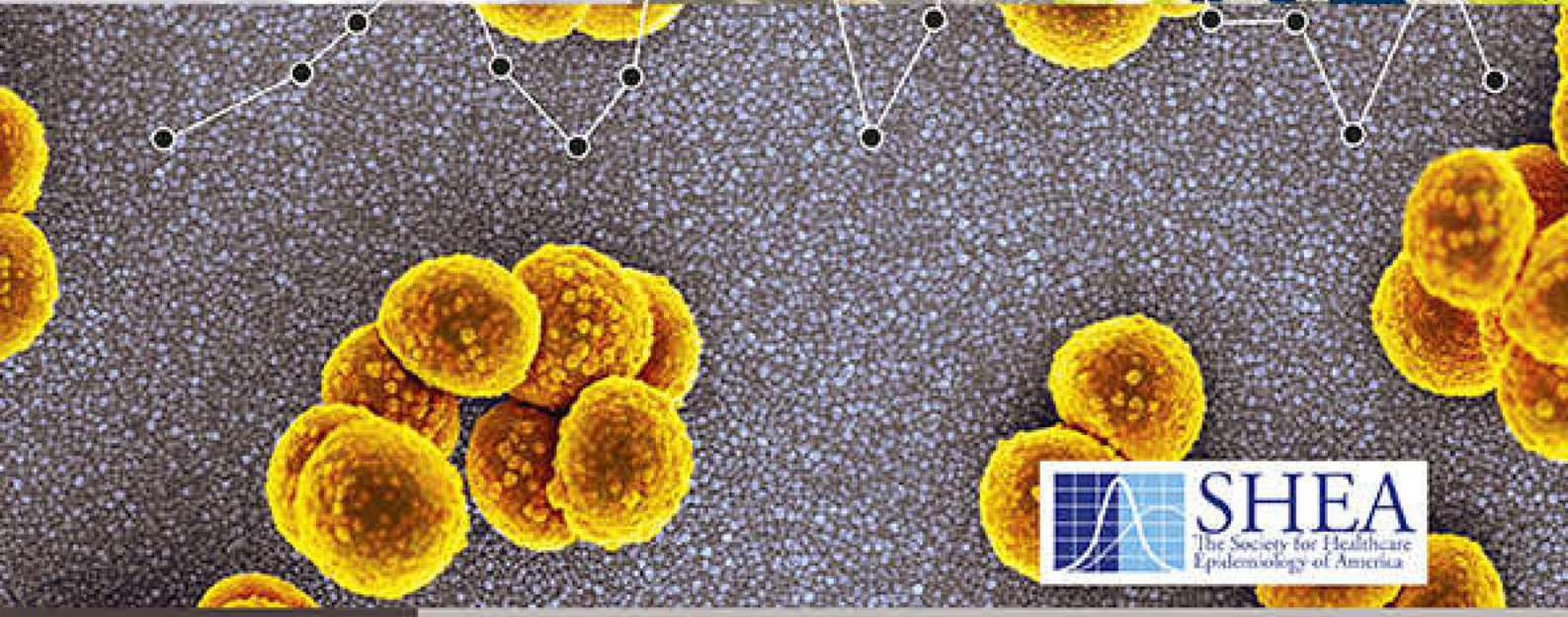
EDITED BY Ebbing Lautenbach, Preeti N. Malani, Keith F. Woeltje, Jennifer H. Han, Emily K. Shuman and Jonas Marschall

Practical Healthcare Epidemiology

FOURTH EDITION



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Practical Healthcare Epidemiology

Fourth Edition

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Preeti To my husband, Mark, and children, Nicholas and Sonya.

Keith For my infection prevention colleagues at Washington University School of Medicine and BJC HealthCare, who work tirelessly to improve the care of the patients we serve.

Ebbing To my wife, Gillian, and children, John, Kate, Thomas, and William.

Jonas To my wife, Maria, and children, Laila and David.

Jennifer For Maddy, Norah, and Vivian.

Emily To my husband, Andy, and my children, Jonah and Lily.

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Preface

An Introduction to Practical Hospital Epidemiology

Ebbing Lautenbach, Preeti N. Malani, Jennifer H. Han, Jonas Marschall, Emily K. Shuman, and Keith Woeltje

It is with great pleasure that we introduce the fourth edition of *Practical Healthcare Epidemiology*. As noted by Dr. Loreen Herwaldt in the introduction to the first edition of this text, "Hospital epidemiology and infection control have become increasingly complex fields."[1] While certainly true then, it is even more so now. The healthcare epidemiologist today faces an abundance of both challenges and opportunities. One need look no further than the recent emergence or reemergence of multidrug-resistant gram-negative bacteria, Middle East Respiratory Syndrome, and Ebola, to appreciate the dynamic nature of this field. Ongoing emphasis on such issues as pandemic preparedness, patient safety, and complex regulatory requirements related to infection prevention, highlights the need for the expertise of the healthcare epidemiologist in many arenas. The requirement for knowledgeable and well-trained healthcare epidemiologists has never been greater.

Healthcare-associated infections (HAIs) exact a tremendous toll in morbidity, mortality, and costs. A recent survey estimated that 4 percent of all patients admitted to US acute-care hospitals in 2011 developed HAIs, for a total of 721,800 such infections.[2] Among these patients, about 75,000 died during their hospitalizations. Total annual costs for the five major HAIs (surgical site infection, central line–associated bloodstream infection, catheter-associated urinary tract infection, *Clostridium difficile* infection, and ventilator-associated pneumonia) have recently been estimated at around $9.8 billion.[3]

The primary focus of the healthcare epidemiologist remains the prevention of HAIs. In this regard, there has been substantial progress over the past several years, with significant reductions in the incidence of several HAIs, including central line–associated bloodstream infection, surgical site infection, and *C. difficile* infection.[4] However, as indicated by the ongoing burden of HAIs noted above, there remains much work to be done. Indeed, the healthcare epidemiologist must deal with all aspects of the healthcare setting to prevent patients or staff from acquiring infection. These include outbreak investigation, surveillance, policy development, audits, teaching, advice, consultation, community links, and research. With the increasing acuity of the hospitalized patient population and the growing utilization of other healthcare settings, (e.g., long-term acute care, outpatient, home care), the need for the healthcare epidemiologist will continue to increase dramatically in the coming years.

The knowledge and skills of the healthcare epidemiologist also lend themselves extremely well to addressing many other issues at the forefront of patient care today. Knowledge of healthcare epidemiology is useful for antimicrobial stewardship, quality improvement, technology assessment, product evaluation, and risk management. In particular, application of healthcare epidemiology–based practices has offered much to the patient safety movement. These include establishing clear definitions of adverse events, standardizing methods for detecting and reporting events, creating appropriate risk adjustments for case-mix differences, and instituting evidence-based intervention programs.[5,6]

We recognize that several comprehensive textbooks of hospital epidemiology exist as excellent resources for infection control professionals.[7–9] This book is not meant to replicate these textbooks but rather to complement them as a pragmatic, easy-to-use reference emphasizing the essentials of healthcare epidemiology. As a starting point, this overview of the important aspects of healthcare epidemiology should provide a good foundation for those entering the field of infection prevention. The practical nature of the book lends itself well to the very nature of healthcare epidemiology as a field that requires constant action (e.g., surveillance, interventions). While daily decisions must be based on a thorough evaluation of the data, they must also be practical in the context of the healthcare setting and surroundings of the practitioner.

This book is also distinguished by its focus on experience. While based solidly on the existing medical literature, this resource also offers real-world advice and suggestions from professionals who have grappled with many of the longstanding and newer issues in infection prevention. As with earlier editions of this book, we asked the authors to write their chapters as if they were speaking to an individual who would be running an infection prevention program and who was just starting in this field. The authors' task was to prepare future

hospital epidemiologists for their new careers by summarizing basic data from the literature and by providing essential references and resources. In addition, we asked the authors to share their own experiences of what works and what does not work in particular situations.

We hope that this book will provide trainees and professionals in infection prevention, particularly the fledgling healthcare epidemiologist, the knowledge and tools to establish and maintain a successful and effective healthcare epidemiology program. Ours is a vibrant and exciting field that presents new challenges and opportunities daily. The prospects for the healthcare epidemiologist are virtually limitless, whether they are in infection prevention, antimicrobial stewardship, patient safety, or beyond. We hope that this textbook provides the foundation upon which many future years of further learning, innovation, and advancement are based.

References

1. Herwaldt LA, Decker MD. An introduction to practical hospital epidemiology. In: Herwaldt LA, Decker M, eds. *A Practical Handbook for Hospital Epidemiologists*. Thorofare, NJ: Slack Inc., 1998.
2. Magill SS, Edwards JR, Bamberg W, et al. Multistate point-prevalence survey of healthcare-associated infections. *N Engl J Med* 2014;**370**:1198–208.
3. Zimlichman E, Henderson D, Tamir O, et al. Health care-associated infections: a meta-analysis of costs and financial impacts on the US health care system. *JAMA Intern Med* 2013;**173**:2039–46.
4. Centers for Disease Control and Prevention. 2014 national and state healthcare-associated infections progress report. Published, March 2016. Available at www.cdc.gov/hai/progress-report/index.html.
5. Scheckler WE. Healthcare epidemiology is the paradigm for patient safety. *Infect Control Hosp Epidemiol* 2002;**23**:47–51.
6. Gerberding JL. Hospital-onset infections: a patient safety issue. *Ann Intern Med* 2002;**137**:665–70.
7. Bennett JV, Brachman PS and eds. *Hospital Infections*. 6th ed. Philadelphia, PA: Wolters Kluwer, 2013.
8. Mayhall CG, ed. *Hospital Epidemiology and Infection Control*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2012.
9. Wenzel RP, ed. *Prevention and Control of Nosocomial Infections*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2003.

Chapter 1

Ethical Aspects of Infection Prevention

Loreen A. Herwaldt, MD, and Lauris C. Kaldjian, MD, PhD

Hospital epidemiologists and infection preventionists make countless decisions every day. In general, we do not make life-or-death decisions, such as whether to withdraw life support or whether to withhold possibly life-sustaining therapies. Few of our decisions require court injunctions or provide the fodder for eager journalists. We simply decide whether to isolate patients, whether to let healthcare workers continue to work, or whether to investigate clusters of infections – all very routine decisions in the life of anyone who practices infection control. These decisions are so ordinary that they could not possibly have any ethical implications. Or could they?

In fact, many of the decisions we make every day, even those we consider quite straightforward, are also ethical decisions – which is to say, they compel us to choose between competing moral values. Such choices are rarely easy, and their intrinsic difficulty is not eased by the fact that few of us have received more than cursory training in ethics. Moreover, if we attempt to train ourselves, we find that very little has been written about the ethics of our specialty, infection prevention and control.

Common Infection Prevention Decisions with Ethical Implications

We may easily overlook the ethical component of our everyday decisions; thus, we may misconstrue the decision confronting us, thinking that it is without ethical consequences when, in fact, ethical principles are at stake. Take, for example, the practice of isolating a patient colonized with a drug-resistant organism. Isolating a patient constrains the patient's freedom of movement but protects the rights of other patients to be treated in an environment without unnecessary risk. Similarly the practice of removing healthcare workers with contagious diseases from patient care follows from epidemiologic data but also from the ethical concepts of beneficence, nonmaleficence, and utility – with an overall goal of maximizing good outcomes and minimizing harm. In such cases, we restrict the freedom of healthcare workers to obtain the greater benefit of protecting patients and fellow workers. Or, when stocking the hospital formulary, we consider the efficacy and cost of drugs, but we also balance the benefit of lower cost (to the patient and the hospital) and the risk of selecting resistant microorganisms against physicians' freedom to prescribe any available drug.

Infection prevention personnel confront additional ethical dilemmas in many of their daily activities. For example, when managing an outbreak, infection prevention personnel must identify the offending pathogen's source and mode of transmission, and then intervene appropriately. This is simple enough if the reservoir is a contaminated drain that is easy to replace or a nursing assistant with no political clout in the hospital. But what if the reservoir is a powerful physician with a large practice and tremendous influence with the administration? Or what if the administration thinks your recommendations are too expensive and excessive? Would you bow to the pressures and recommend interventions that you think are less than optimal, or would you risk the wrath of the physician or the administration and state your best advice regardless of the consequences?

Infection prevention personnel frequently inform patients or healthcare workers that they have been exposed to an infectious disease. When the pathogen is varicella zoster virus, the problem is relatively simple. Yet infection prevention personnel must still consider ethical issues. Do you permit some susceptible employees to continue working, if they wear masks, but restrict others? Or do you restrict all susceptible healthcare workers regardless of their position or their economic status? If you are very busy at work or have plans for the evening, do you delay your response or ignore the exposure altogether? Other exposures, such as those to the hepatitis B virus, the human immunodeficiency virus (HIV), or the prion agent that causes Creutzfeldt-Jakob disease, provoke emotional responses and raise challenging ethical questions. For example, what do you tell employees in the pathology laboratory who were not informed that the patient might have Creutzfeldt-Jakob disease and, therefore, did not use the recommended precautions when they processed the brain tissue? Do you recall and resterilize instruments used for the implicated brain biopsy? Do you notify patients who subsequently had surgical procedures and might have been exposed to instruments that were not sterilized in the manner recommended to kill the infectious agent?

We hope these examples enable you to see that ethical considerations abound within the practice of infection prevention. Clearly, ethics is not the esoteric discipline some misunderstand it to be. Ethics is part of our daily practice. We should not delegate ethical deliberations to others, though we will need to include professional ethicists, hospital managers, accountants, and lawyers in our discussions. We all must recognize that maintaining our ethical integrity is an essential professional responsibility. This chapter is a brief introduction to the intricate intersection of ethics and infection prevention.

Taxonomy

In the introductory paragraphs, we described some routine infection prevention activities that have ethical implications. These descriptions are, in essence, a "narrative taxonomy" of

Table 1.1 A taxonomy of ethical problems in infection prevention

Control of the patient to limit spread of pathogenic organisms
Isolate patients who are colonized or infected with drug-resistant organisms
Isolate patients who are infected with highly infectious and/or dangerous organisms
Control of healthcare workers to limit spread of pathogenic organisms
Restrict the activities of healthcare workers who have been exposed to infectious diseases
Restrict the activities of healthcare workers who have infectious diseases
Restrict the activities of healthcare workers who refuse vaccinations (e.g., influenza vaccine)
Control of medications to limit selection and spread of antimicrobial resistance
Limit the antimicrobial agents included on the hospital formulary
Develop guidelines regarding the use of antimicrobial agents
Provide computer decision support for clinicians' antimicrobial choices
Mandating or recommending best practice and interventions to reduce the risk of infection
Mandate or recommend treatment to eradicate carriage of resistant pathogens
Mandate implementation of isolation precautions
Mandate pre-employment vaccination and/or immunity to certain pathogens
Organize and promote yearly influenza vaccination campaigns
Develop policies and procedures
Mandate postexposure testing of patients and healthcare workers
Recommend postexposure prophylactic treatment of patients and healthcare workers
Resource allocation
Establish a threshold for investigating clusters of infections
Evaluate products to assess their cost relative to their safety and efficacy
Determine whether single-use items may be reused
Guide choices regarding materials, design, number of sinks, etc., for construction projects (cost vs. safety)
Limit hospital formularies to reduce costs and control antimicrobial resistance
Information disclosure
Report exposures to staff and patients
Report outbreaks and cases of reportable diseases to the public health department
Report data on healthcare-associated infections to the Centers for Disease Control and Prevention's National Health Safety Network
Identify patients colonized with resistant organisms before intra- or inter-institutional transfers
Protect the confidentiality of patients' medical records and laboratory results
Protect the identity of index patients in outbreaks
Protect confidentiality of patients who test positive for human immunodeficiency virus
Conflicting and competing interests
Managing outbreaks
Staff, especially institutional leaders, may refuse to comply
Administrators may balk at the cost of investigating outbreaks
Hospital epidemiologists who chose unpopular interventions may lose referrals or their jobs
Managing exposures
Staff, especially institutional leaders, may refuse to comply
Selecting the hospital formulary
Relationships between the staff on the formulary committee and the pharmaceutical industry may compromise decisions
Staff physicians may prefer specific antimicrobial agents not on the formulary
Individual professionalism
Act altruistically (prompt intervention vs. personal convenience)
Mediate in-house disputes between administrators, clinicians, unions, and the hospital
Act courageously when necessary, despite inadequate or conflicting data
Keep up with new developments in the field
Personal
Protect yourself from acquiring infectious diseases
Protect your family from acquiring secondary infections

ethical problems in infection prevention and hospital epidemiology. A taxonomy is an orderly listing or categorization of things. Infection prevention personnel are probably familiar with taxonomy as it refers to microorganisms, but not with respect to our profession. On the basis of our experience in infection prevention (LAH) and ethics (LCK), we developed a taxonomy that we think will be helpful to infection prevention personnel as they think about their own work (Table 1.1).

Table 1.2 Differences in emphasis between epidemiologic ethics and medical ethics

Variable	Epidemiologic ethics	Medical ethics
Scope of concern	Populations	Individuals
Goal	Prevent infection	Treat and prevent infection
Typical principles	Nonmaleficence	Beneficence and nonmaleficence
	Justice (fairness)	Respect for patient autonomy
	Utility	
Purpose of disclosure	Investigation	Diagnosis
Information handling	Confidential reporting	Confidential documentation

Table 1.3 Differences in approach between infection prevention and medical care in the care of a patient with a transmissible infection

Variable	Epidemiologic approach	Medical approach
Microbial colonization	Possible treatment	Observation
Confidentiality	Qualified (e.g., posting signs on patients' doors)	Maintained
Freedom of movement	May limit with isolation precautions	Maintained
Freedom of contact	May limit with isolation precautions	Maintained

The taxonomy not only describes the most important ethical problems in infection prevention but also helps us define the individuals, groups, and organizations to which infection prevention personnel have specific obligations. In particular, infection prevention personnel have obligations to inpatients and outpatients as groups, to individual patients, to visitors as a group, to individual visitors, to healthcare workers as a group, to individual healthcare workers, to the healthcare facility for which they work, to public health entities both local and federal, to facilities to which their facility refers or transfers patients, to referring or transferring facilities, and to the public in general. Different groups often have different interests that are in competition. We can use the taxonomy to help us identify the type of ethical problem we are facing and the competing obligations that may surround that problem.

An Approach to Ethical Problems in Infection Prevention

Most discussions of medical ethics ignore the epidemiologist-population relationship and concentrate instead on the clinician-patient relationship.[1,2] Infection prevention personnel are frequently clinicians; however, we must differentiate our clinical and epidemiologic roles because the fiduciary duties associated with these different roles do not always coincide. Medical ethics are "person-oriented," while epidemiologic ethics are "population-oriented" (Table 1.2).[3–5] Even so, the standard principles of medical ethics also apply to hospital epidemiology. These principles are as follows:[6,7]

- Autonomy (respecting the decisions of a competent patient)
- Beneficence (doing good)
- Nonmaleficence (doing no harm)
- Justice (being fair and allocating resources equitably)
- Utility (maximizing benefits and reducing harms to all concerned)

However, the principles are applied according to the public health model,[5,7] which requires commitment to improving the health of populations, not only individual patients.[8] Although both medical ethics and epidemiologic ethics stress nonmaleficence and confidentiality, medical ethics emphasizes privacy at times when epidemiologic ethics emphasizes investigation and reporting to protect the population. Furthermore, medical ethics stresses patient autonomy, whereas epidemiologic ethics places special priority on justice. Put more practically, medical ethics demands that the clinician treat an infected patient while maintaining the patient's confidentiality, privacy, dignity, freedom, and contact with other human beings (Table 1.3). In contrast, epidemiologic ethics might stress treating both infected and colonized patients to protect patients and healthcare workers. In particular cases, epidemiologic ethics might require healthcare workers to post isolation signs on the doors to patients' rooms; or insist that patients stay in their rooms except when going to essential tests, in which case they must wear surgical masks; or require healthcare workers to wear gowns, gloves, and masks to avoid direct contact with patients.

By now it should be clear that ethically challenging situations are common in the practice of infection prevention and hospital epidemiology. To respond effectively to these challenges, infection prevention staff must address each problem systematically. Kaldjian et al.[9] developed an approach to ethics that is clinically oriented and helps the user state the problem clearly, collect data comprehensively, formulate an impression, and, finally, articulate a justified plan. In outline form, we present a modified version of this approach tailored to the particular demands of infection prevention (Table 1.4), and we employ this approach (in abbreviated form) as we discuss three core topics.

Core Ethical Topics in Infection Prevention

Staff Vaccination Programs

Vaccines were one of the public health movement's major triumphs during the twentieth century, and in that very

Table 1.4 An approach to ethical problems in infection prevention

1.	State the problem plainly
2.	Gather and organize data a. Medical facts b. Goals and procedures of infection prevention and control c. Interests of patients, healthcare workers, hospital, community, and public health agencies d. Context
3.	Ask: Is the problem ethical?
4.	Ask: Is more information or discussion needed?
5.	Determine the best course of action and support it with reference to one or more sources of ethical value a. Ethical principles: beneficence, nonmaleficence, respect for autonomy, justice, utility b. Rights: protections that are independent of professional obligations c. Consequences: estimating the goodness or desirability of likely outcomes d. Comparable cases: reasoning by analogy from prior "clear" cases e. Professional guidelines: for example, APIC/CHICA-Canada professional practice standards[48] f. Conscientious practice: preserving epidemiologists' moral integrity
6.	Confirm the adequacy and coherence of the conclusion

NOTE: APIC, Association for Professionals in Infection Control and Epidemiology; CHICA-Canada, Community and Hospital Infection Control Association–Canada.

triumph are the seeds of a substantial controversy and an ethical problem. Because use of vaccines effectively decreased the incidence of many infectious diseases, the public no longer knows how dreadful these infections can be and how many complications and deaths they have caused. The public is now more aware of vaccine complications than they are of the infections the vaccines were developed to prevent. In addition, parents of "vaccine-damaged children," the natural health movement, television, radio talk shows, and the Internet have all become important participants in this "debate."[10,11]

The controversy about the pertussis vaccine is illustrative. In the 1940s, pertussis was the leading cause of death among children under 14 years of age. Pertussis, in fact, killed more children than measles, scarlet fever, diphtheria, polio, and meningitis combined.[12] The incidence of pertussis was already decreasing before the killed whole-cell vaccine was introduced, which was probably related to changes in social conditions, hygiene, and nutrition. However, the incidence declined significantly after the vaccine was introduced.[13]

Because the whole cell pertussis vaccine is composed of dead Gram-negative bacteria, it includes many toxic components and is, thus, quite reactogenic. Recipients often have significant pain, swelling, and erythema at the vaccination site, and they may develop fever, anorexia, irritability, and vomiting.[14] In addition, some children may develop inconsolable crying, excessive somnolence, seizures, or hypotonic-hyporesponsive episodes.[14] Encephalopathy, which is very rare, is the most severe complication of pertussis vaccination.[14] Opponents of the vaccine allege that the vaccine not infrequently causes serious permanent neurological damage. In some countries, such as Sweden, Japan, and the United Kingdom, the antivaccine movements gained such prominence that the countries either stopped vaccinating children or the rate of vaccination decreased significantly. All three of these countries had outbreaks of pertussis that affected thousands of children and caused numerous deaths.[14]

The controversy over the pertussis vaccine suggests that the ethical debate over vaccines in both the public health arena and in the hospital revolves around providing the greatest good for the greatest number of people (i.e., protecting them against harmful infections) and protecting the individual from harm that could be caused by a vaccination. The ethical dilemma occurs because, in general, the population benefits (i.e., an immunized population that is less susceptible to infection), but individual persons bear the risk of vaccine complications.[15–19] In highly vaccinated populations, a single person can refuse a vaccine and may avoid both the potential complications of the vaccination and the infection itself because he or she is protected by the vaccinated population. However, one may ask whether this is fair to persons who are willing to bear the burdens of being vaccinated (potential complications).[15] Furthermore, if this scenario is repeated often enough, the vaccination rate in the population will drop, and nonimmune people will be at risk.

The ethical dilemma just described also occurs in healthcare facilities that require healthcare workers to be immune to certain infections. For example, most healthcare facilities require that healthcare workers be immune to rubella, which means that employees must present proof that they have had the infection or that they have had at least two rubella vaccinations. The reasons healthcare facilities have this requirement are that rubella is easily transmitted within healthcare facilities and that this virus can cause severe congenital defects if a pregnant woman becomes infected.[20,21] Thus, healthcare facilities caring for pregnant women seek to protect these patients by requiring staff to be immune to this infection. Pregnant employees also benefit from this requirement. However, the individual healthcare provider may not benefit from receiving this vaccine, because rubella causes very mild disease in adults, and an adult vaccine recipient might develop complications. Thus, the hospital puts limits on the autonomy of its staff members to avoid harming pregnant patients and employees.

The approach many facilities take to influenza vaccine illustrates another extreme. The influenza virus is quite contagious and can cause serious complications, hospitalization, and death, particularly among elderly people and people with significant underlying diseases. Healthcare facilities, particularly hospitals, care for many people who are at risk for complications of influenza. Moreover, outbreaks of influenza have occurred in healthcare facilities. These outbreaks are difficult to recognize and, therefore, are underreported.[22] Thus, many hospitals offer the vaccine free of charge to employees each fall. But employees, even those who work with high-risk patients, usually are not required to be vaccinated.[23] In this case, hospitals have elected not to mandate vaccination with a safe and effective vaccine that could prevent at least as many severe complications as does the rubella vaccine. Instead, they have elected to preserve their healthcare workers' autonomy rather than allowing the interests of vulnerable patients to take precedence over that autonomy.[23]

Why do hospitals manage rubella one way and influenza another? To our knowledge, no one has studied this issue. However, we might speculate that society considers the birth of even one child with congenital rubella to be a tragedy. By contrast, we might speculate that society is not as alarmed by the fact that thousands of elderly people die each year from complications of influenza. Moreover, a damaged child represents many impaired life-years, whereas a frail elderly person who dies represents very few life-years lost. Furthermore, because influenza outbreaks in healthcare facilities are rarely recognized, most hospital administrators probably feel that the risk to the patients is very low and, thus, do not require all staff to be vaccinated. In contrast, the hospital would face a huge lawsuit if a woman could document that she acquired rubella while receiving prenatal care in that facility. Though these different approaches to rubella vaccine and influenza vaccine present major ethical issues, healthcare providers seem relatively unaware of these issues even though they often discuss their right to autonomy regarding vaccinations.

We believe that healthcare workers have a moral obligation to restrict their own freedom when it comes to complying with interventions such as influenza vaccine if in so doing they might help preserve their patients' health. Rea and Upshur[23] take this position in their commentary on the issue:

As Harris and Holm wrote of society in general: "There seems to be a strong prima facie obligation not to harm others by making them ill where this is avoidable." But there is a special duty of care for us as physicians not simply to avoid transmission once infected, but to avoid infection in the first place whenever reasonable. Our patients come to us specifically for help in staying or getting well. We have not just the general obligation of any member of our community, but a particular trust: *first* do no harm.[23]

The hepatitis B vaccine illustrates another approach to vaccines within the healthcare setting. The US Occupational Safety and Health Administration requires healthcare facilities to offer hepatitis B vaccine to all employees who will have contact with blood and body fluids to protect them from acquiring this virus through an occupational exposure.[24] In this case, the individual vaccinated gets the benefit and bears the risk associated with the vaccine. In addition, employees are not required to take the vaccine. If they do not want it, they simply sign a waiver stating that they decline the vaccine, in which case they bear the risk if they are exposed to hepatitis B. The institution, thereby, fulfills its ethical and legal obligation to the employee, and the employee maintains his or her freedom to choose whether to be vaccinated.

But a question remains regarding hepatitis B vaccine, and that is whether all healthcare workers should be required to be immune to this virus to protect patients from becoming infected. Given that the risk of transmitting hepatitis B virus is very low with most healthcare-associated activities, there does not seem to be a strong ethical argument for requiring vaccination. However, more than 400 patients have acquired hepatitis B from infected healthcare workers who performed invasive procedures.[25] It is, therefore, appropriate to ask whether all healthcare workers who perform invasive procedures that could expose the patient to the healthcare workers' blood should be vaccinated against hepatitis B. Though some healthcare workers might argue that mandatory hepatitis B vaccination infringes on their right to choose, we think that mandatory vaccination for this group of healthcare workers is ethically justifiable, given the known benefits of vaccinating healthcare workers, the minimal risks associated with the vaccine, and the possible benefits to patients. Because many medical schools now require medical students to be vaccinated and the Centers for Disease Control and Prevention recommend vaccinating all infants, in the near future this question may become moot.

Isolating Patients Who Carry or Are Infected with Resistant Organisms

The incidence of colonization or infection with drug-resistant microorganisms, particularly methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE), has increased substantially over time. One of the primary goals for infection prevention personnel is to protect patients from acquiring pathogenic organisms, including resistant organisms, from other patients, the environment, and healthcare workers. Infection prevention personnel have several means to accomplish this goal: educating staff; implementing isolation precautions, with or without active screening programs to identify carriers (see Chapter 7, on isolation precautions); implementing hand hygiene programs; controlling use of antimicrobial agents (see Chapter 19, on antimicrobial stewardship); and developing cleaning protocols for patients' rooms and equipment. Of these methods for controlling spread of resistant organisms, implementing isolation precautions, with or without active screening, and controlling use of antimicrobial agents have been quite controversial and are associated with significant ethical issues. We discuss the ethical implications of using contact precautions to control spread of MRSA and VRE.

There are numerous reasons to prevent spread of MRSA and VRE. Both organisms can cause serious infections.[26–29] Because MRSA and VRE are resistant to the first-line

antimicrobial agents used to treat serious infections caused by *S. aureus* and enterococci, these infections may be difficult and expensive to treat. Moreover, if MRSA becomes resistant to vancomycin (i.e., if the resistance gene is transferred from VRE to MRSA), infection with such strains might be virtually untreatable with currently available antimicrobial agents. Furthermore, MRSA infections do not replace infections caused by methicillin-susceptible *S. aureus*, rather they are added to them. Thus, in hospitals where the incidence of MRSA colonization and/or infection increases, the overall incidence of healthcare-acquired *S. aureus* infection often increases as well.[26] If MRSA and VRE are transmitted in a hospital, other organisms, such as *Clostridium difficile* and gram-negative organisms that are resistant to extended-spectrum β-lactam agents or to carbapenems may also be transmitted, indicating that the overall infection prevention practice in the hospital is lax.

Some infection prevention personnel argue that data from numerous institutions document the effectiveness of aggressive prevention and control measures.[27] Infection prevention personnel who take this position would also argue that, as healthcare professionals, we should first do no harm. Because MRSA and VRE harm many patients, we should do all we can to prevent both transmission of these organisms and infections caused by these organisms. Therefore, infection prevention programs are obliged to use reasonable means to prevent selection and spread of these organisms.[27]

Other infection prevention personnel argue, to the contrary, that there are numerous reasons not to invest substantial resources and time into MRSA and VRE control efforts.[29,30] They insist that the incidence of colonization or infection with these organisms is already so high that control measures are ineffective and waste precious resources. They would agree that aggressive measures have worked in some instances, primarily in outbreaks, but that the data on the overall incidence of MRSA and VRE colonization or infection indicate that infection control efforts have failed to stop transmission. They also argue that many colonized patients never become infected, colonization per se does not harm these patients, and MRSA and VRE are neither more virulent nor do they cause greater morbidity and mortality than methicillin-susceptible *S. aureus* and vancomycin-susceptible enterococci. Thus, these patients should not be subjected to decolonization or to isolation from which they will not benefit. These infection prevention personnel also state that efforts to control MRSA and VRE impair patient care and, therefore, may actually cause worse patient outcomes than would have occurred if the patients were not isolated.[31–33] Finally, they would argue that eradicating carriage with antimicrobial agents such as mupirocin may actually increase antimicrobial resistance.[34]

Infection prevention personnel who think contact precautions are an important component of a program to prevent spread of MRSA and VRE offer several arguments to support their position:[35] 1) contact precautions have been shown by numerous investigators to stop transmission of these organisms during outbreaks; 2) contact precautions have reduced transmission of MRSA and VRE in situations where they are endemic; 3) data from several studies suggest that proximity to a patient who carries MRSA or VRE is a risk factor for acquiring these organisms;[27] and (4) common sense suggests that housing infected or colonized patients in rooms separate from patients who do not carry these organisms should reduce spread of the resistant organisms.

Other infection prevention personnel present arguments against using isolation precautions to control the spread of MRSA and VRE:[29–33] 1) MRSA and VRE are spreading despite these precautions; 2) patients in contact precautions do not receive the same level of care as do patients with similar problems who are not in contact precautions; 3) contact precautions may actually prevent patients from getting appropriate treatments (e.g., aggressive physical rehabilitation) or from being transferred out of an acute-care facility to a facility better suited to the patients' needs; and 4) contact isolation creates social isolation that may impair patients' psychological well-being.

Other infection prevention experts would argue that the real question is not *whether* to invest resources in attempts to control MRSA and VRE, but *which means* should be used to control spread. The major issue in this discussion has been whether to use intensive active surveillance coupled with contact precautions to control the spread of these organisms [27,36] or to enhance compliance with standard precautions and hand hygiene.[30,32] The crux of this debate revolves around differing interpretations of the extant data. Those who support active surveillance and use of contact precautions believe that the data strongly support this approach,[27,36] while those who support enhancing general infection prevention precautions believe either that current data suggest these measures are not effective[30,32] or that more data are needed before hospitals spend large amounts of money and time performing active surveillance.[37]

As suggested in the preceding paragraphs, the major ethical dilemma with respect to using contact precautions to control the spread of resistant organisms is that the health interests of patients who are not colonized or infected with a resistant organism conflict with those of the patients who are colonized or infected with one or more of these organisms. That is, the patients who are not colonized or infected expect to be treated in the safest possible environment, one that is free of organisms that could complicate or prolong their hospitalizations or could add costs to their hospital bills. They desire to avoid untoward consequences or complications of hospitalization. On the other hand, patients who are colonized or infected with one of these organisms have the right to full treatment for their medical problems, which includes receiving adequate attention from staff and having access to all tests and therapies that are necessary for their care. These patients want to avoid complications of inadequate care, such as slower or impaired rehabilitation, and complications of social isolation, such as depression, anger, and nonadherence to recommendations. Each side in this debate refers to different ethical principles to support their case. Those in favor of contact precautions argue that this type of isolation protects unaffected patients from acquiring organisms that could eventually harm them

and thus supports the ethical principle of nonmaleficence. The opposition argues that use of contact precautions violates affected patients' autonomy and may violate the principles of beneficence and nonmaleficence, as well.

Some infection prevention leaders have begun to question whether contact precautions should be used as a primary component of a program to prevent spread of MRSA and VRE within healthcare facilities.[38–40] They argue that most studies addressing this issue are of low quality and were done before intensive efforts to improve hand hygiene were begun or before hospitals introduced bathing patients with antiseptics like chlorhexidine. Moreover, they argue that contact precautions do not prevent infections in colonized patients, that contact precautions may harm patients, that the incremental benefit of contact precautions is likely to be small, and that contact precautions increase costs and healthcare waste considerably.[38–40] Recent studies by Gandra et al.[41] and Edmond et al.[42] found that MRSA and VRE transmission rates and device-associated hospital-acquired infection rates, respectively, did not change significantly after they stopped using contact precautions for patients colonized or infected with these organisms. While the data are suggestive, neither study assessed whether the rate of MRSA and VRE transmission changed. Both studies had methodological weaknesses, and thus they do not provide a definitive answer to this question.

Those who still support using contact precautions cite the results of recent studies that did not find an increased risk of adverse events among patients treated with contact precautions compared with patients who were not.[43–47] In fact, the cluster randomized trial study conducted by Harris et al. found that universal gown and glove use by healthcare workers caring for patients in intensive care units significantly reduced the risk of MRSA acquisition as measured by routine surveillance cultures and did not increase the risk of adverse events.[45,47]

MRSA and VRE are the two most common resistant bacterial pathogens in most US hospitals. Nevertheless, as we have discussed in this section, experts in infection prevention still debate the merits and the ethics of placing patients in contact precautions simply because they are colonized or infected with one of these organisms. This discussion also illustrates that as medical information changes, one's ethical assessment of the merits of infection prevention interventions may change as well. Consequently, hospital epidemiologists and infection preventionists cannot take refuge in the old adage "we've always done it this way." Rather, we must constantly reassess the literature and then reassess our practices in light of new data and ethical principles.

Ethical Issues Associated with Caring for Patients Infected with Highly Transmissible and Virulent Organisms such as Ebola Virus

Highly transmissible and virulent organisms present special challenges for healthcare providers, including infection prevention staff. Outbreaks of Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and Ebola have demonstrated the ease with which such organisms can spread in healthcare facilities. In fact, spread of these organisms has been amplified in the healthcare setting; many patients and healthcare workers have acquired these infections in healthcare facilities, and many of these patients and healthcare workers have died. Thus, outbreaks of these infections have shown how important protecting patients, visitors, and staff – infection prevention programs' primary responsibility – truly is.

In this section, we will use the example of Ebola virus infection to illustrate how the ethical principles of autonomy, beneficence, nonmaleficence, justice, and utility apply when healthcare workers care for patients infected with a highly transmissible and virulent organism. We will also discuss the following additional ethical values that are relevant when addressing such challenging situations: altruism, solidarity, and conscientious practice.

Infection prevention personnel direct much of their work toward preventing harm to patients, visitors, and healthcare workers. Thus, many routine infection prevention practices are designed to maximize beneficence and nonmaleficence. In contrast, some routine practices, such as implementing isolation precautions or restricting ill healthcare workers, place explicit limits on autonomy for patients or for healthcare workers. In addition, infection prevention personnel generally focus most of their attention on providing benefit and preventing harm to patients while at the same time ensuring that visitors and healthcare workers are also safe. When healthcare workers care for patients with infections caused by highly transmissible and virulent organisms, infection prevention staff members must increase their efforts to ensure that other patients, visitors, and healthcare workers are safe (nonmaleficence) and must place more limits on patients' autonomy. During outbreaks of these infections or during other crises, infection prevention staff may also apply the principle of utility more frequently to ensure that benefits within a healthcare population are maximized, harms are minimized, and scare resources are preserved.

Autonomy: The principle of respect for patient autonomy indicates that patients have the right to request and receive available treatment even for infections caused by highly transmissible and virulent organisms. Healthcare workers must always respect the patient's right to self-determination while balancing this right against the important interests of other patients and of healthcare workers themselves. Because Ebola virus is transmitted easily in healthcare facilities and infections are often severe, infection prevention programs implement more stringent infection prevention practices that necessarily limit the infected patient's autonomy to protect the interests of other patients, visitors, and healthcare workers. Thus, to protect other patients and healthcare workers, healthcare facilities place a patient with Ebola virus infection in rigorously enforced isolation precautions and limit the diagnostic tests and treatments offered.

Beneficence: The principle of beneficence indicates that healthcare workers must promote patients' best interests. In most situations, this means that infection prevention measures address primarily the patient's welfare and that

healthcare professionals work primarily to ensure the patient's welfare when deciding which diagnostic tests and treatments are appropriate. When a patient is infected with a highly transmissible virulent organism such as Ebola virus, infection prevention personnel and clinicians must increase their attention to the welfare of other patients, visitors, and healthcare workers, thereby expanding the extent to which the principle of beneficence is applied also to these groups. When trying to maximize the principle of beneficence, we should try to balance the best interests of all concerned parties (maximizing beneficence in this way can be seen as being related to promoting utility). On the basis of the principles of autonomy and beneficence, healthcare workers should strive to meet the patient's needs and should never abandon the patient.

Nonmaleficence: The principle of nonmaleficence indicates that healthcare workers must avoid harming patients. This principle can be applied to healthcare workers, even during routine patient care. For example, the Centers for Disease Control and Prevention introduced standard precautions to protect healthcare workers from the harm of acquiring pathogenic organisms while caring for infected patients, including those infected with common organisms such as MRSA, hepatitis B, hepatitis C, and HIV.

When a patient is infected with a highly transmissible and highly virulent organism, such as Ebola virus, the principle of nonmaleficence can be seen as indicating that, in addition to protecting the patient from harm, we must also protect other patients, visitors, and healthcare workers from harm. As noted previously, healthcare workers still must accept some risk because they cannot abandon patients. Healthcare facilities and infection prevention programs must do all they reasonably can to minimize the risks for each front-line staff member by providing safeguards such as optimal personal protective equipment, education and practical training, an optimal work environment, and other staff members who monitor and coach the staff members caring for the patients.[48,49]

Justice: In general, the principle of justice indicates that persons should have equal access to healthcare resources, that persons in similar situations should be treated similarly, and that available benefits or necessary burdens should be distributed fairly among the group of individuals under consideration. When healthcare workers must care for patients infected with highly transmissible and virulent organisms, the principle of justice indicates that risks and burdens of caring for these patients should be distributed fairly and consistently among staff. This principle also indicates that healthcare workers who do not accept this risk have likely transferred the risk to someone else. Thus, a healthcare worker who will not care for a patient with Ebola or who does not report to work during an influenza pandemic has shifted to other healthcare workers both the risk intrinsic to caring for the patient and the responsibility for not abandoning the patient.[50]

Utility: The principle of utility indicates that infection prevention programs and healthcare workers should work to maximize benefits and minimize risks to all persons concerned, including the affected patients, other patients, healthcare workers, and members of the community. Under usual circumstances, infection prevention programs' and healthcare workers' primary focus is on maximizing the benefits and minimizing the harms for individual patients while maintaining a safe environment for other patients, visitors, and healthcare workers. However, when caring for a patient infected with Ebola virus or with another highly transmissible virulent organism, infection prevention programs must increase their efforts to ensure that other patients, visitors, and healthcare workers benefit and are not harmed. In these situations, infection prevention personnel and clinicians must consider both the likelihood that the patient will benefit from a diagnostic test or a procedure and the likelihood that healthcare workers or other people will be harmed in the process.[49] For example, clinicians may choose to intubate the patient and insert a central venous catheter before the patient's condition deteriorates (i.e., preemptively) to decrease the likelihood of harm to healthcare workers associated with performing procedures under emergent conditions. Or clinicians may deem the likelihood that a moribund patient will benefit from a procedure, such as dialysis, to be very low and the likelihood that a healthcare worker could be harmed to be high and, therefore, decide not to offer the patient this intervention.[49,51] During widespread outbreaks, such as the Ebola outbreak in West Africa, healthcare administrators, clinicians, infection prevention personnel, and public health officials may justifiably apply the principle of utility (alongside other principles and values) to protect healthcare workers because healthcare workers are a limited resource that is essential to the community's well-being.[49] To protect healthcare workers, it may be necessary to preferentially provide them prophylaxis or treatment, and it may be necessary to triage patients[48] to limit healthcare workers' exposure to patients who are least likely to respond to treatment.

Altruism: The principle of altruism indicates that healthcare workers have a duty to care for infected patients regardless of the causative organism's transmissibility or virulence. Because they have promised to care for the sick and to make patients' needs their primary professional concern, healthcare workers are committed to responding to their patients' needs, even when responding entails some degree of risk to their own welfare. The basis for healthcare workers' duty to care results from:

- A professional's promise to respond to the needs of the sick;
- The actual need of one or more patients;
- The ability of an actual professional to meet that need.

Various professionals, organizations, agencies, employers, and governments have assessed the extent of a professional's duty to care for patients during disasters or outbreaks that pose serious risks to the healthcare workers' lives. However, they have come to very different conclusions.[48–50,52,53] Some have stated that the duty to serve is an absolute duty regardless of the healthcare worker's risk; others have stated that the individual healthcare worker can decide how much risk he or she is

Table 1.5 Range of possible responsibilities based on the assessment of the duty to care in a crisis situation

Expectation	Rationale
Work is mandatory	Duty entails accepting the associated risks
Exceptions exist	Competing duties exist that may mitigate a particular healthcare worker's duty to care
Healthcare workers may volunteer; if a sufficient number of healthcare workers do not volunteer, a lottery system can be used to select additional personnel	Healthcare workers may opt out of caring for patients in risky situations; if some workers must be required to work, a lottery system distributes burdens fairly
Healthcare workers may volunteer, and those who do will receive hazard pay; if a sufficient number of healthcare workers do not volunteer, a lottery system can be used to select additional personnel	Healthcare workers may opt out of caring for patients in risky situations, and those who volunteer should be compensated for accepting the risk; if some workers must be required to work, a lottery system distributes burdens and compensation acknowledges the significance of the risk

willing to assume; and yet others have come down somewhere between these two alternatives.

The American Medical Association's (AMA) Code of Medical Ethics upholds the duty to care, stating: "Because of their commitment to care for the sick and injured, individual physicians have an obligation to provide urgent medical care during disasters. This ethical obligation holds even in the face of greater than usual risks to their own safety, health or life."[54] But the AMA Code includes a note of caution that effectively appeals to the principle of utility: "The physician workforce, however, is not an unlimited resource; therefore, when participating in disaster responses, physicians should balance immediate benefits to individual patients with ability to care for patients in the future."

Unlike most professional societies, some governments have defined healthcare workers' duty to work and treat patients during emergencies as being absolute. In fact, some US states "regard the obligation to treat during an emergency as a legal duty punishable by criminal sanctions for failure to act or for abandonment of patients."[48] Some employers have developed strict policies addressing the duty to work during crises, such as a pandemic. For example, the University of Iowa developed a policy that focuses on utility and also stipulates that the duty to care is extensive, given that the hospital is an essential community resource. The policy states: "The University will be considered a 'community asset' and a 'state asset' in responding to a pandemic. University of Iowa Hospitals and Clinics and Student Health Services will experience increased demand for medical treatment and advice from faculty, staff, students, and the community. For this reason, employees of these facilities are considered essential and required to report to work as scheduled, or may be called to report to work if not scheduled."[55]

Table 1.5 describes a range of possible expectations and rationales relevant to the duty to care in situations that pose infectious or other risks to healthcare professionals.

Solidarity: The principle of solidarity indicates that healthcare facilities and the community should support healthcare workers who serve at risk to their own and their loved ones' welfare. As discussed previously, healthcare facilities have a duty to protect their staff (see nonmaleficence), but attention to this duty is particularly important during times of crisis or high anxiety associated with highly transmissible and virulent organisms. The principle of solidarity indicates that healthcare facilities should: 1) clearly articulate and actively promote the applicable professional standards of duty and the institutional and societal expectations regarding the duty to care so that the healthcare workers understand the situation; and 2) provide venues in which staff members can learn about the infectious agent, the risks posed by caring for a patient infected with this agent, and precautions the facility is implementing to protect and help staff who care for these patients. Opportunities for open dialogue between leadership and frontline staff members will allow the concerned parties to calibrate and communicate their expectations and also acknowledge the boundary between consensus and controversy.

The principle of solidarity also indicates that healthcare facilities have additional responsibilities when their staff members care for patients infected with highly transmissible and virulent organisms, such as Ebola virus.[48,49,52] For example, healthcare facilities must protect the staff who care for the patient from discrimination, stigmatization, and harassment from inside and outside the institution and must help provide for the caregivers' physical needs (e.g., food, water, adequate breaks from work, a place to stay if necessary) and emotional needs (e.g., help making difficult decisions, counseling) given the difficulty of caring for critically ill patients while wearing extensive personal protective equipment and maintaining constant vigilance to avoid exposing themselves to the infecting pathogen. Moreover, because healthcare workers who acquire Ebola while caring for a patient could become seriously ill and could subsequently be disabled or die, healthcare facilities should consider developing compensation provisions for harms suffered by healthcare workers who knowingly accept serious risks when caring for such patients (e.g., death benefits for surviving family members).

Conscientious practice by staff: Conscientious practice refers to the profound role that conscience, or integrity, plays in our moral lives. It indicates that healthcare workers should have the freedom to determine the degree of risk that is acceptable given their life situations and other important responsibilities (such as obligations to dependents). In other words, healthcare workers must balance their duty to care for patients in a particular situation against their duties or obligations to family, friends, society, and, we might say, even themselves.[49,52]

Respecting conscientious practice protects the individual healthcare provider's ability to maintain his or her integrity, and doing so acknowledges that healthcare workers vary in their assessments of how much risk is acceptable based on their personal obligations and their philosophical, religious, or professional beliefs.

Moving from Theory to Practice

As should be apparent, ethical principles and values provide guidance but not absolute or detailed answers to specific ethical issues. Moreover, different principles can suggest different and possibly competing responsibilities and may lead administrators, clinicians, and infection prevention personnel at different healthcare facilities to different conclusions based on their patient populations, their healthcare worker population, their resources, and the guidelines and laws governing their practices. When developing policies and procedures to address either routine or more challenging infection prevention issues, infection prevention personnel, clinicians, and administrators must consider the implications of each principle and determine which principles are most important for specific indications or situations. As new information arises, infection prevention personnel and others must evaluate whether specific policies and procedures still meet the standards implicit in the ethical principles.[9,52] For example, they may need to evaluate whether contact precautions for patients with MRSA or VRE infection or colonization remain an ethical practice given intensive use of alcohol-based products for hand hygiene and antiseptic solutions for bathing patients. If effective treatments are introduced for Ebola or infections caused by other highly transmissible and virulent organisms, infection prevention personnel may need to reevaluate imitations on care offered to patients infected with these organisms.[52]

Ethical codes emphasize a profession's core values and may help guide decisions and behavior. To our knowledge, neither the Society for Healthcare Epidemiology of America nor the Association for Professionals in Infection Control and Epidemiology (APIC), the two societies concerned with infection prevention, have developed codes of ethics. However, APIC and the Community and Hospital Infection Control Association–Canada (CHICA-Canada) have published a document describing "professional and practice standards" for persons practicing infection prevention and control.[56]

A well-developed and clearly stated ethical code is an essential guide, yet it is also insufficient. A code of ethics cannot identify all of the ethical dilemmas that individual hospital epidemiologists and infection preventionists will face in the course of their practice. Nor, despite the fond hopes of professional school administrators, does reciting such a code at graduation guarantee ethical conduct. Alone, an ethical code cannot ensure ethical behavior. It must be taught, learned, affirmed, and lived, if it is to affect our practice. As William Diehl writes: "Formal codes of ethics are hot items these days. [But one] thing is certain: any organization that requires all its employees to review and sign its ethics code each year, and then does nothing else to encourage high moral behavior, is wasting its time on the code."[57]

Any institution that does not act as it preaches wastes time and also, at least implicitly, encourages unethical behavior. Institutions reward the conduct they prize. It should be a warning to us that, at present, we are probably more likely to hear of inconsiderate behavior excused on the grounds of a colleague's academic or technical brilliance than to hear an individual praised for making a difficult but ethically sound decision. Perhaps as a community we need to consider the significance of Ralph Waldo Emerson's startling and humbling remark that "character is higher than intellect."

As our financial and staff resources are stressed without limit and as the pressures under which we work intensify, temptation amplifies. Barbara Ley Toffler of Resources for Responsible Management states:

> For many employees, being ethical is getting to be too risky – something they can't afford any more. . .. The problem grows out of what I call the "move it" syndrome. . .. That's when the boss tells a subordinate to "move it" – just get it done, meet the deadline, don't ask for more money, time, or people, just do it – and so it goes on down the line.[58]

For American companies, this peril from within is as serious as outside threats from competitors. As more employers are forced to "move it," companies are increasingly vulnerable – legally, financially, and morally – to the unethical actions of decent people trying to [move it just to keep their jobs].[58]

To "move it," we may find ourselves declining to issue appropriate sanctions in an outbreak because we are loath to alienate an important doctor or lose referrals from a powerful practice group. Or, fearing management anger over bad publicity and loss of revenue, we may decide against closing a ward affected by an outbreak. Under pressure to reduce budgets, we may approve questionable practices or eliminate effective infection prevention programs. We may be tempted to treat influential administrators or practice groups preferentially because they control our budgets or could curtail our programs. We may be tempted to recommend a particular product because we have received grants from the company that makes the product or whose stock we own. We may feel pressure to withhold information regarding resistant organisms so that we can transfer patients to other institutions and shorten their length of stay in our hospital. Or perhaps we may be tempted to condone altering hospital records to avoid losing accreditation.

What can you as an individual hospital epidemiologist or infection preventionist do? We would recommend that you think about your job and identify the most common questions you answer and decisions you make. Once you have identified these questions and decisions, you can try to identify the ethical choices they represent. You can then develop an approach for dealing with these issues before you face them again, since it is easier to think more clearly and dispassionately when not in the middle of a crisis. When designing such approaches, you should obtain help, if necessary or prudent, from experts in medicine, law, ethics, or other appropriate disciplines.

We have described but a few of the manifold ethical challenges that confront us. Against our ambitions and our fears,

we must rely on our enduring values, commitments, and continual self-examination as we strive to meet the challenges posed by our work. We must ask ourselves difficult questions. Are we serving ourselves or patients and healthcare workers? Are we seeking to keep our jobs, or are we seeking to implement the right interventions? As hospital epidemiologists and infection preventionists, we must keep our attention focused firmly on the needs of our patients and communities.

References

1. Jonsen AR. Do no harm. *Ann Intern Med* 1978;**88**: 827–832.
2. Last JM. Ethical issues in public health. In: Last JM. *Public Health and Human Ecology*. East Norwalk, CT: Appleton & Lange;1987: 351–370.
3. IEA Workshop on Ethics, Health Policy and Epidemiology. Proposed ethics guidelines for epidemiologists. *American Public Health Association Newsletter* (Epidemiology Section) 1990: 4–6.
4. Beauchamp TL, Childress JF. *Principles of Biomedical Ethics*. 2nd ed. New York: Oxford University Press;1983.
5. Phua KL. Ethical dilemmas in protecting individual rights versus public protection in the case of infectious diseases. *Infect Dis (Auckl)* 2013;**6**: 1–5.
6. Soskolne CL. Epidemiology: questions of science, ethics, morality, and law. *Am J Epidemiol* 1989;**129**: 1–18.
7. Herman AA, Soskolne CL, Malcoe L, Lilienfeld DE. Guidelines on ethics for epidemiologists. *Int J Epidemiol* 1991;**20**: 571–572.
8. Beauchamp TL, Cook RR, Fayerweather WE, et al. Appendix: ethical guidelines for epidemiologists. *J Clin Epidemiol* 1991;**44**(1 suppl): 151S–169S.
9. Kaldjian LC, Weir RF, Duffy TP. A clinician's approach to clinical ethical reasoning. *J Gen Intern Med* 2005;**20**: 306–311.
10. Clements CJ, Evans G, Dittman S, Reeler AV. Vaccine safety concerns everyone. *Vaccine* 1999;**17**: S90–S94.
11. Freed GL, Katz SL, Clark SJ. Safety of vaccinations: Miss America, the media, and the public health. *JAMA* 1996;**276**: 1869–1872.
12. Gordon JE, Hood HI. Whooping cough and its epidemiological anomalies. *Am J Med Sci* 1951;**222**: 333–361.
13. Cherry JD. The epidemiology of pertussis and pertussis immunization in the United Kingdom and the United States: a comparative study. *Curr Probl Pediatr* 1984;**14**: 1–78.
14. Mortimer EA. Pertussis vaccine. In: Plotkin SA, Mortimer EA, eds. *Vaccine*. Philadelphia, PA: W.B. Saunders Company;1988.
15. Diekema DS. Public health issues in pediatrics. In: Post SG, ed. *The Encyclopedia of Bioethics*. 3rd ed. Farmington Hills, MI: Thomson Gale;2003.
16. Bazin H. The ethics of vaccine usage in society: lessons from the past. *Endeavour* 2001;**25**: 104–108.
17. Ulmer JB, Liu MA. Ethical issues for vaccines and immunization. *Nat Rev Immunol* 2002;**2**: 291–296.
18. Vermeersch E. Individual rights versus societal duties. *Vaccine* 1999;**17**: S14–S17.
19. Hodges FM, Svoboda JS, Van Howe RS. Prophylactic interventions on children: balancing human rights with public health. *J Med Ethics* 2002;**28**: 10–16.
20. Poland GA, Nichol KL. Medical students as sources of rubella and measles outbreaks. *Arch Intern Med* 1990;**150**: 44–46.
21. Centers for Disease Control and Prevention (CDC). Control and prevention of rubella: evaluation and management of suspected outbreaks, rubella in pregnant women, and surveillance for congenital rubella syndrome. *MMWR Morb Mortal Wkly Rep* 2001;**50**: 1–23.
22. Evans ME, Hall KL, Berry SE. Influenza control in acute care hospitals. *Am J Infect Control* 1997;**25**: 357–362.
23. Rea E, Upshur R. Semmelweis revisited: the ethics of infection prevention among health care workers. *Can Med Assoc J* 2001;**164**: 1447–1448.
24. Department of Labor, Occupational Safety and Health Administration. 29 CFR Part 1920.1030, Occupational exposure to bloodborne pathogens, final rule. *Fed Reg* December 6, 1991;**56**:64, 4–64, 182.
25. Sepkowitz KA. Nosocomial hepatitis and other infections transmitted by blood and blood products. In: Mandell GL, Bennett JE, Dolin R, eds. *Principles and Practice of Infectious Diseases*. 5th ed. New York: Churchill Livingstone;2000: 3039–3052.
26. Herwaldt LA. Control of methicillin-resistant *Staphylococcus aureus* in the hospital setting. *Am J Med* 1999;**106** (5A): 11S–18S.
27. Muto CA, Jernigan JA, Ostrowsky BE, et al. SHEA guideline for preventing nosocomial transmission of multidrug-resistant strains of *Staphylococcus aureus* and *Enterococcus*. *Infect Control Hosp Epidemiol* 2003;**24**: 362–386.
28. Farr BM. Protecting long-term care patients from antibiotic resistant infections: ethics, cost-effectiveness, and reimbursement issues. *J Am Geriatr Soc* 2000;**48**: 1340–1342.
29. Ostrowsky B, Steinberg JT, Farr B, Sohn AH, Sinkowitz-Cochran RL, Jarvis WR. Reality check: should we try to detect and isolate vancomycin-resistant enterococci patients. *Infect Control Hosp Epidemiol* 2001;**22**: 116–119.
30. Teare EL, Barrett SP. Stop the ritual of tracing colonized people. *Br Med J* 1997;**314**: 665–666.
31. Peel RK, Stolarek I, Elder AT. Is it time to stop searching for MRSA? Isolating patients with MRSA can have long term implications. *Br Med J* 1997;**315**: 58.
32. Kirkland KB, Weinstein JM. Adverse effects of contact isolation. *Lancet* 1999;**354**: 1177–1178.
33. Pike JH, McLean D. Ethical concerns in isolating patients with methicillin-resistant *Staphylococcus aureus* on the rehabilitation ward: a case report. *Arch Phys Med Rehabil* 2002;**83**: 1028–1030.
34. Vasquez JE, Walker ES, Franzus BW, Overbay BK, Reagan DR, Sarubbi FA. The epidemiology of mupirocin resistance among methicillin-resistant *Staphylococcus aureus* at a Veterans' Affairs hospital. *Infect Control Hosp Epidemiol* 2000;**21**: 459–464.
35. Farr BM, Jarvis WR. Would active surveillance cultures help control healthcare-related methicillin-resistant *Staphylococcus aureus* infections? *Infect Control Hosp Epidemiol* 2002;**23**: 65–68.
36. Calfee DP, Giannetta ET, Durbin LJ, Germanson TP, Farr BM. Control of endemic vancomycin-resistant *Enterococcus* among inpatients at a university hospital. *Clin Infect Dis* 2003;**37**: 326–332.

37. Diekema DJ. Active surveillance cultures for control of vancomycin-resistant *Enterococcus*. *Clin Infect Dis* 2003;**37**: 1400–1402.
38. Gonzalo Bearman G, Stevens MP. Control of drug-resistant pathogens in endemic settings: contact precautions, controversies, and a proposal for a less restrictive alternative. *Curr Infect Dis Rep* 2012 **14**: 620–626.
39. Morgan DJ, Murthy R, Munoz-Price LS, et al. Reconsidering contact precautions for endemic methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*. *Infect Control Hosp Epidemiol* 2015;**36**: 1163–1172.
40. Morgan DJ, Kaye KS, Diekema DJ. Reconsidering isolation precautions for endemic methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*. *JAMA* 2015;**312**: 1395–1396.
41. Gandra S, Barysauskas CM, Mack DA, Barton B, Finberg R, Ellison RT. 3rd. Impact of contact precautions on falls, pressure ulcers and transmission of MRSA and VRE in hospitalized patients. *J Hosp Infect* 2014;**88**: 170–176.
42. Edmond MB, Masroor N, Stevens MP, Ober J, Bearman G The impact of discontinuing contact precautions for VRE and MRSA on device-associated infections. *Infect Control Hosp Epidemiol* 2015;**36**: 978–980.
43. Morgan DJ, Day HR, Harris AD, Furuno JP, Perencevich EN. The impact of contact isolation on the quality of inpatient hospital care. *PLoS One* 2011;**6**: e22190, doi:10.1371/journal.pone.0022190.
44. Morgan DJ, Pineles L, Shardell M, et al. The effect of contact precautions on healthcare worker activity in acute care hospitals. *Infect Control Hosp Epidemiol* 2013;**34**: 69–73.
45. Harris AD, Pineles L, Belton B, et al. Benefits of Universal Glove and Gown (BUGG) Investigators, Shahryar SK, Price CS, Gadbaw JJ, et al. Universal glove and gown use and acquisition of antibiotic-resistant bacteria in the ICU: a randomized trial. *JAMA* 2013;**310**: 1571–1580.
46. Day HR, Perencevich EN, Harris AD, et al. Depression, anxiety, and moods of hospitalized patients under contact precautions. *Infect Control Hosp Epidemiol* 2013;**34**: 251–258.
47. Croft LD, Liquori M, Ladd J, et al. The Effect of contact precautions on frequency of hospital adverse events. *Infect Control Hosp Epidemiol* 2015;**36**: 1268–1274.
48. Bartlett JG. Planning for avian influenza. *Ann Intern Med* 2006;**145**: 141–144.
49. Evans NG. Balancing the duty to treat patients with Ebola Virus Disease with the risks to dialysis personnel. *Clin J Am Soc Nephrol* 2015 [epub ahead of print]. Accessed November 30, 2015.
50. Upshur RE, Working Group Three. WHO: Project on Addressing Ethical Issues in Pandemic Influenza Planning (2006 Draft Paper, www.who.int/ethics/PI_Ethics_draft_paper_WG3_14Sept06.pdf). Accessed November 30, 2015.
51. Lally JF. Ebola and moral philosophy: the trolley problem as a guide. *Del Med J* 2015;**87**: 25–25.
52. Halpern SD, Emanuel EJ. Ethical guidance on the use of life-sustaining therapies for patients with Ebola in developed countries. *Ann Intern Med* 2015;**162**: 304–305.
53. Singer PA, Benatar SR, Bernstein M, et al. Ethics and SARS: lessons from Toronto. *BMJ* 2003;**327**: 1342–1344.
54. AMA E-9.067 Physician Obligation in Disaster Preparedness and Response (www.ama-assn.org/resources/doc/code-medical-ethics/x-pub/9067a.pdf; paywall). Accessed November 24, 2015.
55. The University of Iowa Disaster Preparedness and University State of Emergency Human Resource Policy (July 23, 2007, http://hr.uiowa.edu/policies/disaster-preparedness). Accessed November 30, 2015.
56. Horan-Murphy E, Barnard B, Chenoweth C, et al. APIC/CHICA-Canada infection control and epidemiology: professional and practice standards. *Am J Infect Control* 1999;**27**: 47–51.
57. Diehl WE. *The Monday connection: a spirituality of competence, affirmation, and support in the workplace*. New York: Harper Collins Publishers;1991: 85–135.
58. Toffler BL. When the signal is "move it or lose it." *NY Times* 1991;Sect F:13.

Chapter 2

The Infection Control Committee

David A. Pegues, MD

Introduction

The infection control committee plays an important role in ensuring patient safety through the prevention and control of infections in healthcare facilities. This committee is a mechanism for the infection prevention program to report activities, including infection metrics, outbreaks, and infection prevention and control interventions. The infection control committee also develops and approves policies and procedures on infection surveillance, prevention, control, and education. The infection control committee is an important liaison between departments responsible for patient care and supporting departments, such as pharmacy, environmental services, and facilities. The committee should report to the facility's medical board and/or senior leadership to ensure executive engagement and support for prevention activities.

Infection control committees vary in their scope of responsibility and membership size, depending on whether they serve a single healthcare facility or a local, regional, or national health system. Regardless of size, most infection control committees function in a reporting capacity, typically reviewing and approving reports and policies developed by content experts who are members of the committee.

Membership

The infection control committee is generally comprised of members from a variety of disciplines within the healthcare facility. Representation may include the following: physicians, nursing staff, infection prevention practitioners, quality assurance personnel, and risk management personnel, as well as representatives from the microbiology laboratory, surgery department, central sterilization and processing, environmental services, pharmacy, facilities management, dietary services, occupational health, and local public health. Physician and nursing staff members often are drawn preferentially from the high-volume and high-risk departments and represent important constituencies in infection control and prevention, including critical care, surgery, and those that care for immunocompromised patients (e.g., hematology/oncology, solid organ transplantation). Members of the committee should hold leadership positions or positions of influence in the hospital in order to serve as opinion leaders and to effect change when necessary. Members may be nominated by their departments and should be engaged and effective communicators. Ordinarily, membership on the committee is ongoing with periodic (e.g., annual) reappointment, but additional staff members may be asked to provide ad hoc input as the need arises.

Role and Functions of the Committee

The infection control committee functions to prevent and control healthcare-associated infections by setting infection control policy and monitoring practices to reduce these risks. Preventing healthcare-associated infections has become highly technical. Therefore, the bulk of the committee's work is best accomplished by a core of experts that include the hospital epidemiologist, infection preventionists, a microbiologist, and the director of employee health. Policies should be developed by this subgroup along with other experts on an ad hoc basis and brought to the entire committee for review, approval, and support from political and administrative standpoints. Committee members then assist in disseminating, gaining buy-in, and monitoring issues associated with new and existing policies from their departments.

There are a number of important core functions of the infection control committee, including the following:

- Reviewing infection control surveillance data and developing appropriate infection control goals and control plan.

  The infection control committee collaborates with the infection prevention team to develop the annual infection prevention objectives and goals and assists in effective implementation and monitoring progress toward these goals. To meet these goals, surveillance data that have been collected and analyzed by the infection prevention program are regularly reviewed, interpreted, and discussed at committee meetings. Surveillance summaries can be electronically distributed before the meeting along with the agenda and other documents for prereview or may distributed at the meeting. The frequency of reporting should be defined (e.g., monthly, bimonthly, quarterly) and surveillance data presented in such a way as to trend performance over time and compare year-to-date performance against internal and external benchmarks. Corrective actions and responsible individuals should be identified and documented in the meeting minutes. Progress and barriers to implementation of the action plan are then discussed and addressed at subsequent meetings.

- Discussing and developing plans for the control of outbreaks and monitoring implementation as needed.

  Reviewing the management of outbreaks is another important function of the infection control committee (see Chapter 11 on outbreak investigations). Members of the

committee undoubtedly will be leading or participating as members of the investigation team. These individuals, and not the committee as a whole, are responsible for making real-time decisions about control measures and assessing their impact. The committee's role primarily should be advisory and consultative, and this function is an important part of the quality improvement process. The committee also is likely to be engaged in preparedness planning and response to emerging global public health threats (e.g., Ebola virus and MERS-CoV) as well as local community threats (e.g., vaccine-preventable disease outbreak in a susceptible population). Successful prevention and control of infections require careful planning, including evaluation of the technical evidence supporting efficacy of an intervention, education, measurement, and monitoring to ensure impact and sustainability. The infection control committee supports the mission of infection control by establishing important alliances and advocacy, and spreading and sustaining prevention and control efforts throughout the hospital or health system.

- Approving infection control–related policies and procedures before submission to the medical board.

  It is more efficient to have working groups of experts draft and edit infection control policies before distributing them to committee members in advance of the next meeting. New and existing policies are then summarized in the meeting where committee members offer comments and formal approval is sought. Once approved by vote of the committee, these policies and procedures are submitted to the medical board for approval.

- Providing infection control input and guidance to ensure the safety of the hospital environmental and employees.

  The infection control committee and its members share responsibility for ensuring the safety of the hospital environment, including hospital construction and renovation activities, environmental services, sterilization and disinfection, and occupational health of employees. The committee should include standing members representing each of these departments. These members typically serve as liaisons to their departments and work collaboratively with infection prevention program personnel on relevant infection control issues both within and outside of the infection control committee meetings.

- Serving in an advisory capacity to senior medical and administrative leadership of the facility.

  The committee serves an important advisory role to senior leadership, informing them of infection control risks and hazards and proposing interventions to address these issues.

- Compliance with benchmarks.

  The infection control committee should periodically review compliance with facility-specific and national infection prevention benchmarks. These may include employee hand hygiene compliance and seasonal influenza coverage rates, or performance on infection control process measures such as perioperative antimicrobial prophylaxis and infection prevention bundles. By reviewing and discussing such data, the committee can help to identify variations in practice at the unit or provider level and address barriers to achieving the goals.

- Compliance with regulatory requirements.

  The infection control committee may need to develop guidelines to help clinicians comply with external regulatory requirements. Examples include institutional guidelines on notifiable disease reporting, consent requirements for human immunodeficiency virus testing, and policies governing work fitness and professional activities of healthcare workers infected with bloodborne pathogens or other communicable diseases. In addition, The Joint Commission requires that hospitals have written infection control policies and procedures needed to conduct the organization's mission effectively. The infection control committee reviews and approves the annual infection control surveillance plan and risk assessment and is charged with evaluating and ensuring compliance with The Joint Commission infection control standards, including all relevant elements of performance and national patient safety goals.

- Promoting and facilitating the education and compliance of all staff in infection control policies and procedures.

  The infection control committee plays an important role in developing and disseminating infection control education for employees. The committee may have primary responsibility for content development or share the responsibility with the education department. This includes required infection control and bloodborne pathogen training for employees at the time of hire and annually thereafter as well as role-specific infection control (e.g., medical device cleaning and disinfection). In addition, the infection control committee also helps to develop, coordinate, and disseminate education plans for new infection control policies and practices. Examples included interventions that directly affect patient care (e.g., chlorhexidine gluconate bathing, catheter dressing products, nurse-driven urinary catheter removal protocols), environmental control (e.g., disinfectant products), or health and safety of employees (e.g., safety sharps devices, latex-free examination gloves). Whatever the education methods used (e.g., in-servicing, huddles, screen savers, posters, email), this information should be effectively messaged to all impacted employees. In these ways, the committee acts as a facilitator between other departments to improve implementation of new infection control practices.

Responsibilities of the Chair

The chair is most often a physician who has training and expertise in infectious diseases and healthcare epidemiology. The chair provides scientific and administrative leadership to the committee and is typically appointed or approved by the

medical board. The chair is responsible for reviewing the membership list annually to ensure adequate representation from appropriate departments and for replacing members who have poor attendance, are unable to fill their role, have accepted different positions, or have left the organization. The chair also may appoint special subcommittees or task forces or ad hoc members to address specific infection control issues that arise.

To be effective, the chair should be familiar with and utilize effective meeting practices. These include attention to meeting preparation, facilitation, participation, and evaluation. An effective chair, along with his/her administrative support, organizes meeting logistics and distributes the agenda and documents that require review before the meeting. The chair ensures that meetings start and end on time, and keep to the agenda. For example, the meeting may open with an optional members "check in," in which members are invited to contribute immediate concerns to the opening of the meeting. This "check in" serves to bring busy people to the purpose of the meeting so that they can receive support or put issues aside for the meeting. The chair must be an effective facilitator, listening attentively and respectfully, and he/she should encourage the participation of many members in the discussions. Verbally summarizing decisions and assigning action items helps to avoid misunderstandings and moves the agenda forward. Minutes record the decisions of the meeting and the actions for follow-up and help to ensure that the plans and actions decided upon by the committee are implemented.

In addition to these administrative functions, the chair serves as an expert consultant to the hospital and departments on infection control and prevention matters. The chair typically acts as spokesperson for the infection control committee when reporting to the medical board and other hospital-wide committees and often is called upon to justify to senior leadership the evidence supporting the committee's infection control recommendations, and their potential costs and benefits.

Responsibilities of the Members

Members of the infection control committee should be selected both for their willingness to serve and for their ability to work collaboratively on committee activities. Members should attend the meetings regularly and, when unable to attend, should identify a delegate to attend in their place. Members need to be effective communicators, as they must bring forward infection control–related concerns and report back committee activities and decisions for those whom they represent. Ideally, members should be in a position of influence and have decision-making capacity for their departments to facilitate implementation and compliance with infection control policies and practices. In addition, many members of the committee have important committee reporting functions. Table 2.1 lists the reports that are often presented to the committee during meetings and the corresponding responsible committee member. Not all reports or responsible members are applicable in all healthcare settings. The frequency of these reports will vary but should occur no less than annually and more often, depending on the local needs.

Administrative Matters

Committee meetings should be held at a recurring day, time, and location with a frequency typically ranging from monthly to quarterly. The agenda should be planned and distributed to committee members before the meeting. In addition, all policies should be distributed before the meeting to allow adequate time for review and comment by committee members and to improve meeting efficiency. As a token of appreciation to members, food and/or beverages should be provided, budget permitting.

The meeting agenda may begin with introduction of new members or visiting attendees and then correction and approval of the minutes of the previous meeting. This may be followed by invitation for the members to provide brief, informal reports or "check ins," as appropriate. Old business should be limited, as much as possible, to updating progress toward completing action items from prior meetings and to ongoing outbreak investigations or response to public health emergencies. A healthcare infection surveillance summary is presented, including infection counts, rates, and benchmark performance and opportunities for improvement are discussed. Brief, 5-to-10 minute department-specific infection control reports are presented on a recurring schedule and should be summarized in the minutes and the reports attached (Table 2.1). New business should focus on in-depth reports of selected current infection prevention and control issues activities. These reports can be presented either by standing or ad hoc members or invited guests. Finally, new and revised policies should be discussed and approved on an ongoing basis to ensure policy content is current and that regulatory requirements are met.

Meeting Minutes

Well-documented minutes should be kept of each committee meeting. These minutes have four major purposes: to serve as communication tools, instruments for guiding current and proposed infection prevention and control practices, legal and regulatory documents, and historic records. Minutes are useful to notify or remind individuals of the tasks assigned to them and the timelines, and to report actions and decisions to the medical board, senior leadership, and other relevant committees (e.g., quality improvement and patient safety). Minutes are important tools for collaborative project management, moving projects forward with the aid of well-written summaries of progress and commitments. Infection control committee minutes are considered to be confidential peer review documents in most states and therefore are not subjected to subpoena. Regardless of applicable law, committee minutes are reviewed by regulatory and accrediting agencies, and they must be accurately and objectively reported and recorded. An institution-specific template is typically used for recording the minutes, and content is guided by the agenda. The minutes should include sections for each topic discussed, which contain the following information: a discussion, which is the analysis of the problem or data; a recommendation, which describes improvement strategies; an action, which includes what is to be done and how; and follow-up, which describes who is responsible for what and when this issue will be revisited to ensure improvement has occurred.

Table 2.1 Infection control committee reports and responsible parties

Responsible party	Reports to the infection control committee
Infection preventionist (IP)	**Recurring reports** • Healthcare-associated infection rates • Invasive device utilization rates • Hand hygiene compliance rates • Isolation compliance monitoring rates • Outbreak investigations • Notifiable disease reports (as applicable) • Construction project surveillance: current class 3 or 4 Infection Control Risk Assessment (ICRA) projects • Mandatory training reports • Pressure ulcers/wound care report (may be assigned to the Wound Care Nurse or long-term care facility member) **Annual Reports** • Infection control report • Infection control plan • Infection control risk assessment • Tuberculosis risk assessment • Infection control education plan • Bloodborne pathogen exposure control plan
Microbiologist or laboratory representative	• Blood culture contamination report • Facility antibiogram (may be assigned to Pharmacy) • Legionella urinary antigen report • Seasonal influenza and respiratory virus surveillance report
Environmental management services representative	• Quality Improvement/Quality Assurance monitors (e.g., high-touch surface cleaning report)
Pharmacist	• Antimicrobial stewardship activities • Facility antibiogram (may be assigned to Microbiology) • Pharmacy compounding area biological environmental monitoring (USP 797 a standard that outlines the requirement for compounding areas)
Wound care nurse	• Pressure ulcers/wound care (may be assigned to the IP or long-term care unit representative)
Long-term care unit representative	• Residents' vaccination rates for influenza and pneumococcal vaccines • Pressure ulcers/wound care (may be assigned to the IP or Wound Care Nurse)
Home health nurse	• Infections in the home setting, including catheter-associated bloodstream infections (CLABSI) • Central line device utilization rates • Visiting nurse hand hygiene compliance (assessed by home care patient survey) • Home health bloodborne pathogen exposure control plan
Occupational health and safety	• Employee communicable disease exposure events • Employee respirator-fit testing report • Employee influenza vaccination rates • Annual employee tuberculosis infection/skin test conversion rate • Annual safety device review • Annual bloodborne pathogens exposure control plan review
Facility maintenance/engineering representative	• Airflow (pressure) reports • Legionella water culture and mitigation report • Temperature and humidity standards for controlled areas, including operating rooms, labor and delivery rooms, and isolation rooms

Table 2.1 (cont.)

Responsible party	Reports to the infection control committee
Food services	• Food safety quality indicator report • Food safety and sanitation inspection reports
Surgical services representative	• Immediate-use steam sterilization (flash) report • Operating room temperature/humidity report • Surgical Care Improvement Project quality measure report (e.g., antibiotic prophylaxis)
Sterile processing representative	• Temperature/humidity report • Sterilizer biologic indicator report • Instrument recall notifications
Public health representative	• Local community outbreaks and communicable disease trends
Dialysis	• Dialysis water and dialysate culture report

Suggested Reading

Friedman C, Barnette M, Buck AS, et al. Requirements for infrastructure and essential activities of infection control and epidemiology in out-of-hospital settings: a consensus panel report. Association for Professionals in Infection Control and Epidemiology and Society for Healthcare Epidemiology of America. *Infect Control Hosp Epidemiol* 1999;**20**: 695–705.

Pigeon Y, Khan O. Leadership lesson: tools for effective team meetings – how I learned to stop worrying and love my team. Available at www.aamc.org/members/gfa/faculty_vitae/148582/team_meetings.html. Accessed October 16, 2015.

Schirling J. Effective meeting management. In: Gassiot CA, Searcy VL, Giles CW, eds. *The Medical Staff Services Handbook: Fundamentals and Beyond*. 2nd ed. Sudbury, MA: Jones & Bartlett Publishers; 2011.

Chapter 3

Product Evaluation

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Background

According to the Association of Value Analysis Professionals, the average healthcare organization utilizes anywhere from 5,000 to 17,000 products, services, and technologies in any given year.[1] Medical product evaluation is the process of appraising the value and significance of quality, safety, cost, standardization, user preference, and serviceability of a device. Product evaluation and selection centers on collaborative decision making within a formal organizational structure, most often consisting of an interdisciplinary committee with defined membership, governance structure, and policies and procedures for reviewing, procuring, and assessing new products for the hospital. A wide range of representatives from all relevant clinical and nonclinical areas of the organization should participate, including nurses, physicians, materials management, hospital administrators, finance, and purchasing, as well as infection prevention. Interdisciplinary and collaborative evaluation allows stakeholders to voice their opinions and concerns and promotes transparency in the product selection process.

Product selection and evaluation is an integral part of the value analysis process, but as illustrated by Figure 3.1, value analysis is more comprehensive, involving the intersection of product selection and evaluation. Value analysis is the organized, systematic application of recognized techniques that identify the functions of a product or service.[3] Value analysis seeks ways to enhance value by providing the desired performance at the lowest overall cost. Value analysis brings together users who have clinical product knowledge, financial analysts, and those with purchasing expertise in order to make best-valued product and service acquisition decisions. In many hospitals, there are separate value and analysis and products committees. Where such a distinction exists, value-analysis committees often focus their evaluation on higher-cost medical devices and technologies whereas products committees typically focus on high-volume medical consumables, such as isolation gowns, gloves, bathing products, and disinfectants.

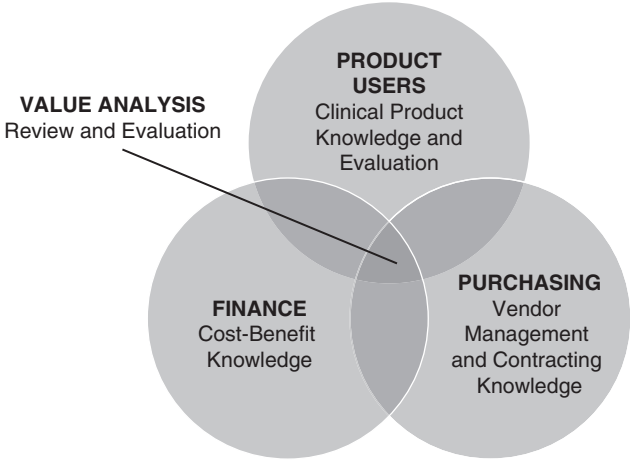

Figure 3.1 Central position of value analysis in relation to product users, purchasing and finance
Source: What Is Value Analysis in Healthcare? WellStarr Health System Georgia, USA. Available at www.iienet.org/uploadedfiles/Webcasts/SHS_VA_Presentation.pdf.

The role of infection prevention in safety product evaluation was initially emphasized in the US Department of Labor Occupational Safety and Health Administration (OSHA) Needlestick Safety Prevention Act of 2000.[2] In recent years, prevention of healthcare-associated infections is increasingly a focus in marketing claims that are used to justify the differential cost of new products and technologies. Infection prevention personnel have an important role in the evaluation of products that may affect rates of healthcare-associated infections to determine whether they are clinically safe, effective, and justify the added cost. This role includes the requirement for technical knowledge and expertise in the following aspects of product evaluation:

- Infection risks to patients and personnel
- Asepsis of sterile products
- Cleaning and disinfection or sterilization of reused products/equipment
- Proper disposal of items/products if not reusable

In addition to the technical expertise that healthcare epidemiologists and infection preventionists possess, there are regulatory considerations that drive infection prevention personnel to be involved in product evaluation. The Joint Commission infection control standards require that organizations reduce the risk of infections associated with the use of medical equipment, devices, and supplies, and products evaluation is a critical step in the process.

Steps in Product Evaluation

The five core product attributes of medical devices are safety, quality, performance, features, and ease-of-use. The process of product evaluation includes the following steps that have been adapted from the Centers for Disease Control and Prevention's (CDC) Workbook for Designing, Implementing, and Evaluating a Sharps Injury Prevention Program:[4]

1. Organize a product selection and evaluation team:
   a. Organizations should designate a team to guide the selection, evaluation, and implementation of infection-prevention devices. This team is usually implemented as a formal, standing product-evaluation committee or designated subcommittee.
   b. Assign responsibility for coordinating the process and obtain input from persons with clinical expertise (e.g., Environmental Services director for surface disinfectants, critical care nurse specialist for central line dressings).

2. Set priorities for product consideration:
   a. Define priorities based upon the facility's rates of healthcare-associated infections, needlesticks, and other data, such as audits of device maintenance practices for defects in processes of care.

3. Gather information on the use of the conventional (existing) device:
   a. Must obtain information on use of the conventional product (device) that it is replacing.
   b. Frequency of use and purchase volume.
   c. Purpose(s) for which device is used.
   d. Compatibility issues with other devices it is used with (e.g., chlorhexidine gluconate and skin care products; central venous catheter (CVC) lock solutions and CVC integrity).
   e. Unique clinical needs. If yes, representatives from these areas should be included in the team.

4. Establish criteria for product selection and identify other issues for consideration:
   a. Design criteria – physical attributes of device, required features for clinical needs.
   b. Performance criteria – how a device functions for its intended patient care and safety needs.
   c. The product's environmental impact should also be assessed, including whether the product will be recycled or reused (e.g., isolation gown) and what method is used for disposal (e.g., high-level disinfectant requiring stringent handling and disposal).

5. Obtain information on available products from the following sources:
   a. Primary peer-reviewed literature, when available.
   b. Evidence reviews from an evaluation organization, such as University HealthSystem Consortium and ECRI Institute.
   c. Professional resources, including professional societies (AORN, APIC, SHEA) and the product manufacturers. Manufacturers' representatives can provide clinical and technical data, including product research, material safety data sheets, and cleaning and disinfection/sterilization methods, as appropriate.
   d. Opinions and experience of materials management and colleagues in other similar facilities.

6. Obtain samples of products under consideration.

7. Develop a product evaluation survey form:
   a. This form must contain the information necessary to make informed decisions for final product selection. Criteria may include safety, performance, quality, efficiency, ease of use, compatibility with other products; clinical effectiveness; financial impact analysis; sterilization parameters; regulatory requirements; standardization; environmental impact; and training requirements.
   b. The form that is easiest to complete is usually one or two pages and allows users to circle or check responses using standardized scoring criteria, such as use of a graded opinion or Likert-type scale (e.g., strongly agree, agree, disagree, strongly disagree).
   c. Allow space for comments. Healthcare personnel should be given an opportunity to comment on a device. Individual comments can provide useful insights and identify areas for further questioning.
   d. Include questions about product users. Unless a product evaluation is confined to a single unit and/or group of staff, information on the respondents (e.g., occupation, length of employment and/or work in the clinical area, training on the new device) is helpful in assessing how different groups react to the new device.

8. Develop a product evaluation plan:
   a. Select clinical areas for evaluation. Include patient-care areas with unique or compelling clinical and at-risk populations (e.g., intensive care units for products focused on device-associated infections).
   b. Determine the duration of evaluation. Consider frequency of device use and learning curve to become familiar with the device. Balance staff interest with need for sufficient product experience. If more than one product is being evaluated, use the same population and trial duration for each product.
   c. Plan for staff training. Healthcare personnel participating in an evaluation must understand how to use the new device properly. Training should be tailored to the audience needs and include discussion about why the change is being proposed, how the evaluation will proceed, and what criteria will be used to evaluate product performance (e.g., ease of use, end-user preference, durability, performance of device)
   d. One efficient approach to training is to utilize a team consisting of in-house staff and device manufacturer's representatives

9. Compile data from the survey forms:
   a. Depending on the number of staff involved and survey forms completed, this can be done either by hand or by use of a computerized database. It is useful to score each question in addition to the overall response, particularly if evaluating two or more devices; responses to each question can be used to compare devices. In addition, categorize individual comments so

they provide a better picture of the clinical experience with the device.

b. Consider calculating response rates by occupation and clinical area and analyzing data by these variables, if the volume of responses permits. This can help identify differences in opinion that may be influenced by variations in clinical needs.

10. Perform financial impact analysis:

a. Should be performed on each product and can help to clarify the choice between different products with equivalent performance and functionality.

b. This analysis should include direct costs (e.g., cost of the replacement product), indirect costs (e.g., costs associated with the use of the device after purchase, including training, disposal, time analysis) and group purchasing organization contract pricing.

11. Select and implement the preferred product:

a. Learning reports from the education and training of staff on the evaluation units are invaluable in spreading use of the product and standardizing practice across patient-care areas.

b. Interdepartmental and health system standardization plan should be developed for each product being evaluated. Standardization can reduce cost and decrease variations in practice that contribute to medical errors. It also reduces inventory and storage requirements and user training.

12. Perform postimplementation monitoring:

a. New product performance and user satisfaction should be evaluated at planned intervals, including the frequency and criteria for reevaluation. This may correspond to the length of the contract.

b. At the provider level, monitoring should focus on compliance and satisfaction with use of the product.

c. At the unit and hospital level, it is important to assess whether the product has been associated with the desired clinical outcome and if not, why not. In the case of devices that impact the risk of healthcare-associated infections, use of surveillance data can help to inform these periodic evaluations, especially when correlated with data on compliance with product use.

Assessing the Evidence

When available, evidence from peer-reviewed medical literature should be utilized when evaluating the clinical efficacy of a medical product and the data quality, consistency, limitations, and potential biases should be considered.[5] However, the Food and Drug Administration's (FDA) regulatory policy is largely responsible for the rapid introduction and large quantity of medical devices coming to market and the lack of clinical efficacy data for the majority of these devices. While all new drugs must undergo rigorous premarketing testing in randomized clinical trials to receive FDA approval, most new medical devices and products do not require such evaluation. Some of the differences between medical devices and drugs are outlined in Table 3.1. About half of medical devices that are marketed each year are considered low-risk products (e.g., bandages, surgical drapes) and are exempt from premarketing review. New products that have undergone incremental change to a previously marketed version (e.g., dialysis catheters, endoscopes) are considered medium-risk. For these products, the FDA requires only a premarketing notification application (510 k), because they are assumed to be essentially equivalent to those already approved.[6] Because the data are not required, manufacturers have little incentive to undertake studies to answer relevant clinical questions, including the impact of devices on reducing the risk of healthcare-associated infections. As a result, many manufacturers rely upon data from in vitro studies or laboratory model systems to support claims of efficacy in reducing healthcare-associated infections.

Table 3.1 Comparison of differences between medical devices and drugs that impact evaluation of clinical efficacy

Devices	Drugs
Constantly evolving	Unchanging compound
Complications decrease with use	Complications increase with use
Results vary with operator skill and experience	Results unrelated to provider skill and experience
Limited premarketing assessment of safety and efficacy	Extensive premarketing assessment of safety and efficacy
Low-quality evidence base	High-quality evidence base

Making the Business Case/Cost Effectiveness

If a change in product that may be more expensive but provides clinical value is being proposed, it must be shown that the product will achieve the desired results (e.g., reduce infections, produce a better clinical outcome).[7] Optimally, cost/benefit analysis should include the facility's actual costs and revenue. For example, the difference between reimbursement for patients and the actual hospital costs associated with patients is their contribution margin. If the product being evaluated is aimed at reducing surgical site infections (SSIs), then one should compare the contribution margin for those patients with SSIs versus those without this complication. That difference (delta) provides data on actual costs and can be compared with clinical/healthcare-associated infection data to determine whether change is warranted.

Another method to assess cost effectiveness of an infection control product is to compare direct cost avoided in preventing infections to the incremental cost of the product. Reductions in rates of the targeted healthcare-associated infection can be estimated from pilot evaluations within the facility and from

Table 3.2 Estimated direct cost avoided by use of ultraviolet germicidal irradiation (UVGI) to reduce the risk of *C. difficile* infection

Location	No. infections observed baseline	Relative risk with UVGI	No. infections avoided	Per patient attributable cost of HAI	Estimated annual direct cost avoided
Non-study units*	108	0.75	27	$6,408–$9,124[8]	$173,016–$246,348
Study units	87	0.75	21	$6,408–$9,124[8]	$134,568–$191,604
Total	**195**		**48**		**$308,584–$437,952**

* Potential costs avoided if UVGI was also used on nonstudy units with an equivalent observed risk reduction.

medical literature, when available. The point estimate of risk reduction associated with the device is then applied to the facility's baseline infection count and multiplied by the direct cost of the target infection to estimate direct costs averted.[8] In the example in Table 3.2, a 12-month evaluation of ultraviolet germicidal irradiation (UVGI) for terminal cleaning of rooms previously occupied by patients with *Clostridium difficile* infection on three target units was associated with 25 percent decline (relative risk, 0.75) in *C. difficile* infection rates.[9] The estimated cost of *C. difficile* infections averted was compared to the direct cost of purchasing and servicing the UV devices and hiring employees to implement the program house-wide in order to justify the capital expenditure.

Indirect cost can also be used in the evaluation of products with safety or infection-reduction features. Safety-engineered sharps devices have a higher acquisition cost than nonsafety devices, but in addition to comparing direct costs of the two devices, you must consider indirect costs of implementation as well as projected cost savings resulting from a reduction in sharps injuries. An example of a template for calculating indirect cost related to implementation of a sharps injury prevention device program is available at www.cdc.gov/sharpssafety/pdf/sharpsworkbook_2008.pdf. This cost model considers the cost of lost productivity, medical evaluation and treatment for occupational needlestick injuries to help organizations determine how much the projected cost for purchasing and implementing a specific device will be offset by injury reductions. Costs incurred due to underperformance in one or more of the healthcare-associated infection metrics in the Centers for Medicare and Medicaid Services value-based purchasing or hospital-acquired conditions programs or other insurance payer quality programs can also be leveraged to justify the higher cost of implementing products that have been demonstrated to reduce infection risk.

References

1. Association of Healthcare Value Analysis Professionals. Statement of Purpose. Available at www.ahvap.org/?page=Statement_of_Purpose. Accessed December 2, 2015.
2. Occupational Safety and Health Administration. Needlestick Safety and Prevention Act. Available at www.osha.gov/SLTC/bloodbornepathogens/standards.html. Accessed December 2, 2015.
3. Ontario Hospital Association. Chapter 4. Product selection and standardization. In: Optimizing Your Perioperative Supply Chain. Available at www.oha.com/_layouts/login.aspx?ReturnUrl=%2fCurrentIssues%2fkeyinitiatives%2fSupplyChain%2fDocuments%2fForms%2fAllItems.aspx. Accessed December 2, 2015.
4. CDC. Workbook for Designing, Implementing, and Evaluating a Sharps Injury Prevention Program. Available at www.cdc.gov/sharpssafety/pdf/sharpsworkbook_2008.pdf. Accessed December 2, 2015.
5. Guyatt GH, Sackett DL, Sinclair JC, Hayward R, Cook DJ, Cook RJ. Users' guides to the medical literature. IX. A method for grading health care recommendations. *JAMA* 1995; **274**: 1800–1804.
6. Ventola CL. Challenges in evaluating and standardizing medical devices in health care facilities. *P & T* 2008;**33**: 348–359.
7. Perenevich EN, Stone PW, Wright SB, et al. Raising standards while watching the bottom line: Making a business case for infection control. *Infect Control Hosp Epidemiol* 2007;**28**: 1121–1133.
8. Scott RD. The Direct medical costs of healthcare-associated infections in U.S. hospitals and the benefits of prevention. National Center for Preparedness, Detection, and Control of Infectious Diseases (U.S.), Division of Healthcare Quality Promotion. 2009. Available at www.cdc.gov/HAI/pdfs/hai/Scott_CostPaper.pdf. Accessed December 2, 2015.
9. Pegues DA, Han J, Gilamr C. McDonell B, Gaynes S. Impact of unltraviolet germicidal irradiation for no-touch terminal room disinfection on Clostridium difficile infection incidence among hematology-oncology patient. Infect Control Hosp Epidemiol 2017;**38**: 39–44.

Chapter 4

The Business Case for Healthcare Epidemiology and Antimicrobial Stewardship

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Introduction

Before the early 1970s, little attention was paid to infection prevention activities in hospitals, and few standalone hospital epidemiology programs existed.[1] However, since the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) established infection prevention standards with requirements for discrete programs, there has been slow but increasing support for infection prevention leadership, staff, and interventions in healthcare settings.

There are numerous internal and external penalties and incentives driving an increased focus on infection prevention activities, through attention to infection rates (outcomes), specific programs (e.g., antimicrobial stewardship programs) or interventions (process measures). For example, despite the limitations of public reporting, the Centers for Medicare and Medicaid Services (CMS) now requires hospitals to submit specific healthcare-associated infection (HAI) rates to receive full annual reimbursement updates (pay for reporting), and as of 2015, these data are now used to reduce Medicare reimbursement rates for the poorest-performing hospitals (pay for performance).[2] Prior to this, the Hospital-Acquired Conditions (HAC) Initiative, mandated by the US Congress in 2005 and implemented in 2008, targeted eight "never" event complications, including catheter-associated urinary tract infections (CAUTIs) and central line–associated bloodstream infections (CLABSIs). Under the Initiative, hospitals could no longer claim higher-level Medicare severity diagnosis-related groups (MS-DRG) reimbursement for these eight complications. A 2012 study limited to 398 hospitals found little evidence that the HAC Initiative was effective in reducing infections.[3] However, a more recent and larger analysis examining the impact of the HAC Initiative in 1381 hospitals found that it was associated with an 11 percent reduction in CLABSI rates and a 10 percent reduction in CAUTI rates.[4] These results suggest that hospitals have responded to economic incentives, and when provided with a business case for new interventions targeting one of these HAC (e.g., CLABSI), may be inclined to support new infection prevention interventions.

Public reporting continues to drive attention toward infection prevention and antimicrobial stewardship. Hospital specific rates are available at Medicare's Hospital Compare website (www.hospitalcompare.hhs.gov), while hospitals in 31 states and the District of Columbia are now mandated to report HAI data through the National Healthcare Safety Network (NHSN).[5] In addition, the risk of litigation has risen drastically, as public awareness surrounding the incidence and preventability of HAI has increased in recent years due to public reporting and increased media attention. For example, a recent study found that higher reported patient satisfaction on Hospital Compare's Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) Patient Survey was correlated with a lower frequency of medical malpractice claims.[6]

Antimicrobial stewardship programs (ASPs) are also receiving increased attention. Since July 2015, all acute-care hospitals in California have been required to develop a policy supporting judicious use of antimicrobials, establish a physician-supervised multidisciplinary committee or work group, and report the activities within the hospital administration.[7] The National Veterans Health Administration (VHA) released VHA Directive 1031, which required all VA medical facilities to develop a stewardship policy with annual review by July 2014.[8] Finally, The President's Council of Advisors on Science and Technology (PCAST) recently recommended that stewardship programs be required for all inpatient and long-term care facilities as a Condition of Participation for CMS by the end of 2017.[9]

Each economic incentive, public reporting initiative or mandate for infection prevention or antimicrobial stewardship is an opportunity to enhance overall programs through increased hospital programmatic support investment in new surveillance technologies, or implementation of infection prevention interventions (e.g., central venous catheter insertion checklists, antimicrobial coated catheters, or automated monitoring technologies). Yet despite the increased attention, there is little evidence that infection prevention programs are receiving the necessary support. A 2014 survey from the Society for Healthcare Epidemiology of America (SHEA) Research Network quantified the increasing burden on infection prevention programs.[10] Overall, 59 percent of programs expected increases in reporting requirements, 31 percent reported increases in time devoted to meetings, and 57 percent reported increasing program responsibilities in 2014, while only 13 percent were expecting increasing financial support for hospital epidemiologists. Furthermore, only 13 percent of programs were expecting an increase in the number of infection preventionists. In the US, 92 percent of 47 programs responding to this SHEA survey had antimicrobial stewardship programs, while 72 percent of the 22 non-US hospitals had such a program. The authors of the survey concluded by saying, "while mandatory reporting of infection rates and other infection control indices have been leveraged in some institutions to garner additional support, the majority of facilities have not seen additional support despite the

growth of responsibilities."[10] While it may seem obvious that hospital administrators should be rushing to fund infection control and antimicrobial stewardship programs, if the past several decades are any indication, expansion of programs will only occur through careful planning and making a business case for infection control and antimicrobial stewardship. In 2007, a SHEA guideline outlined how to make a business case for infection control interventions and programmatic requirements.[11] During the past decade, this approach has been modified to discuss antimicrobial resistant pathogens,[12] targeted infection preventionists issues,[13] and expanded to cover antimicrobial stewardship programs.[14] Yet, the basic steps necessary to make a business case have remained largely the same and are increasingly necessary, in the face of overwhelming programmatic requirements and regulatory burdens. Thus, an updated outline of a business-case analysis is needed to help hospital epidemiologist, infection preventions and antibiotic stewards expand their programmatic resources and ultimately say "yes" to a safer healthcare environment.

Types of Economic Evaluation in Healthcare

Before defining a business-case analysis, it is often helpful to understand what types of economic analyses exist since published economic analyses are often used for parameters in financial calculations. The medical literature contains four basic types of economic analysis including cost minimization analysis, cost-effective analysis, cost-utility analysis, and cost-benefit analysis. In general, the different types of economic analysis, including the related business-case analysis, vary in how they calculate and report clinical outcomes (Table 4.1). Unfortunately, one cannot rely on how authors of published reports describe their analyses in abstracts or methods sections since many published studies purporting to be one type of analysis are actually a different type of analysis. Yet despite the limitations of the published literature, important data are included in many reports and having a better understanding of each type of analysis, including strengths and limitations, can inform an effective business-case analysis.

Table 4.1 Differential valuation and reporting of outcomes based on type of economic analysis completed

Analysis type	Valuation of outcomes	Formulation of final reported outcome
Cost minimization (CMA)	None	Dollars saved
Cost effectiveness (CEA)	Natural units (e.g., infections prevented, life-years saved)	Cost per infection prevented or cost per life year saved
Cost utility (CUA)	Healthy years (quality-adjusted life years: QALYs)	Cost per QALY saved
Cost benefit (CBA)	Monetary units for infections prevented or lives saved	Net benefit (or loss) in dollars
Business case (BCA)	Monetary units for costs averted through infections prevented	Net benefit (or loss) in dollars

Cost-Minimization Analysis

Cost-minimization analysis is frequently used in infection control. Here, the effectiveness of two or more interventions or devices are assumed to be the same, and the analysis is aimed at determining which is the least expensive.[15] For example, when a hospital value-analysis committee is determining which brand of disposable isolation gown should be purchased, it is often assumed that each type of gown is equally effective (side effects and effectiveness). In this example, the least expensive gown would be chosen. However, if the value-analysis committee was trying to determine whether to replace disposable gowns with reusable or laundered gowns, they would not complete a cost-minimization analysis, since disposable gowns are associated with different levels of healthcare worker protection (e.g., liquid barrier) and healthcare worker satisfaction.[16] In situations where different levels of effectiveness exist, one typically completes a cost-effectiveness analysis or cost-utility analysis.

Cost-Effectiveness Analysis

Unlike cost minimization analysis, cost-effectiveness analysis (CEA) compares interventions or devices that have different levels of effectiveness including clinical benefits and side effects. If a new device costs more and is less effective or alternatively costs less and is more effective than an existing intervention, then choosing is relatively simple – one should always select the more-effective as well as less-costly device. Frequently, the choice is more complicated, particularly when a new device delivers increased benefits at a higher cost. In cost-effectiveness analysis, the effectiveness of a device or program is measured in the most natural unit of comparison, such as lives saved or infections prevented.[15] Comparisons are then made in terms of dollars per life-year gained or dollars per infection prevented. Many interventions (in fact most) in healthcare are considered to be cost effective without a cost saving requirement. Clearly, society values a life saved (or infection prevented) over $0, so we should be able to spend resources to prevent an infection, just as we are able to spend resources on a coronary artery bypass graft surgery.

Cost-Utility Analysis

Cost-utility analysis (CUA) is an extension of CEA with the benefits of a specific intervention adjusted by health preference scores or specific utility weights.[15] Here, devices or programs are compared in terms of quality-adjusted life years (QALY) gained. This approach allows the incorporation of disability or adverse effects associated with the infection being prevented and also the side effects of the program or device. Good

examples of CUA in the infection control literature are quite rare.[17] An example worth reviewing is one that analyzed the routine use of vancomycin versus cefazolin as perioperative prophylaxis during coronary-artery bypass graft surgery.[18]

One important parameter to consider when reviewing and reporting the cost-effectiveness of infection control interventions is what is considered cost-effective by society. As discussed above, cost-saving interventions are cost-effective, but since society is willing to spend resources on healthcare, a cost-saving threshold should not be used when determining what is and what is not considered cost-effective. A standard threshold for determining whether a program is cost effective is for the intervention or program to cost less than $50,000/QALY saved; however, some suggest the threshold should be increased to $100,000/QALY saved.[19] The World Health Organization recommends that a threshold for labeling an intervention cost effective be three times a country's gross domestic product per capita, so this threshold is approximately $164,000 in the United States using per capita GDP for the period 2011–2015.[20]

Before discussing cost-benefit analysis or even business-case analysis, it is important to note that CEA and the closely related CUA have emerged as the preferred methods for economic evaluation in healthcare.[21,22] A key strength of both CEA and CUA is that outcomes are reported in standard units, such as cost per lives-saved or QALYs-saved.[21] If an agency wanted to choose between funding a contact-precaution initiative for VRE and a colon cancer–screening program, it would be difficult to compare cost per VRE infection prevented with cost per cancer detected. However, if the clinical outcome comparison between the two programs was cost per life-years saved or cost per QALY saved, an informed decision could be reached.

Cost-Benefit Analysis

Cost-benefit analysis differs significantly from other types of economic evaluation in that all aspects of the analysis, including the clinical consequences of the intervention, are valued in monetary or dollar terms. If a device or program's benefits measured in dollars exceed its costs, then it is considered worthwhile.[21] The major barrier for completing a cost-benefit analysis in healthcare is the requirement to value clinical consequences or a human life in monetary units. For example, few are comfortable estimating or assigning a monetary value to a human life-year. Therefore, the use of cost-benefit analysis has typically been limited to policy-level evaluations outside of healthcare.

Business-Case Analysis

A business-case analysis is a cost analysis from the perspective of what is best for the business, in this instance the health system. Defined for infection prevention, a business case is one where programmatic investments (e.g., hiring full-time employees or purchasing new antimicrobial coated catheters) realize a clinical benefit and a financial return within a set time frame, typically the next fiscal year. The return can be through profit, reduction in losses, or cost avoidance. Specifically, the aim is to determine the dollar costs and benefits of an infection control or stewardship program or changes to such a program to encourage or maintain investment by hospital administrators. In the business case, patient outcomes such as infection-associated morbidity and mortality have not been included since they typically don't impact the hospital economically.[23] Unfortunately, many programs lack the economic expertise necessary to complete a business-case analysis for a program or specific intervention. Prior to considering such an analysis, healthcare epidemiology leadership should contact their local institution's finance administrators or "value-analysis" committees for assistance in using the available local cost data. Additionally, most published studies purporting to be cost-effectiveness analyses of infection control interventions actually take the hospital perspective and are more correctly called business-cases analyses.

Another caveat is that many infection prevention programs have been in existence for years and have helped keep rates of infections low. Similarly, once an antimicrobial stewardship program has reduced fluoroquinolone use to very low levels, it becomes harder to reduce further. The challenge then becomes the continued justification of such programs. Thus, a key role of a business-case analysis is to maintain current funding levels of programs in the face of prior success, since administrators might want to cut such non–revenue generating prevention programs. There are also difficulties when trying to initiate a new intervention, as it is easy to quantify the extra costs (e.g., new hires or new devices) but often very difficult to estimate the incremental financial benefits. This is particularly challenging when there are very few published clinical trials available to convince administrators of the economic costs of HAIs or benefits of infection prevention or stewardship programs and even fewer resources to complete studies at one's own institution.[24]

One partial solution to facilitate saving an existing program is to examine areas where the intervention is not in place and compare infection rates to areas where the intervention is utilized. However, this is becoming increasingly difficult, as there are fewer intensive care units that lack central line–associated bloodstream infection prevention initiatives, for example.[25] Alternatively, if cost reductions or drives for de-implementation force elimination of a specific program (e.g., contact precautions for resistant pathogens), it would be helpful to stagger the elimination of the program in a stepped-wedge fashion, so that if infection rates rise in certain units where an intervention is eliminated, this evidence could be used to reinstitute the program.[26] Interestingly, the University of Maryland eliminated their antimicrobial stewardship program in 2008 resulting in a large increase in antimicrobial utilization and costs.[27] The program elimination led to a now-published economic analysis, which informed the reinitiation of a stewardship program years later. This experience, which will hopefully not be repeated elsewhere, is one that can greatly inform institutions discussing program elimination.

When an identified problem, new mandate, or new technology leads to the desire to introduce a new infection

control intervention, it is important to remember that this is the time to collect outcome, cost, and implementation data that will justify the continuation of the intervention in the future if the institutional support dissipates. To that end, it is often helpful from an analysis, and more importantly, from an implementation perspective to roll out a new intervention in a stepwise or step-wedge fashion.[28,29] This allows comparisons to control populations (e.g., wards or ICUs where the intervention has not yet been implemented) using a higher-level quasi-experimental design.[30] Importantly, when completing a business-case analysis, it is critical to make an honest assessment of the situation. While hospital epidemiologists and infection preventionists want to increase the resources available for infection prevention, it is also important to avoid overestimating benefits or underestimating staff and time costs.[24] Making either or both of these mistakes in an initial analysis may improve the appearance of the situation in the short term, while hindering efforts and necessary trust in the long term after resource audits are performed.

Business-Case Analysis Example: Expanding Services and Programs

The method of completing of a business-case analysis can be broken down into several incremental steps. Over the past decade since the SHEA Business-Case Guideline[11] was published, it has become evident that two additional steps are needed prior to completing a business-case analysis for a specific intervention, policy change, or new hire. These two steps are strategic planning and learning to say "no" to added demands without added resources. If there is one recommendation that that should hang on the walls of every hospital epidemiologist, infection preventionist, and ID pharmacist it would be KEEP CALM AND DON'T WORK FOR FREE, which will be discussed more below.

Step 1: Establishing a Strategic Business Plan for Your Program

Although beyond the scope of this chapter, it is important to be aware of the role that strategic business planning plays in establishing a platform for program success. Soule published one of the few overviews of strategic planning in infection control.[1] She outlined a basic strategic plan that included a mission statement, overall program goals, program assessment, description of existing personnel and roles, the infection control plan, and how the infection control program integrates in the hospital via an organization "org" chart. Whether through "SWOT" analysis that identifies strengths, weaknesses, opportunities, and threats or other strategies like Gap Analysis,[31] understanding where one's program is now (example – high central line–associated bloodstream infections – CLABSI) and where it needs to be (below the NHSN median CLABSI rate) is a critical first step in preparing to make a business case.

Step 2: Learn to Say "No"

Once one has established clinical goals or targets, it becomes easier to identify what is already being done and, therefore, where increased resources are needed. However, many times a program is faced with a request to expand without increased resources. For example, a request from a hospital chief medical officer might be: "Our CLABSI rates are too high, you must attend a national meeting on CLABSI prevention and get the hospital rates cut in half to be in line with other hospitals. However, at this time, we have no additional resources to meet this request."

As outlined in William Ury's important book *The Power of the Positive No*, a typical response to this request is to accommodate the request within the current budget or get angry and say "no" to the request in an attacking way.[32] However, these responses let the entire infection prevention team down by adding more work onto an already overworked program, which can be quantified since a strategic plan was completed in Step 1, above. If anyone gets angry and attacks hospital leadership in a direct or indirect way, the long-term harm to programmatic efforts is immeasurable. Fortunately, there is an effective path that avoids accommodation or confrontation. This strategy is called the "Positive No" and requires uncovering the yes – what the goals are (i.e., your strategic plan), empowering a "no" in a positive way and proposing an alternative strategy that the infection prevention team can say yes to.

The first step in the infection control "Positive No" is saying yes to the infection prevention program including the staff. For example, resources are needed to meet a new request, and if one says yes now, the program will never receive the necessary resources to protect patients and your overworked staff. Thus, the decision is between saying yes to future patients and the existing staff and saying no to reducing CLABSI rates without resources. This small recognition of what one is saying yes to empowers the infection prevention team to make necessary financial requests. The second step is to develop a positive no without anger. This requires time; therefore, it is recommended that decisions or responses to any request not be made immediately. Thus, once the request is received, print the email and save it while a plan B is developed. Finally, once a response or alternative plan is carefully developed, it can be proposed to the CMO: "I really feel that CLABSI are a big problem. At the moment our team is extremely overworked and I'm concerned they may quit. I can't say yes to new initiatives without additional resources, as it will compromise what we are doing and my team. I propose we set up a hospital-wide task force to come up with a plan to address the CLABSI problem." While this response indirectly says no to the initial request, at the same time it has communicated that the clinical problem understood the problem and that the infection prevention program has seriously considered the situation and has a potential plan to improve the CLABSI rates. Now that there is a clinical target and task force, the next steps are to develop a business case to tackle high infection rates.

Step 3: Frame the Problem and Develop a Hypothesis Regarding the Potential Solutions

One may now wish to implement an intervention to reduce CLABSI in hospital ICU settings. However, there are many possible interventions that target CLABSI including antimicrobial catheters, insertion bundles and checklists, and "scrub the hub campaigns." Since a strategic plan has been completed in Step 1, the primary barrier hindering implementation of specific CLABSI interventions has been identified as too few infection preventionists for the hospital census compared to other institutions with similar clinical programs. In order to implement an intervention to reduce these infections, the CLABSI task force recommends hiring additional staff for your department. Thus, the next task is convincing the hospital administration that the cost of an additional full-time employee (FTE) will be offset by cost savings through reduced infections, including CLABSI.

Step 4: Meet with Key Administrators

Prior to the start of the analysis, schedule a meeting with the key administrators (e.g., Chief Quality Improvement Officer, Chief Medical Officer, Chief Nursing Officer) who oversee hospital epidemiology and other groups who will be involved in the program, hire, or intervention. The purpose of this meeting is threefold. First, it is important to obtain agreement that the manner in which the plan is to address the clinical problem (i.e., new FTE) has the backing of leadership. Second, the administrator can assist in identifying critical individuals and departments who may be affected by the proposal and whose needs should be included in the business case. Finally, the administrators can help identify the critical costs and factors that should be included in the analysis, including administrative data.

Step 5: Determine the Annual Cost of the Program

In the current example, the cost is the salary of an FTE plus the price of benefits. This is available from many sources including the hospital's institutional budgets or available on-line surveys.[33] As an example, an FTE infection preventionist might earn $62,000 in Idaho or $110,000 in New York State (ref www.careersinpublichealth.net/careers/infection-preventionist, accessed 12/2/2015). Other interventions may involve more wide-ranging costs. For example, interventions that include contact precautions will include costs associated with purchasing gowns and gloves, excess FTE time (i.e., salary) needed to don and doff the precautions, added FTE time to remove the added waste from the wards, and costs associated with waste disposal.

Step 6: Determine What Costs Can Be Avoided through Reduced Infections

Optimally, the upfront cost of hiring a new infection preventionist can be recouped during a reasonable period of time, usually the current fiscal year. Ideally, local institutional data can be analyzed to determine if CLABSI were reduced after hiring additional staff in the past. Alternatively, the medical literature may be reviewed to see if others have published their data regarding a similar issue. For example, individual local experience or a literature review might suggest that hiring an infection preventionist would be expected to reduce CLABSI by half through improved audit and feedback, and insertion checklist implementation. Thus, if a hospital has 40 CLABSI annually, an effective infection preventionist could directly prevent 20 CLABSI.

Step 7: Determine the Costs Associated with the Infection of Interest at Your Hospital

If local hospital administrative data are readily available, an attributable cost of an ICU-CLABSI could be directly calculated. Alternatively, a literature review might reveal that the average CLABSI is associated with an excess cost of $18,000.[11] Many estimates of the costs associated with CLABSI and other HAI report far higher costs. One major reason for the overestimate of HAI costs is failure to consider time-dependent bias in the study methods.[34] Time-dependent bias is particularly important to consider when estimating the cost and length of stay of HAIs since longer hospitals stays are associated with higher risk of HAI. If the duration of the hospital stay and costs that manifest prior to the infection are included, this would cause a biased overestimate of the outcomes associated with the infection. Studies that use conventional study design methods that fail to take into account hospital stays and costs prior to the development of the infection have been shown to overestimate costs by approximately 30 percent and attributable lengths of stays by 9 to 13 days.[34,35]

At this point, it might be tempting to multiply the expected CLABSI prevented, 20, by the estimated costs per CLABSI and state that hiring an infection preventionist will save $360,000 in CLABSI-associated costs alone. However, a certain percent of these costs might be reimbursed by third-party payers, although this is less common in 2015. For example, if 20 percent of costs are reimbursed, the cost savings from preventing 20 CLABSI would be estimated at $288,000 (80 percent of $360,000). After subtracting the cost of the new infection preventionist, the savings could be as high as $226,000 (288,000–62,000) in Idaho.

An alternative method for calculating the attributable cost of a nosocomial infection is to multiply the average increase in length of stay by the average daily cost for a hospital stay. This cost can be determined specifically for the local institution or

taken from the literature. The average attributable length of stay for a CLABSI is approximately 12 days.[11] Thus, preventing 20 CLABSI, reduces over-all length of stay by a total of 240 days at an average cost of approximately $1,200/day for a cost savings of $288,000.

Step 8: Calculate the Financial Impact of the Proposed Intervention or Program

Completing the business case requires taking the estimated cost savings or additional profits and subtracting the costs of the upfront outlay, in this case the salary and benefits of a full-time infection preventionist. In this example, the total economic impact to the hospital for prevented CLABSI from hiring an additional infection preventionist is estimated to save between $178,000 (New York State) and $226,000 (Idaho).

Step 9: Include Additional Financial or Health Benefits of the Proposed Intervention or Program

Many infection prevention interventions have multiple benefits. For instance, contact precautions introduced in response to an *Acinetobacter baumannii* outbreak would also be expected to reduce MRSA and VRE infections.[36] In this case, the additional FTE would also be expected to reduce rates of surgical site infections and improve hand hygiene compliance. All of these factors should be included in a proper business-case analysis. To further make the business case for an additional FTE, one must include the expected reduced costs associated with reductions of these other preventable infections. After these are included, it would be expected that hiring an additional FTE would save the hospital significant additional costs.

Even though business-case analysis does not include the adverse consequences of healthcare-associated infections, such as patient mortality, hospital administrators do respond to these issues. While patient safety cannot be the whole argument, some calculation of the patient safety improvement associated with the intervention should be included. If mortality associated with preventing a CLABSI is included, it is possible that preventing 20 CLABSI could prevent two to seven additional deaths. Additionally, preventing complications such as CLABSI might be associated with reduced legal costs. Furthermore, with the increased regulations for mandatory reporting of healthcare-associated infections, there are many other financial benefits to the hospital that we have not considered (e.g., pay-for-performance or enhanced reputation of the institution). These must be included in a proper business-case analysis and can influence hospital administration. Thus, a hospital's risk management group should be involved early in any quality improvement program business-case analysis.

Step 10: Make the Case for Your Business Case

Completing the analytical portion of a business case must be followed by effective communication of the results to key stakeholders at the institution through the successful presentation of your analysis. After completing the analysis, schedule individual meetings with the same stakeholders you met with in Step 4. These meetings should include presentation of the initial findings of the business-case analysis, the development of the implementation plan, which may have additional costs that need to be included, and determination of current support for the planned initiative. These meetings will allow the infection prevention leadership to answer most of the questions that might otherwise appear during the final presentation of the business case. Most important, these meetings are the critical first step in developing an implementation plan for the intervention, about which much has been written.[37,38]

Even in interventions, such as the presented example, where the estimates suggest that hiring an FTE will be cost-saving, it is often not easy to initiate cost-saving interventions in hospitals. One of the reasons for the difficulty in initiating interventions is that it is not always clear who should pay for the intervention since the cost-center that benefits (e.g., patient care) is not always where the cost of the intervention arises (e.g., infection control or microbiology). In this example, should the Critical Care service contribute to the hiring of a new infection preventionist since they will see the benefits of the added staff through lower reported infection rates and lower costs? The cost-shifting issues become even more problematic when interventions are effective but not cost-saving. It is often the case that stronger institutional support and understanding of cost-sharing is needed in order to initiate effective and even cost-saving interventions.

Step 11: Prospectively Collect Cost and Outcome Data Once Program Is in Effect

If an infection control or stewardship program or intervention has been in place for an extended period of time, it is often the case that infection rates are already low, so that it may be difficult to justify additional investment. In the above CLABSI example, if CLABSI rates are now below the NHSN median, competing demands may cause administrators to question the need for your now larger infection prevention program. One way to maintain current resources is through continued collection of multidrug-resistant organisms (MDROs) rates, device infection rates, and process measure compliance rates (e.g., hand hygiene) that have been improved through the FTE hire. If one is able to demonstrate a continued reduction in these rates through a well-designed annual report, it will be difficult for administration to eliminate the FTE. Fortunately, the literature continues to support the fact that continued investment in infection prevention programs is cost-effective and pays dividends over the long haul, while the benefits would be lost if the investment was not continued.[39]

Conclusion

Demonstrating the value of infection prevention and antimicrobial stewardship programs increasingly falls to the hospital epidemiologist, infection preventionist, and infectious diseases pharmacist. When accompanying a well-designed strategic plan and thorough annual report, a business-case analysis can help justify new initiatives and maintain or expand existing programs. The future existence of these programs will require up-to-date estimates of the costs and outcomes associated with device infections and multidrug-resistant pathogens.

References

1. Soule BM. From vision to reality: strategic agility in complex times. *Am J Infect Control*. 2002;**30**(2): 107–119.
2. Talbot TR, Bratzler DW, Carrico RM, et al. Public reporting of health care–associated surveillance data: recommendations from the healthcare infection control practices advisory committee. *Ann Intern Med*. 2013;**159** (9): 631–635.
3. Lee GM, Soumerai SB, Jha AK. Nonpayment for preventable infections in U.S. *hospitals. N Engl J Med*. 2013;**368** (2): 191–192.
4. Waters TM, Daniels MJ, Bazzoli GJ, et al. Effect of Medicare's nonpayment for Hospital-Acquired Conditions: lessons for future policy. *JAMA Intern Med*. 2015;**175**(3): 347–354.
5. State-based HAI prevention. 2015; www .cdc.gov/hai/stateplans/required-to -report-hai-NHSN.html. Accessed December 14, 2015.
6. Jones V. Hospital and physician professional liability trends and industry topics. *J Healthc Risk Manag*. 2015;**35**(1): 7–19.
7. The California Antimicrobial Stewardship Program Initiative. 2015; www.cdph.ca.gov/programs/hai/Pages/antimicrobialStewardshipProgramInitiative.aspx. Accessed December 14, 2015.
8. VHA DIRECTIVE 1031: ANTIMICROBIAL STEWARDSHIP PROGRAMS (ASP). 2015; www.va.gov /vhapublications/ViewPublication.asp ?pub_ID=2964. Accessed December 14, 2015.
9. *Report to the President of combatting antibiotic resistance*. Washington, D.C.: Executive Office of the President; September 2014.
10. Morgan DJ, Deloney VM, Bartlett A, et al. The expanding role of the hospital epidemiologist in 2014: a survey of the Society for Hospital Epidemiology of America (SHEA) Research Network. *Infect Control Hosp Epidemiol*. 2015;**36** (5): 605–608.
11. Perencevich EN, Stone PW, Wright SB, et al. Raising standards while watching the bottom line: making a business case for infection control. *Infect Control Hosp Epidemiol*. 2007;**28**(10): 1121–1133.
12. Maragakis LL, Perencevich EN, Cosgrove SE. Clinical and economic burden of antimicrobial resistance. *Expert Rev Anti Infect Ther*. 2008;**6**(5): 751–763.
13. Wright MO, Perencevich EN. Cost-effectiveness of an Infection Control Program. In: Foley SL, Chen AY, Sinjee S, Zervzos MJ, eds. *Molecular Techniques for the Study of Hospital Acquired Infection*. Wiley-Blackwell; 2011: 248.
14. Perencevich EN, Cosgrove SE. Economic evaluation of healthcare-associated infections and infection control and antimicrobial stewardship interventions. In: Jarvis WR, ed. *Bennett & Brachman's Hospital Infections*. 6th ed. Lippincott Williams & Wilkens; 2014.
15. Drummond M, Sculpher M, Torrance G, et al. *Methods for the Economic Evaluation of Health Care Programmes*. 3rd ed. Oxford: Oxford University Press; 2005.
16. Ward WG, Sr., Cooper JM, Lippert D, Kablawi RO, Neiberg RH, Sherertz RJ. Glove and gown effects on intraoperative bacterial contamination. *Ann Surg*. 2014;**259**(3): 591–597.
17. Stone PW, Braccia D, Larson E. Systematic review of economic analyses of health care–associated infections. *Am J Infect Control*. 2005;**33**(9): 501–509.
18. Zanetti G, Goldie SJ, Platt R. Clinical consequences and cost of limiting use of vancomycin for perioperative prophylaxis: example of coronary artery bypass surgery. *Emerg Infect Dis*. 2001;**7**(5): 820–827.
19. Koplan JP, Harpaz R. Shingles vaccine: effective and costly or cost-effective? *Ann Intern Med*. 2006;**145**(5): 386–387.
20. GDP per capita (current US$). 2015; h ttp://data.worldbank.org/indicator/NY .GDP.PCAP.CD. Accessed December 14, 2015.
21. Gold M, Siegel J, Russell L, Weinstein M. *Cost-Effectiveness in Health and Medicine*. 1st ed. New York: Oxford University Press; 1996.
22. Neumann P. *Using Cost-Effectiveness Analysis to Improve Health Care*. 1st ed. New York, NY: Oxford University Press; 2005.
23. Waters HR, Korn R, Jr., Colantuoni E, et al. The business case for quality: economic analysis of the Michigan Keystone Patient Safety Program in ICUs. *Am J Med Qual*. 2011;**26**(5): 333–339.
24. Graves N, Harbarth S, Beyersmann J, Barnett A, Halton K, Cooper B. Estimating the cost of health care-associated infections: mind your p's and q's. *Clin Infect Dis*. 2010;**50**(7): 1017–1021.
25. Furuya EY, Dick A, Perencevich EN, Pogorzelska M, Goldmann D, Stone PW. Central line bundle implementation in US intensive care units and impact on bloodstream infections. *PLoS One*. 2011;**6**(1): e15452.
26. de Hoop E, van der Tweel I, van der Graaf R, et al. The need to balance merits and limitations from different disciplines when considering the stepped wedge cluster randomized trial design. *BMC Med Res Methodol*. 2015;**15**: 93.
27. Standiford HC, Chan S, Tripoli M, Weekes E, Forrest GN. Antimicrobial stewardship at a large tertiary care academic medical center: cost analysis before, during, and after a 7-year program. *Infect Control Hosp Epidemiol*. 2012;**33**(4): 338–345.
28. Brown CA, Lilford RJ. The stepped wedge trial design: a systematic review. *BMC Med Res Methodol*. 2006;**6**: 54.
29. Hussey MA, Hughes JP. Design and analysis of stepped wedge cluster randomized trials. *Contemp Clin Trials*. 2007;**28**(2): 182–191.
30. Harris AD, Lautenbach E, Perencevich E. A systematic review of quasi-experimental study designs in the fields of infection control and antibiotic resistance. *Clin Infect Dis*. 2005;**41**(1): 77–82.
31. Weinshel K, Dramowski A, Hajdu A, et al. Gap analysis of infection control practices in low- and middle-income countries. *Infect Control Hosp Epidemiol*. 2015;**36**(10): 1208–1214.

32. Ury W. *The Power of the Positive No: How to Say No and Still Get to Yes*. New York, NY, Bantam; 2007.
33. 2006 APIC Member Salary and Career Survey. 2006; www.apic.org/AM/Template.cfm?Section=Search&section=SecureWrapper&template=/CM/ContentDisplay.cfm&ContentFileID=5981. Accessed September 1, 2006, 2006.
34. Nelson RE, Samore MH, Jones M, et al. Reducing time-dependent bias in estimates of the attributable cost of health care-associated methicillin-resistant *Staphylococcus aureus* infections: A comparison of three estimation strategies. *Med Care*. 2015;**53**(9): 827–834.
35. Nelson RE, Nelson SD, Khader K, et al. The magnitude of time-dependent bias in the estimation of excess length of stay attributable to healthcare-associated infections. *Infect Control Hosp Epidemiol*. 2015;**36**(9): 1089–1094.
36. Wright MO, Hebden JN, Harris AD, et al. Aggressive control measures for resistant *Acinetobacter baumannii* and the impact on acquisition of methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant Enterococcus in a medical intensive care unit. *Infect Control Hosp Epidemiol*. 2004;**25**(2): 167–168.
37. Sax H, Clack L, Touveneau S, et al. Implementation of infection control best practice in intensive care units throughout Europe: A mixed-method evaluation study. *Implement Sci*. 2013;**8**: 24.
38. Livorsi D, Comer AR, Matthias MS, Perencevich EN, Bair MJ. Barriers to guideline-concordant antibiotic use among inpatient physicians: A case vignette qualitative study. *J Hosp Med*. 2015.
39. Dick AW, Perencevich EN, Pogorzelska-Maziarz M, Zwanziger J, Larson EL, Stone PW. A decade of investment in infection prevention: A cost-effectiveness analysis. *Am J Infect Control*. 2015;**43**(1): 4–9.

Chapter 5

Quality Improvement in Healthcare Epidemiology

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It is not enough to do your best; you must know what to do, and then do your best.
– *W. Edwards Deming*

Healthcare-associated infections (HAIs) account for considerable patient morbidity and mortality, with the majority being preventable.[1,2] There is increasing pressure on hospital epidemiology and infection prevention programs to lead efforts to reduce HAIs nationally by promoting compliance with evidence-based practices. HAIs provide an important measure of quality, and epidemiologists are expected to play a significant role in preventing them. This chapter is a primer on quality improvement applied to infection prevention, from principles, to tools and measures. These quality principles, when integrated with epidemiologic techniques, strengthen infection prevention programs and ensure patient safety and high-quality patient care.

Quality Improvement and Infection Prevention

The focus on quality is traced to medieval times where artisans worked on improving their craftsmanship.[3] The Industrial Revolution brought factories, increasing productivity and incorporating quality control into the products. After World War II, Japanese products had a reputation of being poor-quality, negatively impacting their ability to be sold internationally. The movement for "total quality management" was born as Japanese organizations sought new ways to improve the quality of their products, and these strategies represented the new "total quality" approach.[3] Rather than relying purely on product inspection to ensure quality, Japanese manufacturers focused on improving all organizational processes through the people involved in them. This led to higher-quality products at lower prices, which made Japanese exports competitive in the world market.

Two American quality experts, W. Edwards Deming and Joseph M. Juran, were aware of Japan's progress in the quality arena and predicted that the quality of Japanese goods would overtake the quality of goods produced in the United States by the mid-1970s. Japanese manufacturers began increasing their share in American markets, causing widespread economic effects in the United States. Total quality management, which emphasized approaches that went beyond just statistics and embraced the entire organization, came out of this movement. Several other quality initiatives, such as "continuous quality management," followed. American companies were slow to adopt the principles of quality improvement, and hospitals were even slower.

The Rise of Handwashing: A Quality Improvement Exercise

As epidemiologists, one of the first stories we are taught is that of Dr. Ignaz Semmelweis, a Hungarian obstetrician who in the 1840s showed that cases of puerperal fever could be prevented if doctors washed their hands in a chlorinated lime solution before examining patients.[4] His approach closely followed what we now consider modern quality improvement techniques. First, Semmelweis identified that a problem existed by examining mortality rates in two different obstetrical services. Next he hypothesized that puerperal fever was contagious, and he made observations and started collecting data to prove his hypothesis. He then implemented a practice change, or intervention (handwashing); last, he demonstrated a significant decrease in infection (mortality) through continuous monitoring of data before and after the practice change. Unfortunately, his findings were neither widely adopted, nor were his recommendations implemented by the medical community, and as a result, women in nineteenth-century Vienna continued to die preventable deaths. Even today, the existence of evidence-based practices and quality improvement techniques do not guarantee their adoption nor the successful prevention of errors.

The Birth of Hospital Epidemiology and Infection Prevention Programs

During the 1950s, epidemics of staphylococcal infection and nosocomial infections in hospitals emerged as a major public health issue. At the urging of the American Hospital Association, the CDC, and the Joint Commission (then called the Joint Commission on Accreditation of Healthcare Organizations [JCAHO]), infection control programs were instituted in thousands of hospitals across the country during the 1960s and 1970s. Each program implemented its own prevention and control strategies, with little evidence to definitively determine which interventions, if any, effectively reduced the incidence of infections and the associated costs. In 1974, the CDC initiated the 10-year Study on the Efficacy of Nosocomial Infection Control (SENIC).[5] The study showed that the incidence rate of nosocomial infections decreased and remained lower in hospitals that conducted surveillance for nosocomial infection and that used evidence-based

infection prevention patient care practices. As hospital epidemiology and infection prevention developed as a discipline, quality principles were incorporated and became integral to the functioning of many programs.

The Perfect Storm

During the 1980s and early 1990s, as hospital epidemiology programs continued to evolve, they were impacted by the emergence of the human immunodeficiency virus and the implementation of universal precautions and the Occupational Safety and Health Administration's Blood-borne Pathogens Standard,[6] as well as the resurgence in tuberculosis, including nosocomial outbreaks of multidrug-resistant tuberculosis. At the same time, hospital epidemiology programs were tasked to address the increasing burden of multidrug-resistant organisms and other emerging pathogens that posed a threat to hospitals. In 1999, the Institute of Medicine (IOM) published, *To Err Is Human*, describing the extent of patient harm in the healthcare environment.[7] The IOM estimated about 100,000 preventable deaths per year in the US due to medical errors. It urged that there be a comprehensive approach to patient safety as an ultimate target, at all system levels. *To Err is Human* and subsequent IOM reports were the impetus for US hospitals to embrace safety as priority, and presented an overall framework to improve the delivery of healthcare. The concepts in this framework can be easily applied to infection prevention strategies as well:

Safe: "avoiding injuries to patients from the care that is intended to help them" (e.g., ensuring compliance with hand hygiene)

Timely: "reducing waits and sometimes harmful delays for both those who receive and those who give care" (e.g., administering surgical antibiotic prophylaxis 1 hour prior to the first incision)

Effective: "providing services based on scientific knowledge to all who could benefit and refraining from providing services to those not likely to benefit" (e.g., use maximal sterile barrier precautions during central venous catheter insertion, based on appropriate indications)

Efficient: "avoiding waste, including waste of equipment, supplies, ideas and energy" (e.g., replace administration sets not used for blood, blood products, or lipids at intervals not longer than 96 hours)

Equitable: "providing care that doesn't vary in quality because of personal characteristics such as gender, ethnicity, geographic location, and socioeconomic status" (e.g., implementation of standard precautions and transmission-based precautions)

Patient-centered: "providing care that is respectful of and responsive to individual patient's preferences, needs, and values ensuring that patient values guide all clinical decisions" (e.g., partnering with patients and family members to "speak up" and ask questions, and educating them about what they can expect from healthcare providers and what is being done to reduce their risk of healthcare-associated infection)

The IOM's report *To Err is Human* concluded that "a health care system that achieves major gains in these six areas would be far better at meeting patient needs. Patients would experience care that is safer, more reliable, more responsive to their needs, more integrated, and more available, and they could count on receiving the full array of preventive, acute, and chronic services that are likely to prove beneficial. Clinicians and other health workers also would benefit through their increased satisfaction at being better able to do their jobs and thereby bring improved health, greater longevity, less pain and suffering, and increased personal productivity to those who receive their care."[7]

Very quickly, hospital epidemiology programs found themselves in the crosshairs of hospital administrators, quality management departments, managed-care entities, regulatory and accrediting agencies, lawmakers, and an increasingly worried public, all requesting evidence of effectiveness and increased accountability. Although collaboration with other disciplines is nothing new to hospital epidemiology, this "perfect storm" sometimes required epidemiologists and infection preventionists to use a different language and methodology. "Multidisciplinary collaborations are essential to instigate innovative prevention research, identify new applications for old prevention strategies, maximize synergy among the broad array of professionals engaged in quality promotion efforts, minimize overlap, and conserve scarce resources."[8] Table 5.1 presents perspectives on the quality of healthcare from the points of view of various stakeholders.

Public Reporting and Transparency

Healthcare consumers, regulatory and accreditation agencies, and the insurance industry, including managed-care entities, have an increasing interest in greater transparency in the reporting of healthcare-related outcomes. Publicly reported healthcare-associated events include central line–associated bloodstream infections, catheter-associated urinary tract infections, colon and abdominal hysterectomy surgical site infections, methicillin resistant *Staphylococcus aureus* bacteremia, and *Clostridium difficile* infections.[9] The desire for transparency is based on the belief that these indicators can be used to evaluate those organizations that offer the highest quality of care most cost-effectively. Reported data are becoming increasingly available to the public by way of the Internet. However, questions remain about the accuracy of the reported price, process, and outcome information; the comparability of the results across different populations; and whether and how patients and others use the information in making decisions.

The Concept of Value in Healthcare

Value is a key component to any product we consume. In healthcare, patients, as well as providers and suppliers

Table 5.1 Perspectives on healthcare quality from the point of view of various stakeholders

Perspective	Infection prevention	Quality management	Managed care and accreditation agencies
Focus	Adverse health events	Indicators	Errors, near misses
Determinants	Risk factors	Patient mix	Root cause analysis, human factors
Monitoring	Surveillance, response	Performance measurement, improvement	Reporting, learning
Goal	Prevention	Performance improvement	System improvement
Key professionals	Healthcare epidemiologists, infection preventionists	Quality managers, accreditation officials	System engineers, healthcare purchasers and consumers

Note: Information is from Gerberding.[8]

Table 5.2 Websites with information relevant to quality improvement

Organization	URL
Centers for Disease Control and Prevention (CDC)	www.cdc.gov/
Institute for Healthcare Improvement (IHI)	www.ihi.org/
Agency for Healthcare research and Quality (AHRQ)	www.ahrq.gov/
Centers for Medicare and Medicaid Services (CMS)	www.cms.gov/
The Joint Commission (TJC)	www.jointcommission.org/
National Committee for Quality Assurance (NCQA)	www.ncqa.org/
American Society for Quality (ASQ)	http://asq.org/index.aspx
The American Society for Healthcare Risk Management (ASHRM)	www.ashrm.org/
The World Health Organization (WHO)	www.who.int/en/
The Robert Wood Johnson Foundation (RWJF)	www.rwjf.org/
National Patient Safety Foundation (NPSF)	www.npsf.org/
National Quality Foundation (NQF)	www.qualityforum.org/Home.aspx

benefit from optimizing the value of care, resulting in further economic sustainment of our healthcare delivery system.[10] The focus is on efficiency, and accountability from the providers. The historical organizational structure for healthcare delivery made it difficult to measure value. When we shop for a car, or anything for that matter, we want to purchase the item that gives us the best value. By value, we mean the best quality that we are able to afford. For healthcare, assigning value is a more difficult task but is no less important. We have learned that better care does not equate to higher-cost care, and providers are facing steadily increasing pressure to take excess cost out of the system (i.e., reduce waste) while maintaining or increasing the quality of care.[11] Many agencies and groups have focused on promoting quality nationally and internationally (Table 5.2).

High Reliability Organizations

To achieve the improvements sought and prevent errors, healthcare systems looked for nonmedical organizations where safety has been a priority.[12] High reliability organizations (HROs) have fewer accidents because they work on preventing failure and ensuring reliability.[13] These organizations exhibit a state of "mindfulness" reflected in five practices: preoccupation with failure, reluctance to simplify interpretations, sensitivity to operations, commitment to resilience, and deference to expertise.[14]

HROs address failures with thorough analysis, and treat them as a reflection of the system's reliability. The preoccupation with failure identifies any defect in a process (no matter how small), and directly addresses the issue without waiting until a bad outcome occurs. They encourage identifying multiple potential reasons for the failure and avoid simplification. Often failure may be related to multiple factors, and identifying one defect does not necessarily rule out the presence of additional defects. The sensitivity to operations includes paying very close attention to any changes or deviations in operations and not disregarding these changes as nonsignificant. The commitment to resilience, a containment principle, refers to the organization being functional even in the presence of a stressful environment. Facing the adverse event, the system will work on establishing plans to improve a process to be less susceptible to errors. The system contains the event, and improves the process so that in the situation where a similar event occurs, it will be ready, and harm may be avoided. Finally, expertise is not always related to hierarchy. HROs look to the person who can best achieve the task regardless of his or her position.

Unfortunately, hospitals do not perform as HROs, making them susceptible to frequent failures, resulting in patient

harm.[15,16] Some of the limitations of hospitals include their dependence on efforts of individual healthcare personnel rather than institutionalizing high reliability processes, benchmarking based on available reported outcomes that may not be surrogates of high reliability, and accepting clinician autonomy and variation in patient care even if it does not conform with best practices.[16] Healthcare organizations may work on achieving high reliability through three routes: include a leadership commitment to no harm, establish a safety culture throughout the organization, and incorporate rigorous process improvement tools.[15]

Leadership

Leaders of hospitals and healthcare systems have a key role in influencing safety at their organizations. They can promote safety as a focus for the entire organization with setting clear goals to be achieved.[17,18] A qualitative analysis of 14 US hospitals and their approach to reducing healthcare-associated infections revealed some of the attributes of effective leaders.[19] Successful leaders reflect a culture of excellence when they communicate with their associates; find solutions to overcome barriers; inspire others to lead with clear goals; and are planners, "thinking strategically while acting locally."[19]

Organizational Culture and Safety

The organizational culture of institutions plays a critical role in patient safety. There are four dimensions of organizational culture: group, entrepreneurial, hierarchical, and production-oriented. Hospitals are thought to have a mixture of the four dimensions.[20] A survey of 92 US hospitals evaluated the perceptions of leaders, physicians, and healthcare personnel regarding their institutions' safety climate and their organizational culture.[20] The hierarchical organizational culture was most common, which values predictable operations, and is heavily reliant on structure, policies, and procedures. On the other hand, those who perceived their organization to have a group participation culture scored better in the safety climate survey, suggesting that a high level of hierarchical culture may create barriers to safety efforts. Institutions may have a dominant culture, but at the departmental level variation occurs. For example, the infection prevention department may exhibit a strong group culture supporting safety, compared to a surgical service line where production takes first priority.[21] Still, differing subcultures will support and align to a few beliefs and values of the organization. An organization that thrives on a culture of excellence may be more willing to adopt programs that enhance improvements in patient safety.[22] Finally, external factors or pressures, such as public reporting, hospital-acquired condition program, and value-based purchasing, effectively influence hospitals to closely monitor and intervene in the areas of interest.

Safety Culture

The most effective quality programs provide an environment that places patient safety at the center of all that is done. Clear expectations will enable healthcare personnel to do the right thing, the right way, the first time, every time. A culture of safety incorporates organizational commitment that is conveyed at all levels, supported with resource allocation, and openness in reporting and addressing safety events.[23] Hospitals differ in their adoption of a safety culture, and variation is even recognized at the unit and the individual level.[23] When an error occurs, a "no name, no blame, no shame" culture encourages a focus on the improvement of processes, without negating accountability at the individual level.[24,25] A close evaluation of events clarifies whether the gaps are related to an imperfect process or volitional individual noncompliance. As a step toward greater transparency, some organizations invite members of the public to join patient safety committees and other initiatives. The comprehensive unit safety program (CUSP) focuses on the work at the unit level and promotes safety as a priority for healthcare personnel.[26] It includes the education of staff on the science of safety, creation of a team and engaging senior executives, identifying and learning from defects, and implementing improvements and communication tools. CUSP has been widely used in national efforts to reduce device-related infections.[27,28]

High Reliability Tools

A key to reducing errors is to focus on the environment and process where the errors occur, rather than assuming the error resulted from an unsafe act committed by a healthcare personnel.[29] Most errors represent "system flaws rather than character flaws."[30] Human factors engineering studies the relationship between the person and the system and helps design the system to optimize the worker's performance to reduce any events. James Reason's "swiss cheese" model depicts multiple system failures that escape safeguards thus leading to safety events.[29] Human factors protect against the risk of slips or mistakes of healthcare personnel resulting in safety events. In addition to human factors engineering, process improvement tools such as PDSA, Lean, and Six-Sigma have been used to enhance processes.

Deming's cycle, or PDSA, provides a structure to implement improvements using four steps: plan, do, study, and act.[31] The "plan" stage identifies the process that requires improvement. The "do" stage is when an intervention is implemented; a certain level of imperfection is accepted as the experience itself can lead to learning and improvement. The "study" stage evaluates what worked and what did not. Finally, the "act" stage includes adjustments and additional steps to implement based on the analysis of the difference between actual and expected results. The process is then repeated, till expected results are achieved. Lean process is a quality improvement method that focuses on improving quality by dramatically changing operational processes to become faster and more flexible and to reduce waste.[32] It does this by identifying and reducing steps that do not add value in a process. Finally, six-sigma aims to reduce variation and achieve stable and predictable process results.[33] Achieving a level of six-sigma implies near perfection in an operational process, with only 3.4 defects per 1 million opportunities. Teams follow a process improvement methodology abbreviated DMAIC: define, measure,

analyze, improve, and control. It starts by identifying the problem, then measuring the problem, identifying the root cause of the problem, mitigating the root cause, and finally maintaining the gains. This methodology focuses on finding sources of variation inherent to a process and eliminating them to achieve more consistent results.

High Reliability and Infection Prevention: The Example of the Peripheral Venous Catheter

We describe below how using the five principles of high reliability organizations may improve the infection risk related to peripheral venous catheters (PVCs). The preoccupation with failure leads to the identification of any defect in a process, and directly addressing it before a bad outcome occurs.

- *A PVC is placed without following all the proper steps (not compliant with aseptic technique). I voice my concern even if there are no detectable adverse events.*
- *I notice that the antiseptic used in the kit for placing the PVC has been exchanged with another (not all antiseptics are equal). I investigate the reason.*

The sensitivity to operations includes paying very close attention to any changes or deviations in operations and not disregarding these changes as nonsignificant.

- *With more than half of nurses on one unit being new graduates, the manager recognizes a need for educating them on the proper placement and care of the PVC, and arranges for educational sessions.*
- *An administrative decision is made to abolish the "Intravenous Therapy (IV) Team" because of financial cuts. The IV team had the responsibility to evaluate the PVCs and provide feedback to the nurses. The unit manager evaluates a process to fill the gap in anticipation of any problems before they occur.*

Reluctance to simplify interpretations: Often failure may be related to multiple factors, and finding one factor may not mean other factors are not involved and should still be identified.

- *A patient reports pain at the PVC site shortly after it is placed. The healthcare personnel finds minimal swelling at the site, but the flow of the intravenous fluids was not impeded. Patient was reassured, however, woke up with a swollen and tender arm, and an infiltrated PVC site.*
- *After 3 days of PVC placement, erythema and a mild palpable cord was found at the site. The nurse noted mild phlebitis that was attributed to a potassium infusion. Within 24 hours, the patient developed chills and fever. The patient was diagnosed with peripheral septic thrombophlebitis.*

Commitment to resilience means that the organization will continue to be functional even in the presence of a very stressful environment.

- *An influx of very sick patients present to the emergency department. Healthcare personnel are caring for a much larger number of patients, providing the same treatment without short cuts. If they are not compliant with all the steps of placing the PVC, then they will note this by labeling it as "not placed under aseptic conditions."*
- *Two nurses attend a lecture on the associated risk with PVCs, and multiple case studies are presented. Although they have not previously seen cases with adverse events related to PVCs, their concern about their patients' safety was translated into evaluating every patient's PVC on their unit for any problems.*

Deference to Expertise: Expertise is not always related to hierarchy. It is looking to the person who would be the best to achieve the task regardless of his/her position.

- *An IV team nurse is more knowledgeable than other nurses or physicians in the topic of placement and care of the PVC.*

Implementing and Sustaining Quality Improvement Efforts

Implementation

Implementation is critical to the success of quality improvement efforts.[34] Prior to implementation, a decision to adopt a program is made at the institutional level. The program is usually piloted at a unit level, and then spread hospital-wide. During implementation, the program is refined to best fit the institution, and plans are established to ensure the work is sustainable. Successful implementations strongly influence program outcomes. Implementation may not be universal, and adoption varies among healthcare personnel. Successful implementation depends on multiple factors including the innovation characteristics, organizational capacity and support system, provider characteristics, and community factors.[34]

The planned program needs to be adaptable to and compatible with the institutional workflow. The flexibility of the program will allow enhancements or modifications based on its evaluation during implementation. The closer the program is to the institution's functions, the easier it is for it to be integrated. Moreover, the institution needs to allocate the resources – whether human, technical, or financial – to warrant the optimal support. Leaders play a pivotal role in supporting the work, communicating the importance of the program as a priority, and addressing any barriers that may arise during implementation. Leaders are accountable and demand the same accountability at all levels. The providers should perceive the program as beneficial to them or to their patients' safety, and they should have the skills and the ability to achieve the work. It is essential for the providers to see the new program as a means to improve their work, or at least not burden their daily activities. During implementation, healthcare personnel are trained and evaluated for their competencies, and their feedback and concerns are addressed. Often a few providers emerge as champions, and they identify and engage all the other stakeholders to partner on supporting the program implementation.[35] Successful champions believe in

the safety efforts, have the recognition and respect of their coworkers, and are motivated and early adopters of change.[36] It is beneficial to make the case to each discipline or stakeholder of the program's value to them and to their patients. With each group having different perceptions and needs, it is essential to address any potential effects according to their perspectives.[35]

Sustainability

Sustainability is the long maintenance of a program, where it is continued or improved, becomes integrated into regular activities, and is supported by the different stakeholders.[37,38] Unlike implementation, resources are more limited during the sustainability period. Sustainability is often not well planned for and often overlooked. Programs are more likely to be partially sustained, unless a significant effort is placed in institutionalization, when combined with regular training, audits, and feedback.[38] Factors that influence sustainability include capacity to continue the program, and having processes established to integrate the program as part of the daily activities of healthcare personnel. Integration of the program is easier when it is aligned with the organization's goals (e.g., promoting safety, process, and outcome dashboards). Other supporting factors include updating policies and standard operating procedures, regular competency evaluations, and keeping the focus on the program as a priority. Champions provide essential support for early program adoption;[39] nevertheless, the sole reliance on champions can weaken further acceptance at the institutional level, either through lack of delegation to others or if the champion leaves.[40] The optimal goal is to have a gradual migration from the dependence on the champions to a full integration of the process into the daily work of the healthcare workers, making everyone accountable for the proper steps of the process, and thus, reaching successful results independently of the presence or absence of the champion.

Implementation and Sustainability: The Example of the Urinary Catheter

We describe the example of efforts to reduce urinary catheter risk and catheter associated urinary tract infections (CAUTI). With the public reporting of CAUTI in intensive care units since 2012, and its association of performance with the hospital acquired condition penalty and value based purchasing, the hospital leadership makes the decision to invest significant effort to improve urinary catheter outcomes, and decrease CAUTIs on all patient care units (intensive and non-intensive care units).

As a first step, hospital leadership assigns an executive sponsor of the work who receives regular updates and provides support for any required resources during implementation. Key stakeholders are engaged and educating on why addressing CAUTI is important, and asked for their support and partnership in the effort. Champions are identified and the CAUTI prevention team is formed. The CAUTI team includes physician and nurse champions, in addition to infection preventionists, and other supporting services. The CAUTI team provides expert support to the involved units, identifies progress of the work and plans any changes based on performance. An evaluation of the time requirements for the effort is made to free up resources for implementation. The second step is identifying the units where initial implementation will occur. Implementation plans are discussed with unit managers and representatives of the different pilot units. A key component is to identify how to integrate the new effort as part of the daily activities of the bedside nurse. In our case, this means the daily evaluation of urinary catheter necessity and removal. Plans to provide education and evaluate for competencies are also made. Any feedback from the unit teams is thoroughly examined and addressed. The process (urinary catheters used based on appropriate indications) and outcome (CAUTI) measures are also explained to the teams. Audits and feedback on performance are given regularly to the units involved to help identify gaps and improve the process. The pilot work may identify important opportunities such as the need for evaluating nursing competencies for placement and maintenance of urinary catheters, the importance of integrating the assessment into the electronic medical records, the potential of collaborating with other teams (e.g., wound care and fall prevention) to reduce unnecessary urinary catheter use. The third step is to disseminate the effort hospital-wide. In the case of the urinary catheter, the emergency department, intensive care units, and operating rooms are areas where devices are frequently placed or used. Addressing these different areas will support all other units in reducing inappropriate urinary catheter use house-wide. Having the urinary catheter evaluation for need as a daily activity for every bedside nurse ensures sustainability of the process. Collaboration with the information technology team is essential to the integration of the process. This is achieved through incorporating the reasons for use by the ordering clinician, and having electronic triggers for the daily evaluation. Additional periodic monitoring, from evaluation of competencies, processes and outcomes, to feedback on performance, are essential to continued success. Finally, leadership is kept engaged through incorporating the outcome measures as a part of the institution's quality dashboard.

Measuring Quality

"Doing the Right Things Right."

In 1966, Avedis Donabedian introduced the triad of outcome, process and structure as a model for evaluating medical care.[41] This model is commonly used today in the development of healthcare metrics. Outcome, he suggests, "in terms of recovery, restoration of function and of survival, has been frequently used as an indicator of the quality of medical care." Process, denotes the "attributes or properties of the process of care as goals or objectives of that process," and structure refers to the "adequacy of facilities and equipment; the qualifications of medical staff and their organization; the administrative structure and operations of programs and institutions providing care; fiscal organization."[42] When

attempting to evaluate the quality of healthcare, each type of metric carries with it strengths and limitations that must be considered before selecting.

Measuring quality of care is a key component in improving outcomes.[43–45] Quality improvement projects and initiatives should all have a component that addresses how success or progress toward a goal will be measured. In general, measures fall into one of two categories: process and outcome measures. Each has its strengths and weaknesses that should be taken into account before deciding what data will be collected. Most important, quality measures should be practical. They should also be relevant to the issue, understandable, measurable, and achievable.[46, 47]

Process Measures

Process measures are related to activities performed by providers of care. They include the types of service delivered as well as the appropriateness and timeliness of those services.[48,49] Within the realm of healthcare-associated infections, some examples of process indicators are rates of hand hygiene compliance, timing and appropriateness of surgical antibiotic prophylaxis, appropriate indication for device use, and influenza vaccination. Process measures should be linked to the outcomes of care that are the focus of the quality improvement initiative.[50] Although it is generally believed that improvement in processes of care lead to improvements in outcomes, that is not always the case. It is best to choose processes of care that have been validated in efficacy studies to impact outcomes.[50] Even then, they may not always translate well into real-life settings, and the impact seen in a research study may not be achieved when widely implemented.

Measurable improvement in the given process should translate into clinically meaningful improvements in patient outcomes.[49,51] If a quality improvement project is centered on poor or weak measures, the opportunity costs related to taking resources away from more productive activities will be high. What also remains unknown for many process measures is how good is good enough? Is perfect compliance required or is less than perfect compliance acceptable?

Advantages of process measures include:[46,47 49,52]

- Data can be collected relatively quickly
- Generally easier to measure and interpret
- Lend themselves well to PDSA cycles, as they have smaller sample sizes and quicker feedback, lend themselves to this approach
- Directly actionable: healthcare personnel can identify a single error of commission or omission that can be improved upon, leading to more individual accountability and a sense of ownership over improvement efforts (e.g., indwelling urinary catheter drainage bag not below the bladder, indwelling urinary catheter securement device not used, nonintact central venous access catheter dressing)
- Do not require risk adjustment
- Easily understandable by stakeholders
- Promotes optimizing care to prevent rare or never events

Disadvantages of process measures include:[44,49,52]

- Ensuring the correct denominator may be labor intensive
- Practical limitation of process measurement (e.g., observing insertion of central venous or indwelling urinary catheters)
- Lack of evidence about which processes are important for specific procedures and/or outcomes
- Unmeasured risk factors that impact the outcome more strongly (e.g., host factors such as immunosuppression, obesity)
- Capture only a small portion of the overall care delivered during a hospital stay

The concept of "bundles" has been promoted by the Institute for Healthcare Improvement (IHI) to improve compliance with processes of care.[53] Bundles are a collection of processes or steps that are performed to care effectively for patients undergoing certain treatments that carry inherent risks (e.g., insertion of a central venous catheter). Bundles have been developed for the prevention of central line–associated bloodstream infections, ventilator-associated events (ventilator bundle), catheter-associated urinary tract infections, and surgical site infections. All steps in a bundle must be completed for the bundle to be effective – it is an all or none approach – thus the steps are "bundled" to maximize effectiveness.[54] This is another way to look at process measures. Instead of scoring compliance on individual measures, compliance is scored for the entire bundle (e.g., if one step is missed or performed incorrectly this would be recorded as noncompliance with the entire bundle). Bundles should not be overly complex; they should consist of only 3–5 evidence-based steps that require only yes or no answers for monitoring compliance. The central line–associated blood stream infection (CLABSI) prevention bundle consists of the five following components: hand hygiene, maximal barrier precautions for insertion, chlorhexidine skin antisepsis, optimal catheter site selection, and daily review of line necessity and removal of lines that are no longer needed.[53] It is different from a guideline that will have dozens of recommendations for preventing CLABSI. Following a bundle supports teamwork and doing all steps reliably, in the correct order and with each step adequately documented. When bundles are followed, the variability in clinical care is reduced. Bundles are widely used and have been the cornerstone of successful collaboratives to reduce healthcare-associated infection; however some feel that the evidence behind the effectiveness of bundles requires further study.[54]

Outcome Measures

Outcome indicators are the results of care provided. Traditionally, outcome measures have been related to morbidity, mortality, resource utilization (e.g., readmissions), and quality of life.[48] In the realm of healthcare-associated infections, device- and procedure-related infections are the most common outcome indicators used. Outcome measures are the endpoint that patients care the most about.[50] Outcome

measures have been heavily used for public reporting of healthcare-associated infections, as this is ultimately what patients and payers are most interested in.[46] The Centers for Medicare and Medicaid Services (CMS) has adopted the CDC's *National Healthcare Safety Network (NHSN)* surveillance definitions for evaluating six healthcare-associated infections linked to public reporting and reimbursement. Using the NHSN definitions, and adjusting these outcome measures using standardized infection ratios (SIR), helped standardize the evaluation of outcomes nationally. On the other hand, surveillance definitions have their own limitations, as they do not fully represent clinical events.

Outcome measures are not enough to improve patient care; it is still necessary to know what processes require attention to enhance the outcomes. Understanding and knowing the true connection between process and outcome measures remains a challenge in many instances. The assumption is that if the processes of care are performed correctly and consistently the effect will be noticeable in an improvement in outcomes but that may not always be the case.[52]

Advantages of outcome measures include:[47,49]

- Patient outcomes are the bottom line, of most interest to patients and payers
- Likely to get the most buy-in from clinicians and administrators
- Reflect all aspects of processes of care and not simply those that are measured or measurable
- Data may be more accessible

Disadvantages of outcome measures include:[49,52]

- The measurement may not be reflective of the true clinical outcome
- The outcome may be rare or difficult to track
- Data collection process difficult
- Larger sample size may be needed to capture the outcome measure (this is one of the most important disadvantages)
- May require risk adjustment
- What action tool to use to impact the outcome is not immediately clear, unless audits of process of care measures are undertaken in parallel
- Data abstraction can be expensive
- Factors impacting the outcome of interest may be outside the control of the provider
- Often impractical for ambulatory care settings

The collection of outcome measures has been integral to healthcare epidemiology programs for many decades. However, the collection of such data requires specialized training and is labor/resource intensive even with electronic surveillance tools. With the rise in mandates for more reporting of healthcare associated infections data publicly, some investigators have explored the use of proxy measures rather than continuing to strive for exact measures of outcomes.[55] The goal is to use limited resources more efficiently so more resources are available for prevention efforts targeted to processes of care. Proxy measures promote rapid assessment of healthcare-associated infections and may be best used intrafacility rather than for inter-facility reporting and comparisons.

Choosing Between Process and Outcome Measures

One should be flexible in the approach to measuring quality and developing strategies best suited to meet specific needs. The best measure ultimately depends on the goal of the quality improvement project or initiative.[49] There are situations where one type of measure is likely to be more useful than the other. To assist in making that determination, it is helpful to ask the following question: which factors are influenced by the provider, and if those factors are positively controlled, would they improve outcomes? If the answer is "yes," this might push one toward using process measures possibly in combination with an outcome measure. Also, in situations where how you do something is as important as what you do, process measures do not capture that distinction.[47] What this means is that in situations where technical skill is relatively unimportant (e.g., giving a vaccination), the process measure is appropriate (the outcome would be the rate of vaccine preventable infections). However if one is focused on surgeons' technical skills and how they impact outcomes, for example, then process measures will not distinguish between two surgeons in the way that outcome measures (e.g., surgical site infection rate) can.

Ultimately, the determination of whether to use process, outcome, or a combination of the two measure types needs to be balanced with available resources, time to do the project, and the frequency of the outcome. Stakeholders and those who influence care must select and support the chosen measures; otherwise, they will not believe or act on the data generated and will not support driving positive change and improving care.

Summary

Quality is an integral element of infection prevention and hospital epidemiology. Optimizing outcomes and minimizing infection risk rely on having a structure to implement best practices. High reliability organizations have achieved optimal outcomes through leadership commitment to "no harm," a well established safety culture, and continuous improvement of their processes. Recruiting champions to support the work and engaging the key stakeholders for buy-in are critical for initial successful results. However, a pivotal factor in sustaining the improvements is integration of the process into the daily routine of the healthcare personnel activities. We may evaluate quality by either measuring the processes or outcomes. Both have strengths and weaknesses. The process measures help quickly identify gaps in performance, allowing for prompt remediation and enhancements. Outcome measures are seen as the final results of the care provided, and are increasingly used to assess hospital performance and payments. It is of paramount importance to understand what outcome measures represent and how processes affect them.

References

1. Klevens RM, Edwards JR, Richards CL, Jret al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. *Public Health Rep*. 2007;**122**(2): 160–166.
2. Umscheid CA, Mitchell MD, Doshi JA, Agarwal R, Williams K, Brennan PJ. Estimating the proportion of healthcare-associated infections that are reasonably preventable and the related mortality and costs. *Infect Control Hosp Epidemiol*. 2011;**32**(2): 101–114.
3. Juran, J M, and A B. Godfrey. Juran's Quality Handbook. New York: McGraw Hill, 1998.
4. Best M, Neuhauser D. Ignaz Semmelweis and the birth of infection control. *Qual Saf Health Care*. 2004;**13**(3): 233–234.
5. Haley RW, Quade D, Freeman HE, Bennett JV. Study on the efficacy of nosocomial infection control (SENIC Project): Summary of study design. *Am J Epidemiol*. 1980;**111**(5): 472–485.
6. Beltrami EM, Williams IT, Shapiro CN, Chamberland ME. Risk and management of blood-borne infections in health care workers. *Clin Microbiol Rev*. 2000;**13**(3): 385–407.
7. To err is human: Building a safer health system. In: Linda T. Kohn, and Molla S. Donaldson; *Committee on Quality of Health Care in America, Institute of Medicine*. Washington, DC: National Academy Press; 2000.
8. Gerberding JL. Health-care quality promotion through infection prevention: Beyond 2000. *Emerg Infect Dis*. 2001;**7**(2): 363.
9. Medicare program; hospital inpatient prospective payment systems for acute care hospitals and the long-term care hospital prospective payment system and Fiscal Year 2014 rates; quality reporting requirements for specific providers; hospital conditions of participation; payment policies related to patient status. *Final rules. Fed Regist*. 2013;**78**(160): 50495–1040.
10. Porter ME. What is value in health care? *New Eng J Med*. 2010;**363**(26): 2477–2481.
11. Martin L, Neumann C, Mountford J, Bisognano M, Nolan T. Increasing efficiency and enhancing value in health care: Ways to achieve savings in operating costs per year. *Institute for Healthcare Improvement*. 2009.
12. Roberts KH, Bea R, Bartles DL. Must accidents happen? Lessons from high-reliability organizations. *The Academy of Management Executive*. 2001;**15**(3): 70–78.
13. Weick KE, Sutcliffe KM, Obstfeld D. Organizing for high reliability: Processes of collective mindfulness. *Crisis Management*. 2008;**3**: 81–123.
14. Weick KE, Sutcliffe KM. *Managing the Unexpected: Resilient Performance in an Age of Uncertainty*: Hoboken, NJ: John Wiley & Sons; 2011.
15. Chassin MR, Loeb JM. High-reliability health care: Getting there from here. *Milbank Q*. 2013;**91**(3): 459–490.
16. Resar RK. Making noncatastrophic health care processes reliable: Learning to walk before running in creating high-reliability organizations. *Health Serv Res*. 2006;**41**(4p2): 1677–1689.
17. Pryor D, Hendrich A, Henkel RJ, Beckmann JK, Tersigni AR. The quality "journey" at Ascension Health: How we've prevented at least 1,500 avoidable deaths a year–and aim to do even better. *Health Aff (Millwood)*. 2011;**30** (4): 604–611.
18. Flin R, Yule S. Leadership for safety: Industrial experience. *Qual Saf Health Care*. 2004;**13**(Suppl 2): ii45–ii51.
19. Saint S, Kowalski CP, Banaszak-Holl J, Forman J, Damschroder L, Krein SL. The importance of leadership in preventing healthcare-associated infection: Results of a multisite qualitative study. *Infect Control Hosp Epidemiol*. 2010;**31**(09): 901–907.
20. Singer SJ, Falwell A, Gaba DM, et al. Identifying organizational cultures that promote patient safety. *Health Care Manage Rev*. 2009;**34**(4): 300–311.
21. Cooper MD. Towards a model of safety culture. *Saf Sci*. 2000;**36**(2): 111–136.
22. Krein SL, Damschroder LJ, Kowalski CP, Forman J, Hofer TP, Saint S. The influence of organizational context on quality improvement and patient safety efforts in infection prevention: A multi-center qualitative study. *Soc Sci Med*. 2010;**71**(9): 1692–1701.
23. Singer SJ, Gaba DM, Geppert JJ, Sinaiko AD, Howard SK, Park KC. The culture of safety: Results of an organization-wide survey in 15 California hospitals. *Qual Saf Health Care*. 2003;**12**(2): 112–118.
24. Frankel AS, Leonard MW, Denham CR. Fair and just culture, team behavior, and leadership engagement: The tools to achieve high reliability. *Health Serv Res*. 2006;**41**(4 Pt 2): 1690–1709.
25. Walton M. Creating a "no blame" culture: Have we got the balance right? *Qual Saf Health Care*. 2004;**13**(3): 163–164.
26. Pronovost P, Weast B, Rosenstein B, et al. Implementing and validating a comprehensive unit-based safety program. *J Patient Saf*. 2005;**1**(1): 33–40.
27. Berenholtz SM, Lubomski LH, Weeks K, et al. Eliminating central line-associated bloodstream infections: A national patient safety imperative. *Infect Control Hosp Epidemiol*. 2014;**35** (1): 56–62.
28. Fakih MG, George CM, Edson BS, Goeschel CA, Saint S. Implementing a national program to reduce catheter-associated urinary tract infection: A quality improvement collaboration of state hospital associations, academic medical centers, professional societies, and governmental agencies. *Infect Control Hosp Epidemiol*. 2013;**34**(10): 1048–1054.
29. Reason J. Human error: Models and management. *BMJ*. 2000;**320**(7237): 768–770.
30. Leape LL. Error in medicine. *JAMA*. 1994;**272**(23): 1851–1857.
31. Taylor MJ, McNicholas C, Nicolay C, Darzi A, Bell D, Reed JE. Systematic review of the application of the plan–do–study–act method to improve quality in healthcare. *BMJ Qual Saf*. 2013.
32. D'Andreamatteo A, Ianni L, Lega F, Sargiacomo M. Lean in healthcare: A comprehensive review. *Health Policy* 2015;**119**(9): 1197–1209.
33. Vest JR, Gamm LD. A critical review of the research literature on Six Sigma, Lean and StuderGroup's Hardwiring Excellence in the United States: The need to demonstrate and communicate the effectiveness of transformation strategies in healthcare. *Implement Sci*. 2009;**4**: 35.
34. Durlak JA, DuPre EP. Implementation matters: A review of research on the influence of implementation on program outcomes and the factors affecting implementation. *Am J Community Psychol*. 2008;**41**(3–4): 327–350.
35. Fakih MG, Krein SL, Edson B, Watson SR, Battles JB, Saint S. Engaging health care workers to prevent catheter-associated urinary

tract infection and avert patient harm. *Am J Infect Control*. 2014;**42**(10):S223–S229.

36. Damschroder LJ, Banaszak-Holl J, Kowalski CP, Forman J, Saint S, Krein SL. The role of the champion in infection prevention: Results from a multisite qualitative study. *Qual Saf Health Care*. 2009;**18**(6): 434–440.
37. Shediac-Rizkallah MC, Bone LR. Planning for the sustainability of community-based health programs: Conceptual frameworks and future directions for research, practice and policy. *Health Educ Res*. 1998;**13**(1): 87–108.
38. Wiltsey Stirman S, Kimberly J, Cook N, Calloway A, Castro F, Charns M. The sustainability of new programs and innovations: A review of the empirical literature and recommendations for future research. *Implement Sci*. 2012;**7**: 17.
39. Gruen RL, Elliott JH, Nolan ML, et al. Sustainability science: An integrated approach for health-programme planning. *Lancet*. 2008;**372**(9649): 1579–1589.
40. Hendy J, Barlow J. The role of the organizational champion in achieving health system change. *Soc Sci Med*. 2012;**74**(3): 348–355.
41. Donabedian A. Evaluating the quality of medical care. *Milbank Mem Fund Q*. 1966: 166–206.
42. Donabedian A. Evaluating the quality of medical care. *Milbank Q*. 2005;**83**(4): 691–729.
43. Birkmeyer J, Kerr E, Dimick J. Performance Measurement: Accelerating Improvement. *Committee on Redesigning Health Insurance Performance Measures, Payment, and Performance Improvement Programs*. Washington, DC: The National Academies Press; 2006.
44. Werner RM, Bradlow ET. Relationship between Medicare's hospital compare performance measures and mortality rates. *JAMA*. 2006;**296**(22): 2694–2702.
45. Brook RH, McGlynn EA, Shekelle PG. Defining and measuring quality of care: A perspective from US researchers. *Int J Qual Health Care*. 2000;**12**(4): 281–295.
46. Egidio G, Kyeremanteng K. Why process quality measures may be more valuable than outcome measures in critical care patients. *Biol Med (Aligarh)*. 2015;**7**(132): 2.
47. Mant J. Process versus outcome indicators in the assessment of quality of health care. *Int J Qual Health Care*. 2001;**13**(6): 475–480.
48. White HL, Glazier RH. Do hospitalist physicians improve the quality of inpatient care delivery? A systematic review of process, efficiency and outcome measures. *BMC Med*. 2011;**9**(1): 58.
49. Birkmeyer JD, Dimick JB, Birkmeyer NJ. Measuring the quality of surgical care: Structure, process, or outcomes? *J Am Coll Surg*. 2004;**198**(4): 626–632.
50. Werner RM, Konetzka RT, Kim MM. Quality improvement under nursing home compare: The association between changes in process and outcome measures. *Med Care*. 2013;**51**(7): 582.
51. Ryan AM, Doran T. The effect of improving processes of care on patient outcomes: Evidence from the United Kingdom's quality and outcomes framework. *Med Care*. 2012;**50**(3): 191–199.
52. Gross PA. Editorial process versus outcome measures: The end of the debate. *Med Care*. 2012;**50**(3): 200–202.
53. Institute for Healthcare Improvement (IHI). What is a bundle? www.ihi.org/resources/Pages/ImprovementStories/WhatIsaBundle.aspx. Accessed September 14, 2015.
54. Cooke FJ, Holmes AH. The missing care bundle: Antibiotic prescribing in hospitals. *Int J Antimicrob Agents*. 2007;**30**(1): 25–29.
55. Huang SS. Health care–associated infection: Assessing the value and validity of our measures. *Clin Infect Dis*. 2009;**48**(8): 1116–1122.

Chapter 6

Epidemiologic Methods in Infection Control

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A strong working knowledge of basic epidemiologic principles and approaches is critical for the healthcare epidemiologist. The ability to accurately quantify new patterns of infectious diseases, design rigorous studies to characterize the factors associated with disease, and devise and evaluate interventions to address emerging issues are vital to effective job performance.

Epidemiology is commonly defined as the study of the distribution and determinants of disease frequency in human populations. This definition concisely encompasses the three main components of the discipline of epidemiology. The first, "disease frequency," involves identifying the existence of a disease and quantifying its occurrence. The second, "distribution of disease," characterizes in whom the disease is occurring, where it is occurring, and when it is occurring. Finally, "determinants of disease" focuses on formulating and testing hypotheses with regard to what might be causing the disease.

The value of epidemiological methods in the study of healthcare infections has been recognized for some time.[1–4] Indeed, the past decade has seen a renewed interest and vitality in efforts to explore previously unstudied aspects of epidemiological methods in the study of healthcare infections and antimicrobial resistance.[5–9] While this chapter is meant to provide a broad overview, the reader is also directed to numerous published textbooks that are dedicated to general epidemiology, infectious diseases epidemiology, and statistical analysis.[10–16]

Measures of Disease Frequency

Before setting out to identify the possible causes of a disease, one must first quantify the frequency with which the disease occurs. This is important both for measuring the scope of the problem (i.e., how many people are affected by the disease) and for subsequently allowing comparison between different groups (i.e., people with and people without a particular risk factor of interest). Prevalence and incidence are the most commonly used measures of disease frequency in epidemiology.

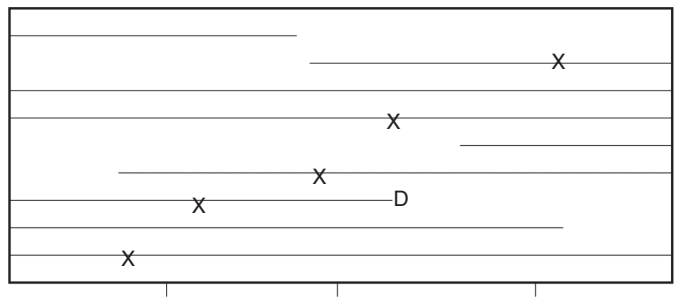
Prevalence

Prevalence is defined as the proportion of people with disease at a given point in time (e.g., the proportion of hospitalized patients who have a nosocomial infection). This is also sometimes referred to as the "point prevalence." It is calculated as the number of individuals with disease divided by the total number of individuals in the population observed.

$$\text{Prevalence} = \frac{\text{number of diseased individuals}}{\text{total number of individuals in the population}}$$

(A related, although infrequently used, measure is the "period prevalence," which is defined as the number of persons with disease in a given *period* of time divided by the number of persons observed during the period.) Prevalence is a proportion and as such has no units. This measure of disease frequency is dependent on both the incidence (i.e., the number of new cases which develop) as well as the duration of disease (i.e., how long a disease lasts once it has developed). The greater the incidence and the greater the duration of disease, the higher the prevalence. Prevalence is useful for measuring the burden of disease in a population (i.e., the overall proportion of persons affected by the disease), which may in turn inform decisions regarding such issues as allocation of resources and funding of research initiatives.

All populations are dynamic; individuals are constantly entering and leaving the population. Depending on the population, the prevalence may vary depending on when it is measured (Figure 6.1). If a dynamic population is at steady state (i.e., the number of individuals leaving is equal to the number of individuals entering the population), the prevalence will be constant over time.



Time point	Prevalence
0.5 years	0/6 cases
1.0 years	1/7 cases
2.5 years	3/6 cases
4.0 years	4/6 cases

Figure 6.1 Measurement of prevalence in a dynamic population

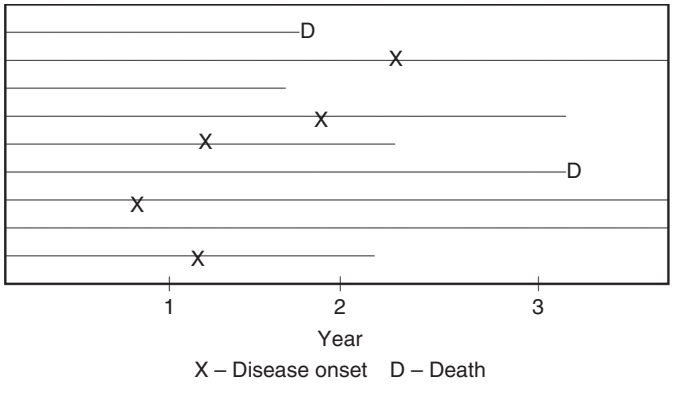
Incidence

Incidence is defined as the number of new cases of diseases occurring in a specified period of time. Incidence may be described in several ways. Cumulative incidence is defined as the number of new cases of disease in a particular time period divided by the total number of disease-free individuals at risk of the disease at the beginning of the time period (e.g., the proportion of patients who develop a nosocomial infection during hospitalization). In infectious disease epidemiology, this traditionally has been termed the "attack rate."

$$\text{Cumulative incidence} = \frac{\text{number of new cases of disease between } t_0 \text{ and } t_1}{\text{total number of disease free individuals at risk of disease } t_0}$$

A cumulative incidence, like a prevalence, is simply a proportion and thus has no units. In order to calculate the cumulative incidence, one must have complete follow-up data on all observed individuals, such that their final disposition with regard to having or not having the disease may be determined. Although this measure describes the total proportion of new cases occurring in a time period, it does not describe when in the time period the cases occurred (Figure 6.2).

For the cumulative incidence of nosocomial infections, the time period implied is the course of hospitalization until an infection event or until discharge without a first infection event. However, patients do not all stay in the hospital and remain at risk for exactly the same period of time. Furthermore, most nosocomial infections are time-related, and comparing the cumulative incidence of nosocomial infection among patient groups with differing lengths of stay may be very misleading. By contrast, if one is investigating infection events that have a point source and are not time-related (e.g., tuberculosis acquired from a contaminated bronchoscope), then the cumulative incidence is an excellent measure of incidence. Surgical site infections are also usually thought of as having a point source (i.e., the operation).



Time point	Cumulative incidence
0.5 years	0/9 cases
1.0 years	1/9 cases
1.5 years	3/9 cases
2.0 years	?

Figure 6.2 Measurement of cumulative incidence

Historically, nosocomial infection rates were often reported as a cumulative incidence (e.g., the number of infections per 100 discharges). This definition had no unique quantitative meaning, as it did not separate first infections from multiple infections in the same patient, and allowed undefi multiple counting of individuals. The implications of a finding of 5 infections per 100 discharges would be entirely different if it represented 5 sequential infections in a single moribund patient or 5 infections in 5 different but otherwise healthy patients, such as women with normal deliveries.

The incidence rate (or incidence density) is defined as the number of new cases of disease in a specified quantity of person-time of observation among individuals at risk (e.g., the number of nosocomial infections per 1,000 hospital-days).

$$\text{Incidence rate} = {}^{1}\Big/_{4}\,\frac{\text{number of new cases of disease during a given time period}}{\text{total person} - \text{time of observation among individuals at risk}}$$

The primary value of this measure can be seen when comparing nosocomial infection rates between groups that differ in their time at risk (e.g., short-stay patients versus long-stay patients). When the time at risk in one group is much greater than the time at risk in another, the incidence rate, or risk per day, is the most convenient way to correct for time, and thus separate the effect of time (i.e., duration of exposure) from the effect of daily risk. For convenience, in hospital epidemiology, incidence rates for nosocomial infections are usually expressed as the number of first infection events in a certain number of days at risk (e.g., the number of nosocomial infections per 1,000 hospital-days), because this usually produces a small single-digit or double-digit number that is practical for comparison across centers.

An incidence rate is usually restricted to counting first infection events (e.g., the first episode of nosocomial infection in a given patient). It is standard to consider only first events because second events are not statistically independent from first events in the same individuals (i.e., patients with a first infection event are more likely to experience a second event). For example, the group of all hospitalized patients who have not yet developed a nosocomial infection would compose the population at risk. After a patient develops an infection, that patient would then be withdrawn from the analysis and would not be a part of the population still at risk for a first event. Each hospitalized patient who never develops an infection would contribute all her hospital-days (i.e., the sum of days the patient is in the hospital) to the total count of days at risk for a first event. However, a patient who develops an infection would contribute only her hospital-days before the onset of the infection.

Unlike cumulative incidence, the incidence rate does not assume complete follow-up for all subjects and thus accounts for different entry and dropout rates. However, even if follow-up data are complete (and thus the cumulative incidence could be calculated), reporting the incidence rate may still be preferable. The cumulative incidence reports only the overall number of new cases occurring during the time period, regardless of whether they occur early or late in the time period.

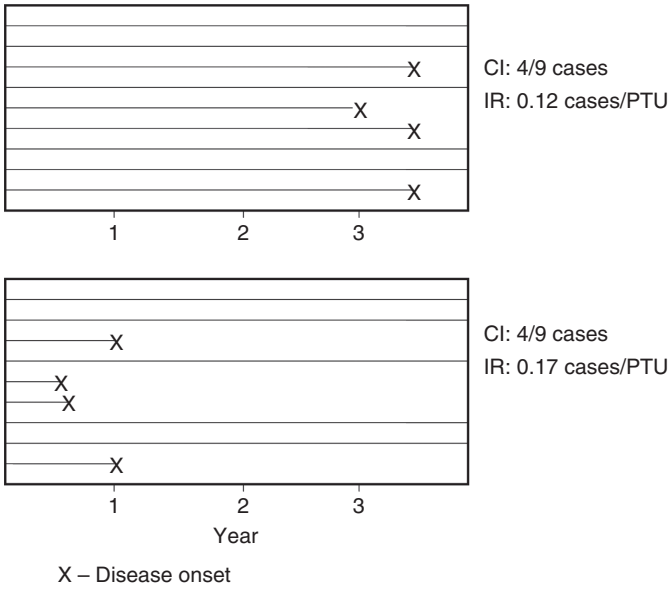


Figure 6.3 Comparison of the cumulative incidence (CI) and the incidence rate (IR); PTU, person-time unit

By comparison, the incidence rate, by incorporating the time at risk, accounts for a potential difference in the time to occurrence of the infection event. In considering the two examples in Figure 6.3, one will note that despite the fact that the cumulative incidence of disease at four years is the same for the two groups, subjects in the second group clearly acquire disease earlier. This information is reflected in the different incidence rates.

Since the incidence rate counts time at risk in the denominator, the implicit assumption is that all time at risk is equal (e.g., the likelihood of developing a nosocomial infection in the first 5 days after hospital admission is the same as the likelihood of developing an infection during days 6–10 of hospitalization). If all time periods are not equivalent, the incidence rate may be misleading, depending on when in the course of their time at risk patients are observed for the outcome.

Study Design

One of the critical components of the field of epidemiology is identifying the determinants of disease (i.e., risk factors for a particular outcome of interest). This aspect of the field focuses on formulating and testing hypotheses with regard to the possible risk factors for disease. A number of study designs are available to the hospital epidemiologist when attempting to test a hypothesis to determine the causes of a disease. These study designs, in order of increasing methodological rigor, include the following types: case report, case series, ecologic study, cross-sectional study, case-control study, cohort study, and randomized controlled trial. Randomized controlled trials, case-control studies, and cohort studies are considered analytic studies, as opposed to the other study designs, which are considered descriptive studies. Analytic studies are most useful in identifying the determinants of disease. In determining the correct study design to use, the hospital epidemiologist must first carefully consider "What is the question?" Once this critical question has been clearly formulated, the optimal study design will likely also become evident. Other considerations (e.g., available time, data sources, access to financial support, and/or ethical considerations) may also influence the decision as to the type of study that should be undertaken.

Case Report or Case Series

A case report is the clinical description of a single patient (e.g., a single patient with a case of bloodstream infection due to vancomycin-resistant enterococcus [VRE]). A case series is simply a report of more than one patient with the disease of interest (e.g., several patients with VRE bloodstream infections in a single center over time). One advantage of a case report or case series is its relative ease of preparation. In addition, a case report or case series may serve as a clinical or therapeutic example for other healthcare epidemiologists who may be faced with similar cases. Perhaps most important, a case report or case series can serve to generate hypotheses that may then be tested in future analytic studies. For example, if a case report notes that a patient had been exposed to several courses of vancomycin therapy in the month prior to the onset of VRE infection, one hypothesis might be that vancomycin use is associated with VRE infection. The primary limitation of a case report or case series is that it describes relatively few patients and may not be generalizable. In addition, since a case report or case series does not include a comparison group, one cannot determine which characteristics in the description of the cases are unique to the illness. While case reports are thus usually of limited interest, there are exceptions, particularly when they identify a new disease or describe the index case of an important outbreak (e.g., the first report of clinical VRE infection).

Ecologic Study

In an ecologic study, one compares geographic and/or time trends of an illness with trends in risk factors (i.e., a comparison of the annual amount of vancomycin used hospital-wide with the annual prevalence of VRE among enterococcal isolates from cases of nosocomial infection). Ecologic studies most often use aggregate data that are routinely collected for other purposes (e.g., antimicrobial susceptibility patterns from a hospital's clinical microbiology laboratory, or antimicrobial drug-dispensing data from the inpatient pharmacy). This ready availability of data provides one advantage to the ecologic study, in that such studies are often relatively quick and easy to do. Thus, such a study may provide early support for or against a hypothesis. However, one cannot distinguish between various hypotheses that might be consistent with the data. Perhaps most important, ecologic studies do not incorporate patient-level data. For example, although both the annual hospital-wide use of vancomycin and the yearly prevalence of VRE among enterococcal isolates from cases of nosocomial infection might have increased significantly over a five-year period, one cannot tell from these data whether the actual patients who were infected with VRE received vancomycin.

Cross-Sectional Study

A cross-sectional study is a survey of a sample of the population in which the status of subjects with regard to the risk factor and disease is assessed at the same point in time. For example, a cross-sectional study to assess VRE infection might involve identifying all patients currently hospitalized and assessing each patient with regard to whether he or she has a VRE infection, as well as whether he or she is receiving vancomycin. One advantage of a cross-sectional study is it is relatively easy to carry out, given that all subjects are simply assessed at one point in time. Accordingly, this type of study may provide early evidence for or against a hypothesis. A major disadvantage of a cross-sectional study is that this study design does not capture information about temporal sequence (i.e., it is not possible to determine which came first, the proposed risk factor or the outcome). Furthermore, a cross-sectional study does not provide information about the transition between health states (e.g., development of new VRE infection or resolution of VRE infection).

Case-Control Study

In distinguishing between the various types of analytic studies (i.e., case-control, cohort, and experimental) it is useful to consider the traditional 2 × 2 table (Figure 6.4). While all 3 study designs seek to investigate the potential association between a risk factor (or exposure) and an outcome of interest, they differ fundamentally in the way that patients are chosen. In a case-control study, patients are entered into the study based on the presence or absence of the outcome (or disease) of interest. The 2 groups (i.e., the case patients with the disease and the control patients without the disease) are then compared to determine if they differ with regard to the presence of risk factors of interest. Case-control studies are retrospective.

A case-control study design is particularly attractive when the outcome being studied is rare, because one may enroll into the study all patients with the outcome of interest. Accordingly, this study design is much more efficient and economical than the comparable cohort study, in which a group of patients with and without an exposure of interest would need to undergo follow-up for a period of time to determine who develops the outcome of interest. Even if a large cohort is available, it may be more economical to conduct a small case-control study within the cohort. Such a "nested" case-control study may produce the same information as would the larger cohort study, at a fraction of the cost (if cost is high for data acquisition). Another advantage of the case-control study is that one may study any number of risk factors (exposures) for the outcome of interest. One disadvantage of a case-control study is that only one outcome may be studied. Another disadvantage of this approach is that one cannot directly calculate the incidence or relative risk from a case-control study, because the investigator fixes the number of case and control patients to be studied.

Thoughtful consideration must be taken when selecting case and control patients in a case-control study. Cases may be restricted to any group of diseased individuals. However, they must derive from a theoretical source population such that a diseased person not selected is presumed to have derived from a different source population. For example, in studying risk factors for nosocomial VRE infection, the theoretical source population could be considered to be the population of patients hospitalized at one institution. Thus, if any patient at that institution were to have a clinical isolate that represented VRE infection, they would be included as a case. However, a patient with VRE infection at a different hospital would not be included. Finally, cases must be chosen in a manner independent of the patient's status with regard to an exposure of interest.

The proper selection control patients for a case-control study is paramount. Controls should be representative of the theoretical source population from which the cases were derived. Thus, if a control patient were to have developed the disease of interest, they would have been selected as a case. In the example above, control patients may be randomly selected from among all patients in the hospital not infected with VRE. In investigating the possible association between prior vancomycin use and VRE infection, these 2 groups (i.e., patients with VRE infection and a random sample of all other hospitalized patients) could be compared to determine what proportion of patients in each group had experienced recent vancomycin exposure. Finally, like cases, controls must be chosen in a manner independent of the patient's status with regard to an exposure of interest and should not be selected because they have characteristics similar to those of case patients.

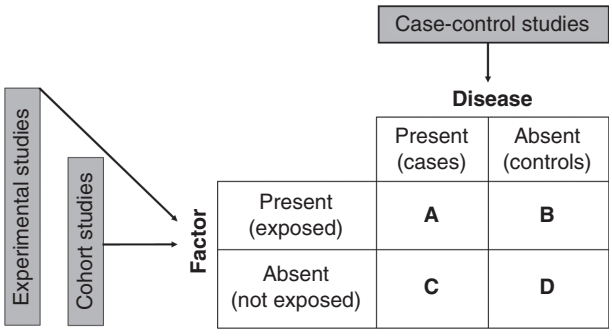


Figure 6.4 Summary of study designs used in infection control and epidemiological studies

Cohort Study

Unlike a case-control study, in which study subjects are selected based on the presence or absence of an outcome or disease of interest, a cohort study selects subjects on the basis of the presence or absence of an exposure (or risk factor) of interest (Figure 6.4). The 2 groups (i.e., the subjects with the exposure and the subjects without the exposure) are then compared to determine if they differ with regard to whether they develop the outcome of interest. The investigator may select subjects randomly or according to exposure.

A cohort study may be either prospective or retrospective. Whether a cohort study is prospective or retrospective depends on when it is conducted with regard to when the outcome of interest occurs. If patients are identified as exposed or unexposed and then follow-up is conducted forward in time to

determine whether the patients develop the disease, it is a prospective cohort study. If the study is conducted after the time the outcome has already occurred, it is a retrospective cohort study. In either case, subjects are entered into the study on the basis of their exposure status, and these groups are then compared on the basis of the outcome of interest. For example, one might identify all patients who receive vancomycin in a hospital (i.e., the exposed group) and compare them to a randomly selected group of patients who do not receive vancomycin (i.e., the unexposed group). These groups could then be followed-up forward in time to determine what proportion of patients in each group develops the outcome of interest (e.g., VRE infection).

One advantage of a cohort study is that one may study multiple outcomes of a single risk factor or exposure. In addition, a cohort study allows the investigator to calculate both an incidence and a relative risk in comparing the 2 groups. Potential disadvantages of a cohort study include heavy cost and time requirements, because patients must be followed-up forward in time until a sufficient number develop the outcome of interest. Depending on the course of the disease, this may be a lengthy period. In addition, if the outcome is rare, a great many subjects will need to be followed-up until the necessary number develop the disease. Finally, the longer the study duration, the more likely that subjects will be lost to follow-up, potentially biasing the results of the study. Some of these limitations are lessened in a retrospective cohort study, since outcomes have already occurred and patients do not need to be followed-up prospectively.

Randomized Controlled Trial

In clinical investigation, the gold standard for establishing an association between an exposure and an outcome is the randomized controlled trial. In comparing the randomized controlled trial to other analytic study designs (Figure 6.4), it is very similar to the cohort study. However, in a cohort study, when patients are enrolled, they already either have or do not have the exposure of interest. In a randomized controlled trial, the investigator assigns the exposure according to some scheme, such as randomization. This study design provides the most convincing demonstration of causality, because patients in both groups should (provided randomization has worked appropriately) be equal with respect to all important variables except the one variable (exposure) manipulated by the investigator. While randomized controlled trials may provide the strongest support for or against an association of interest, they are costly studies, and there may be ethical issues which preclude conducting one. For example, in elucidating the association between vancomycin use and VRE infection, it would be unethical to randomly assign patients to receive vancomycin if they did not require the drug.

Bias and Confounding

Two common issues which arise when designing a study are the potentials for bias and confounding. Bias is the systematic error in the collection or interpretation of data. Types of bias include information bias (i.e., distortion in the estimate of effect because of measurement error or misclassification of subjects with respect to one or more variables) and selection bias (i.e., distortion in the estimate of effect resulting from the manner in which subjects are selected for the study). The potential for bias must be addressed at the time the study is designed, since it cannot be corrected during the analysis of the study. In randomized controlled trials, blinding is a commonly used method to minimize the potential for bias in such studies. In addition to evaluating whether bias may exist, one much also consider the likely impact of the bias on the study results. Bias may be nondifferential (i.e., biasing toward the null hypothesis and making the 2 groups being compared look artificially similar), or differential (i.e., biasing away from the null hypothesis and making the 2 groups being compared look artificially dissimilar).

Confounding occurs when the estimate of the effect of the exposure is distorted because it is mixed with the effect of an extraneous factor. To be a confounder, a variable must be associated with both the exposure and the outcome of interest, but it cannot be a result of the exposure. Unlike bias, a confounding variable may be controlled for in the study analysis. However, to do this, (1) the confounder must be recognized, and (2) data regarding the presence or absence of the confounder must be collected during the study. Thus, it is also important to consider the potential for confounding variables in the design of the study.

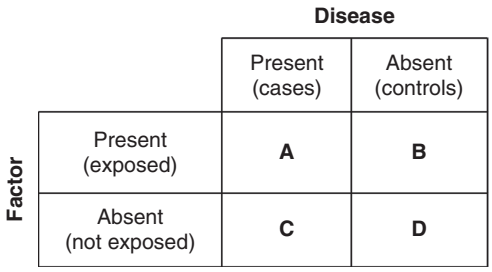
Measures of Effect

Risk Versus Odds

Depending on which type of study one conducts, one will generally calculate either a relative risk (i.e., in a cohort study or a randomized controlled trial) or an odds ratio (i.e., in a case-control study) to characterize the strength of an association between an exposure and an outcome. Before describing these statistical measures in greater detail, it is useful to briefly compare the concepts of risk and odds. For a risk (also referred to as a probability), the numerator contains the event of interest, while the denominator contains all possible events. For example, in throwing a die, the *risk* of throwing a 3 is 1 divided by 6 (since there are 6 possible events when throwing a die). Thus, the risk of throwing a 3 is 0.167, or 16.7 percent. In an odds, the numerator again contains the event of interest, while the denominator contains all possible events minus the event of interest. Using again the example of throwing a die, the *odds* of throwing a 3 is 1 divided by 5 (i.e., 6 minus 1). Thus, the odds of throwing a 3 is 0.2, or 20 percent. Since the denominator for an odds is always smaller, the value for the odds is always somewhat greater than the comparable risk, though this diminishes with small proportions.

Relative Risk

The relative risk (also called the risk ratio) is the ratio of 2 probabilities: the probability of the outcome among the exposed subjects divided by the probability of the outcome in



Relative risk

Risk of disease among exposed persons = A/(A + B)
Risk of disease among unexposed persons = C/(C + D)

$$\text{Relative risk} = \frac{A/(A+B)}{C/(C+D)}$$

Odds ratio

Odds of exposure, given disease = A/C
Odds of exposure, given no disease = B/D

$$\text{Disease odds ratio} = \frac{A/C}{B/D} = \frac{AD}{BC}$$

Relationship between relative risk and odds ratio

When disease is rare, B >> A and D >>> C

$$\text{Relative risk} = \frac{A/(A+B)}{C/(C+D)} \sim \frac{AD}{BC} = \text{odds ratio}$$

Figure 6.5 Comparison of relative risk and the odds ratio, showing how the case-control formula approaches the formula for relative risk when the rare outcome criterion is met

the unexposed subjects (Figure 6.5). A relative risk can be calculated from a cohort study or a randomized controlled trial, because one can derive population-based rates or proportions from these study designs. A relative risk of 1.0 is called the value of no effect or the null value. A relative risk equal to 2.0 means the exposed subjects were twice as likely to have the outcome of interest as were the unexposed subjects. On the other hand, a relative risk of 0.5 means that the exposed subjects were half as likely to experience the outcome as the unexposed subjects, indicating that the exposure had a protective effect (if the outcome is perceived to be negative).

Odds Ratio

As noted previously, in a case-control study, subjects are enrolled into the study on the basis of the outcome of interest. One then compares the 2 groups (i.e., the subjects with the outcome and the subjects without the outcome) to determine what proportion of subjects in each group have a risk factor of interest. In this type of study, without additional information, one cannot determine how common the outcomes or the exposures are in the entire study population. Thus, unlike in a cohort study, one cannot directly calculate a relative risk. What one can calculate in a case-control study is the odds ratio. The odds ratio is defined as the odds of exposure in subjects with the outcome divided by the odds of exposure in subjects without the outcome (Figure 6.5). An odds ratio of 1.0 is called the value of no effect or the null value.

As noted above, one cannot calculate a relative risk from a case-control study because the case-control study offers no insights into the absolute rates or proportions of disease among subjects. However, in situations in which the disease under study is rare (i.e., a prevalence of less than 10 percent in the study population), the odds ratio derived from a case-control study closely approximates the relative risk that would have been derived from the comparable cohort study. Figures 6.4–6.5 show how the case-control formula approaches the formula for relative risk when outcomes are rare.

Measures of Strength of Association

P Value

The most common method of measuring the strength of association in a 2 × 2 table is to use the chi-squared (χ^2) test for the comparison of 2 binomial proportions. This calculation is identical for all 2 × 2 tables, whether or not the data were derived from a cohort study or case-control study. When one has calculated the value for the χ^2test, one can identify the associated probability that the observed difference between binomial proportions could have arisen by chance alone. The conventional interpretation of these probabilities is that a *P* value of less than.05 indicates that an effect at least as extreme as that observed in the study is unlikely to have occurred by chance alone. Although this is the conventional interpretation, there is nothing magical about the.05 cutoff for statistical significance. One limitation of the *P* value is that it reflects both the magnitude of the difference between the groups being compared as well as the sample size. Consequently, with a large sample size, even a small difference between groups (if the sample size is large enough) may be statistically significant, even if it is not clinically important. Conversely, a larger effect that would be clinically important may not achieve statistical significance if the sample size is insufficient. Thus, reporting both the magnitude of the effect and the confidence interval is important.

95 percent Confidence Interval

With the limitations of the *P* value, it is generally preferable to report the 95 percent confidence interval (95 percent CI) for a given point estimate. The 95 percent CI provides a range within which the true magnitude of the effect (i.e., either the relative risk or the odds ratio) lies with a certain degree of assurance. Observing whether the 95 percent CI crosses 1.0 (i.e., the value of null effect), provides the same information as the *P* value. If the 95 percent CI crosses 1.0, the *P* value will almost never be less than.05. In addition, the effect of the sample size can be ascertained from the width of the confidence interval. The narrower the confidence interval, the less variability was present in the estimate of the effect, reflecting a larger sample size. The wider the confidence interval, the greater the variability in the estimate of the effect and the smaller the sample size. When interpreting results that are not significant, the width of the confidence interval may be very helpful. A narrow confidence interval implies that there is most likely no real effect or exposure, whereas a wide interval suggests that the data

are also potentially compatible with a true effect and that the sample size was simply not adequate.

Special Issues in Healthcare Epidemiology Methods

Quasi-Experimental Study Design

In addition to the study designs reviewed previously, the quasi-experimental study is a design frequently employed in healthcare epidemiology investigations.[17] This design is also frequently referred to as a "before-after" or "pre-post intervention" study.[18,19] The goal of a quasi-experimental study is to evaluate an intervention without using randomization. The most basic type of quasi-experimental study involves the collection of baseline data, the implementation of an intervention, and the collection of the same data after the intervention. For example, the baseline prevalence of VRE infection in a hospital would be calculated, an intervention to limit use of vancomycin would then be instituted, and, after some prespecified time period, the prevalence of VRE infection would again measured. Numerous variations of quasi-experimental studies exist and can include the following features: (1) use of multiple pretests (i.e., collection of baseline data on more than one occasion), (2) use of repeated interventions (i.e., instituting and removing the intervention multiple times in sequence), and (3) inclusion of a control group (i.e., a group from whom baseline data and subsequent data are collected but for whom no intervention is implemented).

While often employed in evaluations of interventions in hospital infections, a thorough understanding of the advantages and disadvantages of quasi-experimental studies is critical. Greater attention has recently been focused on increasing the quality of the design and performance of quasi-experimental studies to enhance the validity of the conclusions drawn regarding the effectiveness of interventions in the areas of infection control and antibiotic resistance.[17,20,21]

The quasi-experimental study design offers several advantages. Few study designs are available when one wishes to study the impact of an intervention. In general, a well-designed and adequately powered randomized controlled trial provides the strongest evidence for or against the efficacy of an intervention. However, there are several reasons why a randomized controlled trial may not be feasible in the study of infection control interventions. Randomizing individual patients to receive an infection control intervention is often not a reasonable approach, given the structure of healthcare delivery (e.g., doctors and nurses taking care of multiple patients at a time). One might consider randomizing specific units or floors within one institution to receive the intervention. However, these units are not self-contained, and patients and healthcare workers frequently move from unit to unit. Thus, any reduction noted in the number of transmissions or acquisitions of new drug-resistant infections in the intervention units is likely to also result in some reduction in the number of drug-resistant infections in nonintervention areas (i.e., because of contamination). This would bias the results toward the null hypothesis (i.e., the intervention had no effect). In such a situation, a well-designed quasi-experimental study offers a compelling alternative approach. In addition, this study design is frequently used when it is not ethical to conduct a randomized controlled trial. Finally, when an intervention must be instituted rapidly in response to an emerging issue (e.g., an outbreak), the first priority is to address and resolve the issue. In this case, it would be infeasible and unethical to randomize patient groups to receive an intervention.

Potential limitations of quasi-experimental studies include regression to the mean, uncontrolled confounding, and maturation effects. Implementation of an intervention is often triggered in response to a rise in the rate of the outcome of interest above the norm.[20] The principle of regression to the mean predicts that such an elevated rate will tend to decline, even without intervention. This may serve to bias the results of a quasi-experimental study, as it may be falsely concluded that an effect is due to the intervention.[18,19] Several approaches may be employed to address this potential limitation. First, incorporating a prolonged baseline period prior to implementation of an intervention permits an evaluation of the natural fluctuation in the rate of the outcome of interest over time and a more comprehensive assessment of possible regression to the mean. Second, changes in the rate of the outcome of interest may be measured at a control site (e.g., another institution that has not implemented the intervention) during the same time period. Finally, the use of segmented regression analysis may assist in addressing possible regression to the mean, in that it will assess both the immediate change in prevalence coincident with the intervention and also the change in slope over time.[22–25]

Another potential limitation in quasi-experimental studies is uncontrolled confounding, which is most likely to occur when variables other than the intervention change over time or differ between the preintervention and postintervention periods.[18,19] This limitation can be addressed by measuring known confounders (e.g., hospital census or number of admissions) and controlling for them in analyses. However, not all confounders are known or easily measured (e.g., the quality of medical and nursing care). To address this, one may assess a nonequivalent dependent variable to evaluate the possibility that factors other than the intervention influenced the outcome.[17,20] A nonequivalent dependent variable should have similar potential causal and confounding variables as the primary dependent variable, except for the effect of the intervention. For example, in assessing the impact of an intervention to limit fluoroquinolone use on the prevalence of fluoroquinolone-resistant *Escherichia coli* infection, one might consider the incidence of catheter-associated bloodstream infection as a nonequivalent dependent variable. Although the prevalence of fluoroquinolone-resistant *Escherichia coli* infection and the incidence of catheter-associated bloodstream infection might both be affected by such factors as the patient census, it is unlikely that fluoroquinolone use specifically would affect the incidence

of catheter-associated bloodstream infection. Nonequivalent dependent variables are often difficult to identity and measure, but are quite useful when they can be incorporated into the quasi-experimental study.

The quasi-experimental study design has been used widely for evaluating infection control initiatives targeting hand hygiene,[2] central-line associated bloodstream infections,[27] and catheter-associated urinary tract infections.[28] Measuring the impact of antimicrobial stewardship programs, often led by hospital epidemiologists, is also best accomplished through quasi-experimental study design.[29-31] Thus, understanding the methods, limitations, and interpretation of the quasi-experimental design and analysis is central to the role of the hospital epidemiologist.[32]

Control Group Selection in Studies of Antimicrobial Resistance

Many studies have focused on identifying risk factors for infection or colonization with an antimicrobial-resistant organism. The majority of these studies have had a case-control design. As noted previously, how controls are selected in case-control studies is critical to ensure the validity of study results. Recent work has highlighted this issue of control group selection specifically for studies of antimicrobial-resistant pathogens.[5,33–36]

Two types of control groups have historically been used in studies of antimicrobial-resistant organisms.[5] The first type of control group is selected from patients who do not harbor the resistant pathogen. The second type of control group is selected from subjects infected with a susceptible strain of the organism of interest. For example, in a study of risk factors for infection with VRE in hospitalized patients, the first type of control group would be selected from among the general hospitalized patient population, whereas the second control group would be selected from among those patients infected with vancomycin-susceptible enterococci. As always, the choice of control group should be based primarily on the clinical question being asked. Although use of this second type of control group (e.g., patients infected with the susceptible form of the organism) has historically been a more common approach, it has recently been demonstrated that it may result in an overestimate of the association between antimicrobial exposure and infection with a resistant strain.[36,38] For our example of VRE infection, the postulated explanation for this finding is as follows: if the control patients are infected with vancomycin-susceptible enterococci, it is very unlikely that these patients would have recently received vancomycin (i.e., the risk factor of interest), since exposure to vancomycin may have eradicated colonization with vancomycin-susceptible enterococci. Thus, the association between vancomycin use and VRE infection would be overestimated.[28] A limitation of using the first type of approach (i.e., using patients without infection as controls) is that, in addition to identifying risk factors for infection with a resistant strain of the organism, this approach also identifies risk factors for infection with that organism in general (regardless of whether the strain is resistant or susceptible). Thus, there is no formal way to distinguish between the degree to which a risk factor is associated with being infected with the resistance phenotype and the degree to which it is associated with being infected with the organism in general.[36]

One concern with using the first type of control group (i.e., selected from the group of all hospitalized patients) is the potential for misclassification bias. Specifically, subjects selected as controls based on not having a resistance who have never had a clinical culture performed may in fact be colonized with the resistant organism under study.[35] Thus, if patients colonized with the resistant organism truly had greater prior exposure to antimicrobials than did subjects not colonized but were not identified as such, this misclassification would likely result in a bias toward the null (i.e., the case and control subjects would appear falsely similar with regard to prior antimicrobial use). Another concern with using the first type of control group (i.e., identifying as controls those patients who have never had a clinical culture performed) is that differences between the case and control groups may reflect the fact that clinical cultures were performed for case patients but not for control subjects. Since procurement of samples for culture is not a random process but based on the clinical characteristics of patients, it is possible that the severity of illness or the level of antibiotic exposure may be greater among cases, regardless of the presence of infection with the antibiotic resistant organism.[5] One potential approach would be to limit eligible controls to those patients for whom at least 1 clinical culture has been performed and has not revealed the resistant organism of interest. Such a negative culture result would suggest that the patient is likely not colonized with the resistant organism. However, recent work has demonstrated that using clinical cultures to identify eligible controls leads to the selection of a control group with a higher comorbidity score and greater exposure to antibiotics, compared with a control group for whom clinical cultures were not performed.[24]

One proposed approach to addressing the difficulties in control-group selection in studies of infection with antimicrobial-resistant organisms is to use the case-control study design.[34,38–40] In this design, 2 distinct but related case-control studies are performed. In the first, cases are defined as those patients who harbor the resistant organism, and controls are defined as those patients who do not harbor the pathogen of interest. In the second, cases are instead defined as those patients harboring a susceptible strain of the pathogen of interest, and controls, as in the first approach, are defined as those patients who do not harbor the pathogen of interest.[34] These two separate studies are then carried out with risk factors from the two studies compared qualitatively. This approach allows for the comparison of risk factors identified from the 2 studies to indicate the relative contribution of the resistant infection, over and above simply having the susceptible infection. A potential limitation in this approach is the difficulty of matching for potential confounders because of the use of only 1 control group. Since there are 2 different case groups, variables relevant to the case group (e.g., the duration of hospitalization and

patient location) cannot be used for matching. In addition, the qualitative comparison of results from the 2 studies in this design leaves open the question of how much of a difference in results in meaningful.

Definitions of Antibiotic Exposure

Many studies have sought to uncover risk factors for infection or colonization with antimicrobial-resistant organisms.[8,41] Elucidating such risk factors is essential to inform interventions designed to curb the emergence of resistance. Past studies have particularly focused on antimicrobial use as a risk factor, as it can often be safely modified in the clinical setting.[42,43] However, because antibiotic exposure is not typically a simple binary event, the approaches used to define prior antibiotic exposure have varied considerably across studies.[5] Only recently have attempts been made to identify the impact of differences in these approaches on study conclusions.

A study by Hyle et al.[44] investigated methods used in past studies to describe the extent of prior antibiotic use (e.g., presence or absence of exposure versus duration of exposure), as well as the impact of different methods on study conclusions. A systematic review of all studies investigating risk factors for harboring extended-spectrum b-lactamase–producing *E. coli* and *Klebsiella* species (ESBL-EK) was conducted. Of the 25 studies included, 18 defined prior antibiotic use as a categorical variable, 4 studies defined prior antibiotic exposure as a continuous variable, and 3 studies included both a categorical and a continuous variable to describe prior antibiotic exposure. Only 1 study provided an explicit justification for its choice of variable to describe prior antibiotic exposure. Hyle et al.[44] then reanalyzed a data set from a prior study of risk factors associated with ESBLEK infection[36] and developed 2 separate multivariable models, one in which prior antibiotic use was described as a categorical variable (i.e., exposure present or absent) and one in which antibiotic use was described as a continuous variable (i.e., number of antibiotic-days of exposure). Results of the 2 multivariable models differed substantially: specifically, third-generation cephalosporin use was a risk factor for ESBL-EK infection when antibiotic use was described as a continuous variable but not when antibiotic use was described as a categorical variable.[35]

These results suggest that describing prior antibiotic use as a categorical variable may mask significant associations between prior antibiotic use and infection with a resistant organism. For example, when the categorical variable is used, a subject who received an antibiotic for only 1 day would be considered identical to a subject who received the same antibiotic for 30 days. However, the risk of infection with a resistant organism is almost certainly not the same in these 2 individuals. Describing prior antibiotic use as a continuous variable allows for a more detailed characterization of the association between length of exposure and presence of a resistant pathogen. Recent work in the medical statistics literature emphasizes that the use of cut-off values can result in misinterpretation and that dichotomizing continuous variables reduces analytic power and makes it impossible to detect nonlinear relationships.[37] Indeed, the relationship between prior antimicrobial use and infection with a resistant organism may not be linear (i.e., the risk of such infection may not increase at a constant rate with increasing antimicrobial exposure). It is possible that the risk of infection with a resistant organism does not increase substantially until a certain amount of antimicrobial exposure has been attained (e.g., a "lower threshold"). A more precise characterization of this "lower threshold" would serve to better inform antibiotic use strategies.

Another issue regarding defining prior antimicrobial use centers around how specific antimicrobial agents are grouped. For example, antibiotic use could be classified by agent (e.g., cefazolin), class (e.g., cephalosporins) or spectrum of activity (e.g., activity against gram-negative organisms). Antibiotics are frequently grouped together in classes, even though individual agents within the class may differ significantly,[47] and such categorizations may mask important associations. It is unknown whether using different categorization schemes results in different conclusions regarding the association between antibiotic use and infection with a resistant organism. A recent study explored these issues, focusing on ESBL-EK infection as a model.[48] In a systematic review, 20 studies of risk factors for ESBL-EK infection that met the inclusion criteria revealed tremendous variability in how prior antibiotic use was categorized. Categorization of prior antibiotic use was defined in terms of the specific agents, drug class, and often a combination of both. No study justified its choice of categorization method. There was also marked variability across studies with regard to which specific antibiotics or antibiotic classes were assessed. As expected, a majority (16 studies) specifically investigated the use of b-lactam antibiotics as risk factors for ESBL-EK infection. A variable number of studies also examined the association between use of other antibiotics and ESBL-EK infection: aminoglycosides (9 studies), fluoroquinolones (10 studies), and trimethoprim sulfamethoxazole (7 studies). In a reanalysis of data from a prior study of risk factors for ESBL-EK infection,[45] 2 separate multivariable models of risk factors were constructed: one with prior antibiotic use categorized by class and the other with prior antibiotic use categorized by spectrum of activity.[48] The results of these multivariable models differed substantially. Recent work has reported similar findings when focusing on risk factors for infection with carbapenem-resistant *Pseudomonas aeruginosa*.[49]

Another important issue is timing of exposure. The previously mentioned systematic review of studies investigating risk factors for ESBL-EK infection[44] found that the time window during which antibiotic use was reviewed ranged from 48 hours to 1 year prior to the onset of the drug-resistant infection. Furthermore, studies often did not explicitly state how far back in time prior antibiotic use was assessed.[44]

Conclusion

A basic understanding of epidemiologic principles and study design approaches is essential for the healthcare epidemiologist. The ability to compute measures of disease occurrence, to design and conduct appropriate studies to characterize the factors associated with disease, and to rigorously evaluate the results

of such studies are increasingly vital functions of someone in this position. To build on the foundation provided in this chapter, the healthcare epidemiologist is encouraged to refer to more comprehensive texts and to consult with other professionals (e.g., epidemiologists and biostatisticians) as needed.

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References

1. Haley RW, Quade D, Freeman HE, Bennett JV. The SENIC Project. Study on the efficacy of nosocomial infection control (SENIC Project): summary of study design. *Am J Epidemiol* 1980;**111**: 472–485.
2. Haley RW, Schaberg DR, McClish DK, et al. The accuracy of retrospective chart review in measuring nosocomial infection rates: results of validation studies in pilot hospitals. *Am J Epidemiol* 1980;**111**: 516–533.
3. Freeman J, McGowan JEJr . Methodologic issues in hospital epidemiology. I. Rates, case-finding, and interpretation.*Rev Infect Dis* 1981;**3:** 658–667.
4. Freeman J, McGowan JEJr . Methodologic issues in hospital epidemiology. II. Time and accuracy in estimation. *Rev Infect Dis* 1981;**3**: 668–677.
5. D'Agata EM. Methodologic issues of case-control studies: a review of established and newly recognized limitations. *Infect Control Hosp Epidemiol* 2005;**26**: 338–341.
6. Paterson DL. Looking for risk factors for the acquisition of antibiotic resistance: a 21st century approach. *Clin Infect Dis* 2002;**34**: 1564–1567.
7. Schwaber MJ, De-Medina T, Carmeli Y. Epidemiological interpretation of antibiotic resistance studies – what are we missing? *Nat Rev Microbiol* 2004;**2**: 979–983.
8. Harbarth S, Samore M. Antimicrobial resistance determinants and future control. *Emerg Infect Dis* 2005;**11**: 794–801.
9. Schechner V, Temkin E, Harbarth S, Carmeli Y, Schwaber MJ. Epidemiological interpretation of studies examining the effect of antibiotic usage on resistance. *Clin Microbiol Rev* 2013 Apr;**26**(2): 289–307.
10. Agresti A. *Categorical Data Analysis*. Vol. **3**. New York, NY: Wiley Interscience; 2012.
11. Hennekens CH, Buring JE, Mayrent SL. *Epidemiology in Medicine*. 1st ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 1987.
12. Hosmer DW, Lemeshow SL. *Applied Logistic Regression*. 3rd ed. New York, NY: Wiley Interscience; 2013.
13. Kleinbaum DG, Kupper LL, Morgenstern H. *Epidemiologic Research: Principles and Quantitative Methods*. New York, NY: Van Nostrand Reinhold; 1982.
14. Nelson KE, Williams CM, Graham NMH. *Infectious Disease Epidemiology: Theory and Practice*. 1st ed. New York, NY: Aspen Publishers; 2000.
15. Rothman KJ, Greenland S., Lash TL. *Modern Epidemiology*. Philadelphia, Pa: Lippincott Williams & Wilkins; 2012. Epidemiologic Methods in Infection Control 41.
16. Thomas JC, Weber DJ. *Epidemiologic Methods for the Study of Infectious Diseases*. 1st ed. Oxford, UK: Oxford University Press; 2001.
17. Harris AD, Lautenbach E, Perencevich E. A systematic review of quasi-experimental study designs in the fields of infection control and antibiotic resistance. *Clin Infect Dis* 2005;**41**: 77–82.
18. Shadish WR, Cook TD, Campbell DT. *Experimental and Quasi-experimental Designs for Generalized Causal Inference*. Boston, Mass: Houghton Mifflin Company; 2002.
19. Cook TD, Campbell DT. *Quasi-Experimentation: Design and Analysis Issues for Field Settings*. Chicago, Ill: Rand McNally Publishing; 1979.
20. Harris AD, Bradham DD, Baumgarten M, Zuckerman IH, Fink JC, Perencevich EN. The use and interpretation of quasiexperimental studies in infectious diseases. *Clin Infect Dis* 2004;**38**: 1586–1591.
21. Shardell M, **Harris AD**, El-Kamary SS, Furuno JP, Miller RR, Perencevich EN. Statistical analysis and application of quasi experiments to antimicrobial resistance intervention studies. *Clin Infect Dis* 2007 Oct 1;**45**(7): 901–907.
22. Morton V, Torgerson DJ. Effect of regression to the mean on decision making in health care. *BMJ* 2003;**326**: 1083–1084.
23. Ramsay CR, Matowe L, Grilli R, Grimshaw JM, Thomas RE. Interrupted time series designs in health technology assessment: lessons from two systematic reviews of behavior change strategies. *Int J Technol Assess Health Care* 2003;**19**: 613–623.
24. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. *J Clin Pharm Ther* 2002;**27**: 299–309.
25. Matowe LK LC, Crivera C, Korth-Bradley JM. Interrupted time series analysis in clinical research. *Ann Pharmacother* 2003;**37**: 1110–1116.
26. Allegranzi B, Gayet-Ageron A, Damani N, et al. Global implementation of WHO's multimodal strategy for improvement of hand hygiene:quasi-experimental study. *Lancet Infect Dis* 2013 Oct;**13**(10): 843–851.
27. Rinke ML, Chen AR, Bundy DG, et al Implementation of a central line maintenance care bundle in hospitalized pediatric oncology patients. *Pediatrics* 2012 Oct;**130**(4): e996–e1004.
28. Lee GM, Kleinman K, Soumerai SB, et al. Effect of nonpayment for preventable infections in U.S. hospitals. *N Engl J Med* 2012 Oct 11;**367**(15): 1428–1437.
29. Cosgrove SE, Seo SK, Bolon MK, et al CDC Prevention Epicenter Program: Evaluation of postprescription review and feedback as a method of promoting rational antimicrobial use: a multicenter intervention. *Infect Control Hosp Epidemiol* 2012 Apr;**33** (4): 374–380.
30. Newland JG, Stach LM, De Lurgio SA, et al. Impact of a Prospective-Audit-With-Feedback Antimicrobial Stewardship Program at a Children's Hospital. *J Pediatric Infect Dis Soc* 2012 Sep;**1**(3): 179–186.
31. Mehta JM, Haynes K, Wileyto EP, et al. Centers for Disease Control and Prevention Epicenter Program: Comparison of prior authorization and prospective audit with feedback for

antimicrobial stewardship. *Infect Control Hosp Epidemiol* 2014 Sep;**35**(9): 1092–1099.

32. Moody J, Cosgrove SE, Olmsted R, et al. Antimicrobial stewardship: a collaborative partnership between infection preventionists and healthcare epidemiologists. *Infect Control Hosp Epidemiol* 2012 Apr;**33**(4): 328–30.
33. Harris AD, Carmeli Y, Samore MH, Kaye KS, Perencevich E. Impact of severity of illness bias and control group misclassification bias in case-control studies of antimicrobial-resistant organisms. *Infect Control Hosp Epidemiol* 2005;**26**: 342–345.
34. Kaye KS, Harris AD, Samore M, Carmeli Y. The case-case-control study design: addressing the limitations of risk factor studies for antimicrobial resistance. *Infect Control Hosp Epidemiol* 2005;**26**: 346–351.
35. Harris AD, Karchmer TB, Carmeli Y, Samore MH. Methodological principles of case-control studies that analyzed risk factors for antibiotic resistance: a systematic review. *Clin Infect Dis* 2001;**32**: 1055–1061.
36. Harris AD, Samore MH, Lipsitch M, Kaye KS, Perencevich E, Carmeli Y. Control-group selection importance in studies of antimicrobial resistance: examples applied to *Pseudomonas aeruginosa*, Enterococci, and *Escherichia coli*. *Clin Infect Dis* 2002;**34:** 1558–1563.
37. Carmeli Y, Samore MH, Huskins C. The association between antecedent vancomycin treatment and hospital-acquired vancomycin-resistant enterococci. *Arch Intern Med* 1999;**159**: 2461–2468.
38. Kaye KS, Harris AD, Gold H, Carmeli Y. Risk factors for recovery of ampicillin-sulbactam-resistant *Escherichia coli* in hospitalized patients. *Antimicrob Agents Chemother* 2000; **44**: 1004–1009.
39. Harris AD, Smith D, Johnson JA, Bradham DD, Roghmann MC. Risk factors for imipenem-resistant *Pseudomonas aeruginosa* among hospitalized patients. *Clin Infect Dis* 2002; **34**: 340–345.
40. Harris AD, Perencevich E, Roghmann MC, Morris G, Kaye KS, Johnson JA. Risk factors for piperacillintazobactam-resistant *Pseudomonas aeruginosa* among hospitalized patients. *Antimicrob Agents Chemother* 2002; **46**: 854–858.
41. Livermore DM. Can better prescribing turn the tide of resistance? *Nat Rev Microbiol* 2004;**2**: 73–78.
42. Patterson JE. Antibiotic utilization: is there an effect on antimicrobial resistance? *Chest* 2001;**119** (Suppl 2): 426S–430S.
43. Safdar N, Maki DG. The commonality of risk factors for nosocomial colonization and infection with antimicrobialresistant *Staphylococcus aureus, Enterococcus*, gram-negative bacilli, *Clostridium difficile*, and *Candida*. *Ann Intern Med* 2002;**136**: 834–844.
44. Hyle EP, Bilker WB, Gasink LB, Lautenbach E. Impact of different methods for describing the extent of prior antibiotic exposure on the association between antibiotic use and antibiotic-resistant infection. *Infect Control Hosp Epidemiol* 2007;**28**: 647–654.
45. Lautenbach E, Patel JB, Bilker WB, Edelstein PH, Fishman NO. Extended-spectrum b-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae*: risk factors for infection and impact of resistance on outcomes. *Clin Infect Dis* 2001;**32**: 1162–1171.
46. Royston P, Altman D, Sauerbrei W. Dichotomizing continuous predictors in multiple regression: a bad idea. *Stat Med* 2006;**25**: 127–141.
47. Donskey CJ. The role of the intestinal tract as a reservoir and source for transmission of nosocomial pathogens. *Clin Infect Dis* 2004;**39**: 219–226.
48. MacAdam H, Zaoutis TE, Gasink LB, Bilker WB, Lautenbach E. Investigating the association between antibiotic use and antibiotic resistance: impact of different methods of categorizing prior antibiotic use. *Int J Antimicrob Agents* 2006;**28**: 325–332.
49. Gasink LB, Zaoutis TE, Bilker WB, Lautenbach E. The categorization of prior antibiotic use: Impact on the identification of risk factors for drug resistance in case control studies.*Am J Infect Control* 2007;**35:** 638–642.

Chapter 7

Isolation

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Patients potentially infected or colonized with certain microorganisms must be placed in isolation while in a healthcare facility to prevent healthcare transmission of these pathogens. Isolation systems enable healthcare workers to more readily identify patients who need to be isolated and to institute the appropriate precautions. This chapter presents an overview of isolation precautions, emphasizing the recommendations of the isolation guidelines from the Centers for Disease Control and Prevention (CDC).[1] Resources listed at the end of this chapter should be consulted on specific issues related to isolation.

The goal of isolation is to prevent transmission of microorganisms from infected or colonized patients to other patients, hospital visitors, and healthcare workers. Use of personal protective equipment (e.g., masks, eye wear, gloves, and gowns) and specific room requirements are the tools for such precautions.

The importance of appropriate isolation cannot be overstated. The medical literature is replete with examples of healthcare outbreaks of influenza, tuberculosis, varicella, severe acute respiratory syndrome (SARS), and even hepatitis A infection, all of which might have been prevented if isolation practices had been optimal. Isolation efforts incur costs, but the direct and indirect costs of healthcare-associated outbreaks are substantial. Hand hygiene and appropriate isolation remain the cornerstones of infection prevention and are assuming greater importance as the prevalence of multidrug-resistant organisms (MDROs) increases.

The ideal isolation system is described in Table 7.1. While no system meets all of these characteristics, infection prevention personnel should consider these ideals when designing and implementing a system.

Table 7.1 Characteristics of the ideal isolation system

Utilizes current understanding of the mechanisms of transmission of infectious pathogens
Requires isolation precautions for all patients with infectious diseases that may be transmitted in the healthcare setting (i.e., eliminates transmission of infection in the hospital)
Avoids isolation of patients who do not require it ("over-isolation"); is easily understood by all members of the healthcare team
Is easily implemented; encourages compliance
Is environmentally friendly (avoids unnecessary use of disposable products)
Is inexpensive
Interferes minimally with patient care
Poses no detrimental impact on patient safety Minimizes patient discomfort

In assessing appropriate infection control for any infectious disease, one needs to know the mode of transmission (via small droplets in the air, large droplets, contact, blood and body fluids, or a combination of any of these). Moreover, it is necessary to also know the times of onset and termination of infectivity, since the patient may be infectious before and after the symptomatic period. The emergence of SARS and Middle East Respiratory Syndrome (MERS) demonstrate the difficulties of implementing appropriate infection control measures when the mode of transmission and infective period are unclear.

The CDC has led the effort to formalize guidelines for isolation, with the first such guidance published in 1970. Subsequently, the CDC has modified and simplified these guidelines several times to address emerging problems in infectious diseases, such as multidrug-resistant *Mycobacterium tuberculosis* infection, pandemic influenza, and vancomycin-resistant enterococcal infection, to incorporate an increased understanding about mechanisms of transmission for other diseases and realization of the importance of simple, easy to follow isolation practices.

The CDC and the Hospital Infection Control Practices Advisory Committee (HICPAC) issued a guideline in 1996 for a new system of isolation. This system replaced the previous complicated category-specific and disease-specific systems and integrated universal precautions and body substance isolation. It remains the basis for typical practices in United States hospitals. The guideline was updated in 2007.[1] Recommendations relating to use of Contact Precautions included carbapenem-resistant *Enterobacteriaceae* in 2012[2] and enhanced precautions for unique pathogens such as Ebola in 2014.[3] Still, individual healthcare institutions may find it necessary to adapt basic guidelines to their needs.

This chapter presents an overview of isolation so that infection prevention personnel can implement an appropriate system. Infection prevention personnel should also consult the detailed guidelines for implementing isolation precautions that are referenced at the end of this chapter.

Current CDC Guidelines

The CDC and HICPAC developed a system for isolation that has 2 levels of precautions: standard precautions, which apply to all patients, and transmission-based precautions, employed for patients with documented or suspected colonization or infection with certain microorganisms.[1]

Table 7.2 Requirements for standard precautions

Hand hygiene
After touching blood, body fluids, secretions, excretions, and/or contaminated items or inanimate objects in the immediate vicinity of the patient
Immediately after removing gloves
Before and after patient contact
Gloves
For touching blood, body fluids, secretions, excretions, and/or contaminated items
For touching mucous membranes and/or nonintact skin
Mask, eye protection, face shield
To protect mucous membranes of the eyes, nose, and mouth during procedures and patient-care activities likely to generate splashes or sprays of blood, body fluids, secretions, and/or excretions
Gown
To protect skin and prevent soiling of clothing during procedures and patient-care activities likely to generate splashes or sprays of blood, body fluids, secretions, and/or excretions
Patient-care equipment
Soiled patient-care equipment should be handled in a manner to prevent skin and mucous membrane exposures, contamination of clothing, and transfer of microorganisms to other patients and environments
Reusable equipment must be cleaned and reprocessed before being used in the care of another patient
Environmental control
Requires procedures for routine care, cleaning, and disinfection of patient furniture and the environment
Linen
Soiled linen should be handled in a manner to prevent skin and mucous membrane exposures, contamination of clothing, and transfer of microorganisms to other patients and environments
Sharp devices
Avoid recapping used needles
Avoid removing used needles from disposable syringes by hand
Avoid bending, breaking, or manipulating used needles by hand; place used sharp devices in puncture-resistant containers
Patient resuscitation
Use mouthpieces, resuscitation bags, or other ventilation devices to avoid mouth-to-mouth resuscitation
Patient placement
Patients who contaminate the environment or cannot maintain appropriate hygiene should be placed in a private room

NOTE: Modified from Siegel et al.[1]

Standard Precautions

Standard precautions, previously known as universal precautions, apply to blood, all body fluid secretions and excretions, except sweat, nonintact skin and to mucous membranes. The intent of standard precautions is primarily to protect the healthcare worker from pathogens transmitted via blood and body fluids. Requirements for standard precautions are outlined in Table 7.2.

Transmission-Based Precautions

Whereas standard precautions apply to all patients, transmission-based precautions apply to selected patients on the basis of either a clinical syndrome or a suspected or confirmed specific diagnosis.[1] Transmission-based precautions are used primarily in the acute-care setting and *not* other healthcare settings. Transmission-based precautions are divided into 3 categories that reflect the major modes of transmission of infectious agents in the healthcare setting: airborne transmission precautions (hereafter, "airborne precautions"), droplet precautions, and contact precautions (Tables 7.3 and 7.4). Some diseases require more than 1 isolation category.

Airborne Precautions

Airborne precautions prevent diseases transmitted by aerosols containing droplet nuclei or contaminated dust particles.[1] Droplet nuclei are less than 5 mm in size and may remain suspended in air, allowing them to migrate for long periods of time. Aerosol transmission of pathogens may be obligate, preferential, or opportunistic.[4] *M. tuberculosis* is probably the only pathogen that is transmitted exclusively via aerosol and is thus an example of obligate aerosol transmission. Pathogens that are preferentially but not exclusively transmitted via aerosols include rubeola (measles) virus and varicella virus. Opportunistic pathogens typically are transmitted by other routes but under special circumstances may be transmitted by the airborne route; examples include smallpox virus, SARS-associated coronavirus, influenza virus, and noroviruses.

Patients with suspected or confirmed tuberculosis (pulmonary or laryngeal), measles, varicella, or disseminated zoster should be placed under airborne precautions. In addition, empirical use of airborne precautions should be strongly considered for human immunodeficiency virus–infected patients with cough, fever, and unexplained pulmonary infiltrates in any location until tuberculosis can be ruled out. Appropriate isolation requires an airborne infection isolation room (AIIR): a private room with negative air-pressure and 12 air exchanges per hour. Air from the room should be exhausted directly to the outside or through a high-efficiency particulate air (HEPA) filter. The door to the room must be kept closed at all times.

If the patient must be transported from the isolation room to another area of the hospital, the patient should put on a standard surgical mask before leaving the isolation room. All persons entering the room should wear respirators (either masks or powered air-purifying respirators (PAPRs)). In the United States, the Occupational Safety and Health

Table 7.3 Summary of transmission-based precautions

Variable	Airborne precautions	Droplet precautions	Contact precautions
Room	Negative air-pressure, single-patient room required with air exhausted to outside or through HEPA filters; door must be closed	Single-patient room preferred; door may remain open	Single-patient room preferred; door may remain open; use disposable noncritical patient-care equipment or dedicate equipment to a single patient
Masks	N-95 or portable respirator (PAPR) for those entering room; place surgical mask on patient if transport out of room is required	Surgical or isolation mask for those entering room; place surgical or isolation mask on patient if transport out of room is required	**NA**
Gowns	**NA**	**NA**	When entering room
Gloves	**NA**	**NA**	When entering room

NOTE: Modified from Siegel et al.[1] HEPA, high-efficiency particulate air filter; PAPR, powered air–purifying respirators; NA, not applicable.

Table 7.4 Isolation precautions required for various diseases and pathogens

Airborne precautions
Measles
Monkeypox[a]
Tuberculosis, pulmonary or laryngeal; draining lesion[a]
SARS[a]
Smallpox[a]
Varicella[a]
Zoster, disseminated or in an immunocompromised patient until dissemination ruled out[a]

Droplet precautions
Adenovirus pneumonia[a]
Diphtheria, pharyngeal
Haemophilus influenzae meningitis, epiglottitis; pneumonia (in an infant or child)
Influenza
Meningococcal infections
Mumps
Mycoplasma pneumonia
Parvovirus B19 infection
Pertussis
Plague, pneumonic
Rhinovirus infection[a]
Rubella
MERS
SARS[a]
Group A streptococcal pneumonia; serious invasive disease; major skin, wound, or burn infection;[a] pharyngitis, scarlet fever (in an infant or young child)
Viral hemorrhagic fever[a]

Contact precautions
Adenovirus conjunctivitis
Adenovirus pneumonia[a]
Burkholderia cepacia pneumonia in cystic fibrosis
Article I. *Clostridium difficile* diarrhea
Article II. Conjunctivitis, acute viral
Decubitus ulcer, infected and drainage not contained
Diarrhea, infectious (in a diapered or incontinent patient)
Diphtheria, cutaneous
Enterovirus infection (in an infant or young child)
Furunculosis (in an infant or young child)
Hepatitis A, hepatitis E (in a diapered or incontinent patient)
HSV infection, neonatal or disseminated or severe primary mucocutaneous
Human metapneumovirus infection
Impetigo
Lice
Infection or colonization with MDR bacteria (e.g., MRSA, VRE, VISA, VRSA, ESBL producers, CRE, drug-resistant *Streptococcus pneumoniae*)
Monkeypox[a]
Parainfluenza infection (in an infant or child)
Rhinovirus infection[a]
Rotavirus infection
RSV infection (in an infant, child, or immunocompromised patient)
Rubella, congenital
SARS[a]
Scabies
Smallpox[a]
Staphylococcus aureus major skin, wound or burn infection
Group A streptococcal major skin, burn or wound infection[a]
Tuberculous draining lesion
Vaccinia, fetal, generalized, progressive, or eczema vaccinatum
Varicella[a]
Viral hemorrhagic fever[a]
Zoster, disseminated or in an immunocompromised patient[a]

Enhanced Precautions[a]
Ebola

NOTE: Modified from Siegel et al.1 ESBL, extended-spectrum β-lactamases; HSV, herpes simplex virus; CRE, carbapenem-resistant *Enterobacteriaceae*; MDR, multidrug-resistant; MERS, Middle East Respiratory Syndrome; MRSA, methicillin-resistant *S. aureus;* RSV, respiratory syncytial virus; SARS, severe acute respiratory syndrome; VISA, vancomycin-intermediate *S. aureus;* VRE, vancomycin-resistant enterococci; VRSA, vancomycin-resistant *S. aureus*.
[a] Condition requires 2 types of precautions.

Administration (OSHA) requires mask respirators to meet the following 4 performance criteria:[5]

1. Filter 1-mm particles with an efficiency of at least 95%.
2. Fit different facial sizes and characteristics.
3. Can be fit-tested to obtain a leakage rate of less than 10%, at least annually.
4. Can be checked for fit each time the healthcare worker puts on the mask.

There are numerous products available that are certified by the National Institute for Occupational Safety and Health (NIOSH) as meeting the N-95 standard (i.e., filters 95% of airborne particles). Mask respirators are generally superior to PAPRs due to ease of use.

The standard for individuals not able to use a mask respirator due to facial hair, inability to do fit testing, or claustrophobia with masks is a PAPR. A PAPR program requires training, supply, and upkeep of hoods, pumps, and batteries.

Patients with suspected or confirmed tuberculosis should be instructed to cover their mouth and nose with a tissue when coughing or sneezing. Those with suspected tuberculosis should remain in isolation until tuberculosis can be ruled out. Patients with confirmed tuberculosis who are receiving effective antituberculous treatment can be moved out of the negative air-pressure rooms when they are improving clinically and when 3 consecutive sputum smears of samples collected at least 8 hours apart have no detectable acid-fast bacilli. Patients with multidrug-resistant tuberculosis may need to be isolated for longer.

If the patient has suspected or confirmed measles, varicella, or disseminated zoster, nonimmune individuals should not enter the room. If a nonimmune healthcare worker must enter the room, he or she should wear a respirator mask (as described above). For immune healthcare workers, there are no clear guidelines. Some facilities require respirators for all healthcare workers entering any airborne isolation rooms, for the sake of consistency. Other facilities do not require respirators for immune healthcare workers to enter the room of a patient with measles or varicella.

Droplet Precautions

Droplet precautions prevent the transmission of micro-organisms by particles larger than 5 mm. These droplets are produced when the patient talks, coughs, or sneezes. Droplets also may be produced during some medical procedures. Some illnesses that require droplet precautions include bacterial diseases, such as invasive *Haemophilus influenzae* type B infections, meningococcal infections, multidrug-resistant pneumococcal disease, pharyngeal diphtheria, *Mycoplasma* pneumonia, and pertussis. Some viral diseases, including seasonal influenza, mumps, rubella, and parvovirus infection, also require these precautions.

Droplet precautions require patients to be placed in a private room or cohorted with another patient who is infected with the same organism. The door to the room may remain open. Those entering the room should wear standard surgical or isolation masks. When transported out of the isolation room, the patient should wear a mask; however, a mask is not required for those transporting the patient.

Contact Precautions

Contact precautions prevent transmission of epidemiologically important organisms from an infected or colonized patient through direct contact (touching the patient) or indirect contact (touching surfaces or objects in the patient's environment).[1] Contact precautions require patients to be placed in a private room or cohorted with another patient who is infected with the same organism. Healthcare workers should wear a gown and gloves when entering the room. They should change the gloves while caring for the patient if they touch materials that have high concentrations of microorganisms. While still in the isolation room, healthcare workers should remove their gown and gloves, taking care to not contaminate clothing or skin, and perform hand hygiene. They must take care not to contaminate their hands before leaving the room. Noncritical patient care items (e.g., stethoscopes and bedside commodes) that are used for the patients who are in contact isolation should not be used for other patients. If such items must be shared, they should be cleaned and disinfected before reuse. Patients should leave isolation rooms infrequently.

Contact isolation is recommended by the CDC for patients infected or colonized with multidrug-resistant bacteria (e.g., methicillin-resistant *Staphylococcus aureus* or vancomycin-resistant enterococci). It is also indicated for patients with active *Clostridium difficile* or rotavirus enteritis and for diapered or incontinent patients who are infected or colonized with other agents transmitted by the oral-fecal route (e.g., *Escherichia coli* O157:H7, *Shigella* species, rotavirus, or hepatitis A virus). Infants and young children with respiratory syncytial virus, parainfluenza, or enteroviral infection also require contact isolation, as do patients with severe herpes simplex virus infection (i.e., neonatal, disseminated, or severe primary mucocutaneous disease), impetigo, scabies, or pediculosis. Patients with varicella or disseminated zoster infection require both contact and airborne precautions.

Enhanced Precautions for Special Pathogens

The emergence of Ebola led the CDC to develop more aggressive isolation practices for rare circumstances where this or other emerging pathogens are possible. Precautions involve a more aggressive version of contact isolation with impermeable gowns and airborne isolation if a patient is particularly infectious along with standardized methods for donning and doffing gowns and gloves. CDC guidance should be consulted for further details.

Instituting Isolation Precautions Empirically

Frequently, patients are admitted to the hospital without a definitive diagnosis. However, they may have an infectious process that may place other patients and healthcare

Table 7.5 Appropriate empirical isolation precautions for specific clinical syndromes

Airborne precautions
Vesicular rash[a]
Maculopapular rash with cough, coryza, and fever Cough, fever, and upper lobe pulmonary infiltrate
Cough, fever, any pulmonary infiltrate in a patient infected with HIV (or at high risk for HIV infection)
Cough, fever, any pulmonary infiltrate, and recent travel to countries with outbreaks of SARS or avian influenza[a]
Droplet precautions
Meningitis
Petechial or ecchymotic rash with fever
Paroxysmal or severe persistent cough during periods of pertussis activity
Contact precautions
Acute diarrhea with likely infectious etiology in incontinent or diapered patient
Vesicular rash[a]
Respiratory infections in infants and young children History of infection or colonization with MDR organisms
Skin, wound, or urinary tract infection in a patient with a recent hospital or nursing home stay in a facility where MDR organisms are prevalent
Abscess or draining wound that cannot be covered
Cough, fever, any pulmonary infiltrate, and recent travel to countries with outbreaks of SARS or avian influenz[a]

NOTE: Modified from Siegel et al.1 HIV, human immunodeficiency virus; MDR, multidrug-resistant; SARS, severe acute respiratory syndrome.
[a] Condition requires 2 types of precautions.

workers at risk. Therefore, patients with certain clinical syndromes should be placed in isolation while a definitive diagnosis is confirmed. Table 7.5 delineates appropriate empirical isolation precautions for various clinical syndromes on the basis of the potential mechanisms of transmission.

Unintended Effects of Isolation Precautions

Isolation precautions require specific behaviors by all healthcare personnel (HCP) and therefore affect how care is provided. All forms of isolation precautions have the potential to impact care, but contact isolation is the only form studied extensively. Contact isolation appears to decrease frequency of HCP visits and improve hand hygiene after glove removal.[6–7]

Contact isolation has been hypothesized to lead to greater patient depression and anxiety, worse patient satisfaction, and more adverse events.[6] The literature on these effects is mixed, and the impact likely depends on the way isolation is implemented and the degree of HCP and patient education.

Discontinuing Isolation Precautions

The discontinuation of isolation precautions is pathogen-specific and based on the duration of infectivity. For some types of infection (e.g., acute bacterial infection), the duration of infectivity is shortened by the initiation of effective antimicrobial therapy. For other infections (e.g., viral infections) or colonization with multidrug-resistant pathogens, therapy has less impact on the duration of infectivity. The CDC isolation guideline[1] should be consulted for pathogen-specific recommendations on the duration of isolation precautions.

Foregoing Isolation Precautions for MRSA or VRE

Citing a lack of definitive evidence of benefit and potential harms, including HCP burden, contact isolation is not used by a small minority of US hospitals for MRSA or VRE. Full discussion of such an approach can be found elsewhere.[7]

Visitor Use of Isolation Precautions

Visitors to patients may be at risk of contracting infections. Most are not at risk for transmitting organisms to other patients. Visitors cohabitating with patients outside the hospital are likely at similar risk at home as in the hospital (for example, from *M. tuberculosis*). Hand hygiene remains the cornerstone of infection prevention and should be encouraged in visitors. Visitors particularly susceptible to infection or complications of infection are recommended against visiting patients on isolation.

Recent expert guidance makes the following recommendations for visitors and isolation:[8]

1) *Airborne isolation*: visitors are not trained on PAPRs or fit tested for N95s, and their use is inappropriate. Visitors may use surgical masks. If they cohabitate with the patient outside of the hospital, they may visit them. If they have low risk exposure outside of the hospital, they should be asked not to visit.
2) *Contact isolation*: Outside of outbreaks, visitors are not recommended to use contact isolation for MRSA or VRE, as colonization is prevalent in the community and limiting contact is likely not an effective intervention. Contact isolation has been shown to potentially protect against enteric pathogens and is often used with visitors of patients with enteric disease. Furthermore, it is recommended for CRE given the relative rarity of colonization and severity of infection.
3) *Droplet isolation*: Visitors are recommended to use surgical masks to protect themselves from exposure.

References

1. Siegel JD, Rhinehart E, Jackson M, Chiarello L, the Health Care Infection Control Practices Advisory Committee (HICPAC). 2007 Guideline for isolation precautions: preventing transmission of infectious agents in health care settings. *Am J Infect Control* 2007;**35**(10 Suppl 2): S65–S164.
2. Centers for Disease Control and Prevention (CDC). Guidance for control of infections with carbapenem-resistant or carbapenemase-producing *Enterobacteriaceae* in acute care facilities. *MMWR Morb Mortal Wkly Rep* 2009;**58**(10): 256–260.
3. Centers for Disease Control and Prevention (CDC). Guidance on personal protective equipment (PPE) to be used by healthcare workers during management of patients with confirmed Ebola or persons under investigation (PUIs) for Ebola who are clinically unstable or have bleeding, vomiting, or diarrhea in U.S. hospitals, including procedures for donning and doffing PPE. www.cdc.gov/vhf/ebola/healthcare-us/ppe/guidance.html. Accessed October 5, 2015.
4. Roy CJ, Milton DK. Airborne transmission of communicable infection: the elusive pathway. *N Engl J Med* 2004;**350**: 1710–1712.
5. Jensen PA, Lambert LA, Iademarco MF, Ridzon R. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR Morb Mortal Wkly Rep* 2005;**54** (RR-17): 1–141.
6. Morgan DJ, Diekema DJ, Sepkowitz K, Perencevich EN. Adverse outcomes associated with Contact Precautions: a review of the literature. *Am J Infect Control* 2009;**37**(2): 85–93.
7. Morgan DJ, Murthy R, Munoz-Price LS, et al. Reconsidering Contact Precautions for endemic methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus* (VRE). *Infect Control Hosp Epidemiol* 2015;**36**(10): 1163–1172.
8. Munoz-Price LS, Banach DB, Bearman G, et al. Isolation precautions for visitors. *Infect Control Hosp Epidemiol* 2015:**36**(7): 747–758.

Suggested Reading

Centers for Disease Control and Prevention (CDC). Guidelines for environmental infection control in health-care facilities: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR Morb Mortal Wkly Rep* 2003;**52**(RR-10): 1–42. www.cdc.gov/hicpac/pdf/guidelines/ eic_in_HCF_03.pdf. Accessed October 5, 2015.

Centers for Disease Control and Prevention. Guideline for hand hygiene in health-care settings: recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force.*MMWR Morb Mortal Wkly Rep* 2002;**51**(RR-16): 1–44. www.cdc.gov/mmwr/preview/mmwrhtml/rr5116a1.htm. Accessed October 5, 2015.

Centers for Disease Control and Prevention. Bioterrorism Web Site. www.bt.cdc.gov/bioterrorism/. Accessed May 25, 2009.

Centers for Disease Control and Prevention. Severe Acute Respiratory Syndrome Web site. www.cdc.gov/sars/infection/index.html. Accessed October 5, 2015.

Jarvis WR, ed. *Bennett & Brachman's Hospital Infections*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007.

Mayhall CG, ed. *Hospital Epidemiology and Infection Control*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2004.

Pickering LK, ed. *2009 Red Book: Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009.

Siegel JD, Rhinehart E, Jackson M, Chiarello L, the Healthcare Infection Control Practices Advisory Committee. Management of multidrug-resistant organisms in healthcare settings, 2006. www.cdc.gov/hicpac/pdf/guidelines/MDROGuideline2006.pdf. Accessed October 5, 2015.

Wenzel RP, ed. *Prevention and Control of Nosocomial Infections*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins;2003.

Chapter 8

Disinfection and Sterilization in Healthcare Facilities

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Introduction

In the United States in 2010, approximately 51.4 million inpatient surgical procedures and an even larger number of invasive medical procedures were performed.[1] In 2009, there were over 6.9 million upper gastrointestinal (GI), 11.5 million lower GI, and 228,000 biliary endoscopies performed.[2] Each of these procedures involves contact by a medical device or surgical instrument with a patient's sterile tissue or mucous membranes. A major risk of all such procedures is the introduction of pathogenic microbes, which can lead to infection. Failure to properly disinfect or sterilize equipment may lead to transmission via contaminated medical and surgical devices (e.g., endoscopes contaminated with carbapenem-resistant *Enterobacteriaceae* [CRE]).[3,4]

Achieving disinfection and sterilization through the use of disinfectants and sterilization practices is essential for ensuring that medical and surgical instruments do not transmit infectious pathogens to patients. Since it is not necessary to sterilize all patient-care items, healthcare policies must identify whether cleaning, disinfection, or sterilization is indicated, based primarily on each item's intended use.

Multiple studies in many countries have documented lack of compliance with established guidelines for disinfection and sterilization.[5] Failure to comply with scientifically based guidelines has led to numerous outbreaks and patient exposures.[6–8] Due to noncompliance with recommended reprocessing procedures, the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) issued a health advisory alerting healthcare providers and facilities about the public health need to properly maintain, clean, and disinfect and sterilize reusable medical devices in September 2015.[9] In this chapter, which is an updated and modified version of earlier chapters,[10–13] a pragmatic approach to the judicious selection and proper use of disinfection and sterilization processes is presented, based on well-designed studies assessing the efficacy (via laboratory investigations) and effectiveness (via clinical studies) of disinfection and sterilization procedures.

A Rational Approach to Disinfection and Sterilization

Almost 50 years ago, Earle H. Spaulding[14] devised a rational approach to disinfection and sterilization of patient-care items or equipment. This classification scheme is so clear and logical that it has been retained, refined, and successfully used by infection prevention professionals and others when planning methods for disinfection or sterilization.[10–13] Spaulding believed that the nature of disinfection could be understood more readily if instruments and items for patient care were divided into three categories based on the degree of risk of infection involved in the use of the items. The three categories he described were critical, semicritical, and noncritical. This terminology is employed by the CDC's "Guidelines for Environmental Infection Control in Healthcare Facilities"[15] and the CDC's "Guideline for Disinfection and Sterilization in Healthcare Facilities."[13] These categories and the methods to achieve sterilization, high-level disinfection, and low-level disinfection are summarized in Table 8.1. Although the scheme remains valid, there are some examples of disinfection studies with prions, viruses, mycobacteria, and protozoa that challenge the current definitions and expectations of high- and low-level disinfection.[16]

In May 2015, the FDA convened a panel to discuss recent reports and epidemiologic investigations of the transmission of infections associated with the use of duodenoscopes in endoscopic retrograde cholangiopancreatography (ERCP) procedures.[17] After presentations from industry, professional societies, and invited speakers, the panel made several recommendations to include reclassifying duodenoscopes based on the Spaulding classification from semicritical to critical to support the shift from high-level disinfection to sterilization.[18] This could be accomplished by shifting from high-level disinfection for duodenoscopes to sterilization and modifying the Spaulding definition of critical items from "objects which enter sterile tissue or the vascular system or through which blood flows should be sterile" to "objects which directly or secondarily (i.e., via a mucous membrane such as duodenoscope) enter normally sterile tissue of the vascular system of through which blood flows should be sterile."[18,19] Implementation of this recommendation requires sterilization technology that achieves a sterility assurance level of 10^{-6} of complex medical instruments such as duodenoscopes. Ideally, this shift would eventually involve not only endoscopes that secondarily enter normally sterile tissue (e.g., duodenoscopes, bronchoscopes) but also other semicritical devices (e.g., gastrointestinal endoscopes).[18,19]

Critical Items

Critical items are so called because of the high risk of infection if such an item is contaminated with any microorganism, including bacterial spores. Thus, it is critical that objects that

Table 8.1 Methods for disinfection and sterilization of patient-care items and environmental surfaces[a]

Process	Level of microbial inactivation	Method	Examples (with processing times)	Healthcare application (examples)
Sterilization[b]	Destroys all microorganisms, including bacterial spores	High temperature Low temperature Liquid immersion	Steam (~40 min), dry heat (1–6 hr depending on temperature) Ethylene oxide gas (~15 hr), hydrogen peroxide gas plasma (28–52 min), hydrogen peroxide and ozone (46 min), hydrogen peroxide vapor (55 min) Chemical sterilants[c]: >2% glut (~10 hr); 1.12% glut with 1.93% phenol (12 hr); 7.35% HP with 0.23% PA (3 hr); 8.3% HP with 7.0% PA (5 hr); 7.5% HP (6 hr); 1.0% HP with 0.08% PA (8 hr); ≥0.2% PA (12 min at 50–56°C)	Heat-tolerant critical (surgical instruments) and semicritical patient-care items Heat-sensitive critical and semicritical patient-care items Heat-sensitive critical and semicritical patient-care items that can be immersed
High-level disinfection (HLD)	Destroys all microorganisms except some bacterial spores	Heat-automated Liquid immersion	Pasteurization (65–77°C, 30 min) Chemical Sterilants/HLDs[c]: >2% glut (20–90 min at 20–25°C); >2% glut (5 min at 35–37.8°C); 0.55% OPA (12 min at 20°C); 1.12% glut with 1.93% phenol (20 min at 25°C); 7.35% HP with 0.23% PA (15 min at 20°C); 7.5% HP (30 min at 20°C); 1.0% HP with 0.08% PA (25 min); 400–450 ppm chlorine (10 min at 20°C); 2.0% HP (8 min at 20°C); 3.4% glut with 26% isopropanol (10 min at 20°C)	Heat-sensitive semicritical items (e.g., respiratory therapy equipment) Heat-sensitive semicritical items (e.g., GI endoscopes, bronchoscopes, endocavitary probes)
Low-level disinfection	Destroys vegetative bacteria, some fungi and viruses but not mycobacteria or spores	Liquid contact	EPA-registered hospital disinfectant with no tuberculocidal claim (e.g., chlorine-based products, phenolics, improved hydrogen peroxide, hydrogen peroxide plus peracetic acid, quaternary ammonium compounds-exposure times at least 1 min) or 70–90 percent alcohol.	Noncritical patient care item (blood pressure cuff) or surface (bedside table) with no visible blood

[a] Modified from Rutala and Weber,[11–13] and Kohn et al.[186] Abbreviations: glut-glutaraldehyde; HP-hydrogen peroxide; PA-peracetic acid; OPA-ortho-phthalaldehyde; ppm-parts per million; EPA-Environmental Protection Agency; FDA-Food and Drug Administration; GI-gastrointestinal.

[b] Prions (such as Creutzfeldt-Jakob disease) exhibit an unusual resistance to conventional chemical and physical decontamination methods and are not readily inactivated by conventional sterilization procedures.[187]

[c] Consult the FDA cleared package insert for information about the cleared contact time and temperature, and see reference[25] for discussion why >2% glutaraldehyde products are used at a reduced exposure time (2% glutaraldehyde at 20 min, 20°C). Increasing the temperature using an automated endoscope reprocess (AER) will reduce the contact time (e.g., OPA 12 min at 20°C but 5 min at 25°C in AER). Exposure temperatures for some high-level disinfectants above vary from 20°C to 25°C; check FDA-cleared temperature conditions.[20] Tubing must be completely filled for high-level disinfection and liquid chemical sterilization. Material compatibility should be investigated when appropriate (e.g., HP and HP with PA will cause functional damage to endoscopes). Intermediate-level disinfectants destroy vegetative bacteria, mycobacteria, most viruses, most fungi but not spores and may include chlorine-based products, phenolics, and improved hydrogen peroxide). Intermediate-level disinfectants are not included in Table 8.1 as there is no device or surface for which intermediate-level disinfection is specifically recommended over low-level disinfection

enter sterile tissue or the vascular system be sterile because any microbial contamination could result in disease transmission. This category includes surgical instruments, cardiac and urinary catheters, and implants used in sterile body cavities. The items in this category should be purchased as sterile or be sterilized by steam sterilization if possible. If heat-sensitive, the object may be treated with ethylene oxide (ETO), hydrogen peroxide gas plasma, vaporized hydrogen peroxide, hydrogen peroxide vapor plus ozone or by liquid chemical sterilants/high-level disinfectants if other methods are unsuitable. Tables 8.1–3 summarize sterilization processes and liquid chemical sterilants and the advantages and disadvantages of each. With the exception of 0.2 percent peracetic acid (12 minutes at 50–56°C), the indicated exposure times for liquid chemical

Table 8.2 Summary of advantages and disadvantages of chemical agents used as chemical sterilants[1] or as high-level disinfectants (HLD)

Sterilization method	Advantages	Disadvantages
Peracetic acid/ hydrogen peroxide	• No activation required • Odor or irritation not significant	• Material compatibility concerns (lead, brass, copper, zinc) both cosmetic and functional • Limited clinical experience • Potential for eye and skin damage
Glutaraldehyde	• Numerous use studies published • Relatively inexpensive • Excellent material compatibility	• Respiratory irritation from glutaraldehyde vapor • Pungent and irritating odor • Relatively slow mycobactericidal activity (unless other disinfectants added such as phenolic, alcohol) • Coagulates blood and fixes tissue to surfaces • Allergic contact dermatitis
Hydrogen peroxide	• No activation required • May enhance removal of organic matter and organisms • No disposal issues • No odor or irritation issues • Does not coagulate blood or fix tissues to surfaces • Inactivates *Cryptosporidium* • Use studies published	• Material compatibility concerns (brass, zinc, copper, and nickel/silver plating) both cosmetic and functional • Serious eye damage with contact
Ortho-phthalaldehyde (OPA)	• Fast acting high–level disinfectant • No activation required • Odor not significant • Excellent materials compatibility claimed • Does not coagulate blood or fix tissues to surfaces claimed	• Stains protein gray (e.g., skin, mucous membranes, clothing, and environmental surfaces) • Limited clinical experience • More expensive than glutaraldehyde • Eye irritation with contact • Slow sporicidal activity • Anaphylactic reactions to OPA in bladder cancer patients with repeated exposure to OPA through cystoscopy
Peracetic acid	• Standardized cycle (e.g., Liquid Chemical Sterilant Processing System using peracetic acid, rinsed with extensively treated potable water) • Low temperature (50–55°C) liquid immersion sterilization • Environmental-friendly by-products (acetic acid, O_2, H_20) • Fully automated • Single-use system eliminates need for concentration testing • May enhance removal of organic material and endotoxin • No adverse health effects to operators under normal operating conditions • Compatible with many materials and instruments • Does not coagulate blood or fix tissues to surfaces • Sterilant flows through scope facilitating salt, protein, and microbe removal • Rapidly sporicidal • Provides procedure standardization (constant dilution, perfusion of channel, temperatures, exposure)	• Potential material incompatibility (e.g., aluminum anodized coating becomes dull) • Used for immersible instruments only • Biological indicator may not be suitable for routine monitoring • One scope or a small number of instruments can be processed in a cycle • More expensive (endoscope repairs, operating costs, purchase costs) than high-level disinfection • Serious eye and skin damage (concentrated solution) with contact • Point-of-use system, no sterile storage • An AER using 0.2% peracetic acid not FDA-cleared as sterilization process but HLD
Improved hydrogen	• No activation required • No odor	• Material compatibility concerns due to limited clinical experience

Table 8.2 (cont.)

Sterilization method	Advantages	Disadvantages
peroxide (2.0%); high-level disinfectant	• Nonstaining • No special venting requirements • Manual or automated applications • 12-month shelf life, 14-day reuse • 8 min at 20°C high-level disinfectant claim	• Antimicrobial claims not independently verified • Organic material resistance concerns due to limited data

Modified from Rutala and Weber,[10–13] Abbreviations: AER-automated endoscope reprocessor; FDA-Food and Drug Administration.
[1] All products effective in presence of organic soil, relatively easy to use, and have a broad spectrum of antimicrobial activity (bacteria, fungi, viruses, bacterial spores, and mycobacteria). The above characteristics are documented in the literature; contact the manufacturer of the instrument and sterilant for additional information. All products listed above are FDA-cleared as chemical sterilants except OPA, which is an FDA-cleared high-level disinfectant.

sterilants range from 3 to 12 hours.[20] Liquid chemical sterilants can be relied upon to produce sterility only if cleaning, which eliminates organic and inorganic material, precedes treatment and if proper guidelines as to concentration, contact time, temperature, and pH are met. Another limitation to sterilization of devices with liquid chemical sterilants is that the devices cannot be wrapped during processing in a liquid chemical sterilant; thus it is impossible to maintain sterility following processing and during storage. Furthermore, devices may require rinsing following exposure to the liquid chemical sterilant with water that, in general, is not sterile. Therefore, due to the inherent limitations of using liquid chemical sterilants in a nonautomated (or automated) reprocessor, their use should be restricted to reprocessing critical devices that are heat-sensitive and incompatible with other sterilization methods.

In contrast to semicritical items that have been associated with >100 outbreaks of infection,[6] critical items have rarely,[21] if ever, been associated with disease transmission. For example, any deviation from proper reprocessing (such as crevices associated with the elevator channel) of an endoscope could lead to failure to eliminate contamination with a possibility of subsequent patient-to-patient transmission due to a low or nonexistent margin of safety. This low (or nonexistent) margin of safety associated with endoscope reprocessing compares to the 17-$\log_{10}$ margin of safety associated with cleaning and sterilization of surgical instruments. (i.e., 12-$\log_{10}$ reduction via sterilization and at least a net 5-$\log_{10}$ reduction based on the microbial load on surgical instruments [2-logs][22] and microbial reduction via a washer disinfector[7-logs]).[23]

Semicritical Items

Semicritical items are those that come in contact with mucous membranes or nonintact skin. Respiratory therapy and anesthesia equipment, gastrointestinal endoscopes, bronchoscopes, laryngoscopes, endocavitary probes, prostate biopsy probes,[24] cystoscopes, hysteroscopes, infrared coagulation devices, and diaphragm fitting rings are included in this category. These medical devices should be free of all microorganisms (i.e., mycobacteria, fungi, viruses, bacteria), although small numbers of bacterial spores may be present. Intact mucous membranes, such as those of the lungs or the gastrointestinal tract, generally are resistant to infection by common bacterial spores but susceptible to other organisms such as bacteria, mycobacteria, and viruses. Semicritical items minimally require high-level disinfection using chemical disinfectants. Glutaraldehyde, hydrogen peroxide, orthophthalaldehyde (OPA), and peracetic acid with hydrogen peroxide, and chlorine are cleared by the Food and Drug Administration[20] and are dependable high-level disinfectants, provided the factors influencing germicidal procedures are met (Tables 8.1 and 8.2). The exposure time for most high-level disinfectants varies from 8 to 45 minutes at 20–25°C.[20]

Since semicritical equipment has been associated with reprocessing errors that result in patient lookback investigations and patient notifications, it is essential that control measures be instituted to prevent patient exposures.[7] Before new equipment (especially semicritical equipment, as the margin of safety is less than that for sterilization)[19] is used for patient care on more than one patient, reprocessing procedures for that equipment should be developed. Staff should receive training on the safe use and reprocessing of the equipment and be competency tested. For example, at the University of North Carolina Hospitals, to ensure patient-safe instruments, all staff that reprocess semicritical instruments (e.g., instruments that contact a mucous membrane such as vaginal probes, endoscopes, prostate probes) are required to attend a three-hour class on high-level disinfection of semicritical instruments. The class includes the rationale for and importance of high-level disinfection, discussion of high-level disinfectants and exposure times, reprocessing steps, monitoring minimum effective concentration, personal protective equipment, and the reprocessing environment (establishing "dirty-to-clean" flow). Infection prevention rounds or audits should be conducted annually in all clinical areas that reprocess critical and semicritical devices in order to ensure adherence to the reprocessing standards and policies. Results of infection prevention rounds should be provided to the unit managers, and deficiencies in reprocessing should be corrected and the corrective measures documented to infection prevention within two weeks.

Table 8.3 Summary of advantages and disadvantages of commonly used sterilization technologies

Sterilization method	Advantages	Disadvantages
Steam	• Nontoxic to patient, staff, environment • Cycle easy to control and monitor • Rapidly microbicidal • Least affected by organic/inorganic soils among sterilization processes listed • Rapid cycle time • Penetrates medical packing, device lumens	• Deleterious for heat-sensitive instruments • Microsurgical instruments damaged by repeated exposure • May leave instruments wet, causing them to rust • Potential for burns
Hydrogen peroxide gas plasma	• Safe for the environment and healthcare personnel • Leaves no toxic residuals • Cycle time is ≥28 minutes and no aeration necessary • Used for heat- and moisture-sensitive items since process temperature <50°C • Simple to operate, install (208 V outlet), and monitor • Compatible with most medical devices • Only requires electrical outlet	• Cellulose (paper), linens, and liquids cannot be processed • Endoscope or medical device restrictions based on lumen internal diameter and length (see manufacturer's recommendations) • Requires synthetic packaging (polypropylene wraps, polyolefin pouches) and special container tray • Hydrogen peroxide may be toxic at levels greater than 1 ppm TWA
100% ethylene oxide (ETO)	• Penetrates packaging materials, device lumens • Single-dose cartridge and negative-pressure chamber minimizes the potential for gas leak and ETO exposure • Simple to operate and monitor • Compatible with most medical materials	• Requires aeration time to remove ETO residue • ETO is toxic, a carcinogen, and flammable • ETO emission regulated by states, but catalytic cell removes 99.9% of ETO and converts it to CO_2 and H_2O • ETO cartridges should be stored in flammable liquid storage cabinet • Lengthy cycle/aeration time
Vaporized hydrogen peroxide; sterilization process	• Safe for the environment and healthcare personnel • It leaves no toxic residue; no aeration necessary • Cycle time, 55 min • Used for heat and moisture-sensitive items (metal and nonmetal devices)	• Medical devices restrictions based on lumen internal diameter and length-see manufacturer's recommendations, e.g., stainless steel lumen 1 mm diameter, 125 mm length • Not used for liquid, linens, powders, or any cellulose materials • Requires synthetic packaging (polypropylene) • Limited materials compatibility data • Limited clinical use and comparative microbicidal efficacy data
Hydrogen peroxide and ozone; sterilization process	• Safe for the environment and healthcare personnel • Uses dual sterilants, hydrogen peroxide and ozone • No aeration needed due to no toxic by-products • Compatible with common medical devices • Cycle time, 46 min • FDA-cleared for general instruments, single channel flexible endoscopes, and rigid and semirigid channeled devices	• Endoscope or medical device restrictions based on lumen internal diameter and length (see manufacturer's recommendations) • Limited clinical use (no published data on material compatibility/penetrability/organic material resistance) and limited microbicidal efficacy data • Requires synthetic packaging (polypropylene wraps, polyolefin pouches) and special container tray

Modified from Rutala and Weber.[10–13]
Abbreviations: ETO-ethylene oxide; CFC-chlorofluorocarbon, HCFC-hydrochlorofluorocarbon; FDA-Food and Drug Administration; TWA-time-weighted average.

Table 8.4 Summary of advantages and disadvantages of disinfectants used as low-level disinfectants

Disinfectant active	Advantages	Disadvantages
Alcohol	• Bactericidal, tuberculocidal, fungicidal, virucidal • Fast acting • Noncorrosive • Nonstaining • Used to disinfect small surfaces such as rubber stoppers on medication vials • No toxic residue	• Not sporicidal • Affected by organic matter • Slow acting against non-enveloped viruses (e.g., norovirus) • No detergent or cleaning properties • Not EPA registered • Damages some instruments (e.g., hardened rubber, deteriorates glue) • Flammable (large amounts require special storage) • Evaporates rapidly making contact time compliance difficult • Not recommended for use on large surfaces • Outbreaks ascribed to contaminated alcohol[188]
Sodium hypochlorite	• Bactericidal, tuberculocidal, fungicidal, virucidal • Sporicidal • Fast acting • Inexpensive (in dilutable form) • Not flammable • Unaffected by water hardness • Reduces biofilms on surfaces • Relatively stable (e.g., 50% reduction in chlorine concentration in 30 days)[189] • Used as the disinfectant in water treatment • EPA registered	• Reaction hazard with acids and ammonias • Leaves salt residue • Corrosive to metals (some ready-to-use products may be formulated with corrosion inhibitors) • Unstable active (some ready-to-use products may be formulated with stabilizers to achieve longer shelf life) • Affected by organic matter • Discolors/stains fabrics • Potential hazard is production of trihalomethane • Odor (some ready-to-use products may be formulated with odor inhibitors); irritating at high concentrations
Improved hydrogen peroxide	• Bactericidal, tuberculocidal, fungicidal, virucidal • Fast efficacy • Easy compliance with wet-contact times • Safe for workers (lowest EPA toxicity category, IV) • Benign for the environment • Surface compatible • Non-staining • EPA registered • Not flammable	• More expensive than most other disinfecting actives • Not sporicidal at low concentrations
Iodophors	• Bactericidal, mycobactericidal, virucidal • Not flammable • Used for disinfecting blood culture bottles	• Not sporicidal • Shown to degrade silicone catheters • Requires prolonged contact to kill fungi • Stains surfaces • Used mainly as an antiseptic rather than disinfectant
Phenolics	• Bactericidal, tuberculocidal, fungicidal, virucidal • Inexpensive (in dilutable form) • Nonstaining • Not flammable • EPA registered	• Not sporicidal • Absorbed by porous materials and irritated tissue • Depigmentation of skin caused by certain phenolics • Hyperbilirubinemia in infants when phenolic not prepared as recommended

Table 8.4 (cont.)

Disinfectant active	Advantages	Disadvantages
Quaternary ammonium compounds (e.g., didecyl dimethyl ammonium bromide, dioctyl dimethyl ammonium bromide)	• Bactericidal, fungicidal, virucidal against enveloped viruses (e.g., HIV) • Good cleaning agents • EPA registered • Surface compatible • Persistent antimicrobial activity when undisturbed • Inexpensive (in dilutable form)	• Not sporicidal • In general, not tuberculocidal and virucidal against non-enveloped viruses • High water hardness and cotton/gauze can make less microbicidal • A few reports documented asthma as result of exposure to benzalkonium chloride • Affected by organic matter • Multiple outbreaks ascribed to contaminated benzalkonium chloride[188]
Peracetic acid/hydrogen peroxide	• Bactericidal, fungicidal, virucidal, and sporicidal (e.g., *C. difficile*) • Active in the presence of organic material • Environmental friendly by-products (acetic acid, O_2, H_20) • EPA registered • Surface compatible	• Lack of stability • Potential for material incompatibility (e.g., brass, copper) • More expensive than most other disinfecting actives • Odor may be irritating

Modified from Rutala and Weber.[55] Abbreviations: EPA, Environmental Protection Agency; HIV, human immunodeficiency virus; m, minutes; s, seconds; if low-level disinfectant is prepared on-site (not ready-to-use), document correct concentration at a routine frequency

Although the most common method of performing high-level disinfection of contaminated endocavitary probes is by immersion in an FDA-cleared high-level disinfectant (e.g., glutaraldehyde), an alternative procedure for disinfecting the endocavitary and surface probes is a proprietary hydrogen peroxide mist system, which uses 35 percent hydrogen peroxide at 56°C with the probe reaching no more than 40°C (i.e., Trophon®). The effectiveness of this technology, which has been cleared by the FDA for high-level disinfection, has recently been published. The results demonstrated complete inactivation (>6-$\log_{10}$ reduction) of vancomycin-resistant *Enterococcus* (VRE) and a carbapenem-resistant *Klebsiella pneumoniae* strain, both in the presence and absence of 5 percent fetal calf serum (FCS). The Trophon® EPR system showed good, but not complete, inactivation of *Mycobacterium terrae* (5.2-$\log_{10}$ reduction for *M. terrae* with FCS, a 4.6-$\log_{10}$ reduction for *M. terrae* without FCS) and *Clostridium difficile* spores.[25]

Noncritical Items

Noncritical items are those that come in contact with intact skin but not mucous membranes. Intact skin acts as an effective barrier to most microorganisms; therefore, the sterility of items coming in contact with intact skin is "not critical." Examples of noncritical items are bedpans, blood pressure cuffs, crutches, bed rails, linens, bedside tables, patient furniture, and floors. In contrast to critical and some semicritical items, most noncritical reusable items may be decontaminated where they are used and do not need to be transported to a central processing area. There is virtually no documented risk of transmitting infectious agents to patients via noncritical items[26] when they are used as noncritical items and do not contact nonintact skin and/or mucous membranes. However, these items (e.g., bedside tables, bed rails) could potentially contribute to secondary transmission by contaminating hands of healthcare personnel or by contact with medical equipment that will subsequently come in contact with patients.[27] Tables 8.1 and 4 list several low-level disinfectants that may be used for noncritical items. Table 8.4 lists the advantages and disadvantages of the low-level disinfectants that are used on noncritical patient care items (e.g., blood pressure cuffs) and noncritical environmental surfaces. The exposure time for low-level disinfection of noncritical items is at least 1 minute.

Current Issues in Disinfection and Sterilization

Reprocessing of Endoscopes

Physicians use endoscopes to diagnose and treat numerous medical disorders. While endoscopes represent a valuable diagnostic and therapeutic tool in modern medicine and the incidence of infection associated with use has been reported as very low (about 1 in 1.8 million procedures),[28] more healthcare-associated outbreaks have been linked to contaminated endoscopes than to any other reusable medical device.[6,8] Additionally, endemic transmission of infections associated with GI endoscopes may go unrecognized for several reasons, including: inadequate surveillance of outpatient procedures; long lag time between colonization and infection; low frequency of infection; and pathogens are the "usual" enteric flora. In addition, the risk of some procedures might be lower than others

(e.g., colonoscopy versus ERCP) where normally sterile areas are contaminated in the latter. In order to prevent the spread of healthcare-associated infections, all heat-sensitive endoscopes (e.g., GI endoscopes, bronchoscopes, nasopharyngoscopes) must be properly cleaned and, at a minimum, subjected to high-level disinfection following each use. High-level disinfection can be expected to destroy all microorganisms, although, when high numbers of bacterial spores are present, a few spores may survive.

Recommendations for the cleaning and disinfection of endoscopic equipment have been published and should be strictly followed.[13,29,30] Unfortunately, audits have shown that personnel often do not adhere to guidelines on reprocessing,[5] and outbreaks of infection continue to occur.[3,6,8,31] Additionally, recent studies have suggested that current reprocessing guidelines are not sufficient to ensure successful decontamination.[32] In order to minimize patient risks and ensure that reprocessing personnel are properly trained, there should be initial and annual competency testing for each individual who is involved in reprocessing endoscopic instruments.[13,29,30]

In general, endoscope disinfection or sterilization with a liquid chemical sterilant or high-level disinfectant involves five steps after leak testing: 1) clean – mechanically clean internal and external surfaces, including brushing internal channels and flushing each internal channel with water and an enzymatic cleaner or detergent; 2) disinfect – immerse endoscope in high-level disinfectant (or chemical sterilant) and perfuse disinfectant (which eliminates air pockets and ensures contact of the germicide with the internal channels) into all accessible channels such as the suction/biopsy channel and the air/water channel; ensure exposure for the time recommended for the specific product; 3) rinse – rinse the endoscope and all channels with sterile water, filtered water (commonly used with automated endoscope reprocessors), or tap water; 4) dry – rinse the insertion tube and inner channels with alcohol and dry with forced air after disinfection and before storage; and 5) store – store the endoscope in a way that prevents recontamination and promotes drying (e.g., hung vertically).

Occasionally, there are instances where the scientific literature and recommendations from professional organizations regarding the use of disinfectants and sterilants may differ from the manufacturer's label claim. One example is the contact time used to achieve high-level disinfection with 2 percent glutaraldehyde. Based on requirements by the FDA (which regulates liquid sterilants and high-level disinfectants used on critical and semicritical medical devices), manufacturers test the efficacy of their germicide formulations under worst-case conditions (i.e., using the minimum recommended concentration of the active ingredient) and in the presence of organic soil (typically 5 percent serum). The soil is used to represent the organic load to which the device is exposed during actual use and that would remain on the device in the absence of cleaning. These stringent test conditions are designed to provide a margin of safety by ensuring that the contact conditions for the germicide provide complete elimination of the test bacteria (e.g., 10^5 to 10^6 *M. tuberculosis* organisms in organic soil and dried on an endoscope) inoculated into the most difficult areas for the disinfectant to penetrate and in the absence of cleaning. However, the scientific data demonstrate that *M. tuberculosis* levels can be reduced by at least 8-$\log_{10}$ with cleaning (4-$\log_{10}$) followed by chemical disinfection for 20 minutes at 20°C (4 to 6-$\log_{10}$).[13,20,29,33] Because of these data, professional organizations (at least 14 worldwide) that have endorsed an endoscope reprocessing guideline recommend contact conditions of 20 minutes at 20°C (or less than 20 minutes outside the United States) with 2 percent glutaraldehyde to achieve high-level disinfection that differs from that of the manufacturer's label.[29] It is important to emphasize that the FDA tests do not include cleaning, a critical component of the disinfection process. When cleaning has been included in the test methodology, use of 2 percent glutaraldehyde for 20 minutes has been demonstrated to be effective in eliminating all vegetative bacteria. Other high-level disinfectants commonly used for reprocessing endoscopes and other semicritical items include orthophthalaldehyde, accelerated hydrogen peroxide and peracetic acid.

Outbreaks of Carbapenem-Resistant *Enterobacteriaceae* Infection Associated with Duodenoscopes: What Can We Do to Prevent Infections?

In the past three years, multiple reports of outbreaks have led the FDA, the CDC, and national news organizations to raise awareness among the public and healthcare professionals that the complex design of duodenoscopes (used primarily for ERCP) may impede effective reprocessing. Several recent publications have associated multidrug-resistant (MDR) bacterial infections, especially due to carbapenem-resistant *Enterobacteriaceae* (CRE), in patients who have undergone ERCP with reprocessed duodenoscopes.[3,4,19,31,34] Unlike other endoscope outbreaks,[6] these recent outbreaks occurred even when the manufacturer's instructions and professional guidelines were followed correctly.[3,4]

The key concern raised by these outbreaks is that current reprocessing guidelines are not adequate to ensure a patient-safe GI endoscope (one devoid of potential pathogens) as the margin of safety associated with reprocessing endoscopes is minimal or non-existent. There are at least two (and maybe three) reasons for this reprocessing failure and why outbreaks continue to occur. First, studies have shown that the internal channel of GI endoscopes, including duodenoscopes, may contain 10^{7-10} (7–10-$\log_{10}$) enteric microorganisms.[35,36] Investigations have demonstrated that the cleaning step in endoscope reprocessing results in a 2–6-$\log_{10}$ reduction of microbes and the high-level disinfection step results in another 4–6-$\log_{10}$ reduction of mycobacteria for a total 6–12-$\log_{10}$ reduction of microbes.[33,35,36] Thus, the margin of safety associated with cleaning and high-level disinfection of GI endoscopes is minimal or non-existent (level of contamination: 4-$\log_{10}$ [maximum contamination, minimal cleaning/HLD] to -5-$\log_{10}$ [minimum contamination, maximum cleaning/HLD]). Therefore, any deviation from proper reprocessing (such as crevices associated with the elevator channel) could lead to failure to eliminate contamination with a possibility of subsequent patient-to-patient transmission. This low (or non-existent) margin of safety associated with endoscope reprocessing

compares to the 17-$\log_{10}$ margin of safety associated with cleaning and sterilization of surgical instruments.[19]

Second, GI endoscopes not only have heavy microbial contamination (10^7–10^{10} bacteria) but they are complex with long, narrow channels; right-angle turns; difficult to clean and disinfect components (e.g., elevator channel). The elevator channel in duodenoscopes is unique to side-viewing endoscopes. It has a separate channel and provides orientation of catheters, guide wires, and accessories into the endoscopic visual field.[19] This channel is complex in design and has crevices that are difficult to access with a cleaning brush and may impede effective reprocessing.[37] Based on this and other recent studies, it is likely that MDR pathogens are acting as a "marker" or "indicator" organism for ineffective reprocessing of the complex design of duodenoscopes, which is an infectious risk to patients.

Third, biofilms could impact endoscope reprocessing failure and continued endoscope-related outbreaks.[38] Biofilms are multilayered bacteria plus exopolysaccharides that cement cells to surfaces. They develop in a wet environment. If reprocessing is performed promptly after use and the endoscope is dry, the opportunity for biofilm formation is minimal.[39,40] However, the formation of endoscopic biofilm during clinical practice may be related to reuse of reprocessing methods such as reuse of detergent, manual cleaning, and incomplete drying.[41] Ideally, reprocessing should be initiated within an hour of use; however, there are no evidence-based guidelines on delayed endoscope reprocessing.[42] It is unclear if biofilms contribute to failure of endoscope reprocessing.

What should we do now? Unfortunately, there is currently no single, simple and proven technology or prevention strategy that hospitals can use to guarantee patient safety. Of course, we must continue to emphasize the enforcement of evidenced-based practices, including equipment maintenance and routine audits with at least yearly competency testing of reprocessing staff.[13,29,30] All reprocessing personnel must be knowledgeable and thoroughly trained on the reprocessing instructions for duodenoscopes. This includes the new recommendations to use a small bristle cleaning brush and for additional flushing and cleaning steps of the elevator channel (http://medical.olympusamerica.com/sites/default/files/pdf/150326_TJF-Q180 V_Customer_letter.pdf). Although these steps were described as "validated," no public data are available on the ability of these new cleaning recommendations to yield an ERCP scope devoid of bacteria. However, we must do more; otherwise, additional outbreaks will likely continue. For example, all hospitals that reprocess duodenoscopes should select one of the enhanced methods for reprocessing duodenoscopes. These enhanced methods have been priority ranked, with the first providing the greatest margin of safety.[19] They include: 1) ethylene oxide (ETO) sterilization after high-level disinfection with periodic microbiologic surveillance; 2) double high-level disinfection with periodic microbiologic surveillance; 3) high-level disinfection with endoscope quarantine until negative culture results are returned; 4) liquid chemical sterilant processing system using peracetic acid (rinsed with extensively treated potable water) with periodic microbiologic surveillance; 5) other FDA-cleared low-temperature sterilization technology (provided material compatibility and sterilization validation testing has been performed using the sterilizer and endoscope) after high-level disinfection, with periodic microbiologic surveillance; and 6) high-level disinfection with periodic microbiologic surveillance. These supplemental measures to enhance duodenoscope reprocessing made in May–June 2015[19] were reinforced by the FDA in August 2015.[37] UNC Hospitals has chosen ETO sterilization after high-level disinfection with periodic microbiologic surveillance as its primary reprocessing method for duodenoscopes; if the ETO sterilizer is not available, then double high-level disinfection with periodic microbiologic surveillance is used.[43]

Role of the Environment in Disease Transmission

There is excellent evidence in the scientific literature that environmental contamination plays an important role in the transmission of several key healthcare-associated pathogens including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), *Acinetobacter* spp, norovirus, and *Clostridium difficile*.[44–47] All these pathogens have been demonstrated to persist in the environment for days (in some cases months), frequently contaminate the environmental surfaces in rooms of colonized or infected patients, transiently colonize the hands of healthcare personnel, be transmitted by healthcare personnel, and cause outbreaks in which environmental transmission was deemed to play a role. Importantly, a study by Stiefel et al. demonstrated that contact with the environment was just as likely to contaminate the hands of healthcare personnel as was direct contact with the patient.[48] Further, admission to a room in which the previous patient had been colonized or infected with MRSA, VRE, *Acinetobacter* or *C. difficile*, has been shown to be a risk factor for the newly admitted patient to develop colonization or infection.[49–51]

Monitoring and Improving the Thoroughness of Cleaning/Disinfection

The cleaning and disinfection of noncritical surfaces in hospitals is essential for reducing microbial contamination and healthcare-associated infections.[52–55] A recent Agency for Healthcare Research and Quality (AHRQ) systematic review offers an overview of monitoring modalities.[52,53] These include: visual inspection; microbiologic methods; fluorescent markers; and adenosine triphosphate (ATP) assays. At present, polymerase chain reaction–based technology has a limited role for assessing environmental contamination, is investigational, and does not differentiate between the presence of viable and nonviable microorganisms.[53]

Hospital cleanliness continues to attract patient attention and in the United States it is still primarily assessed via visual cleanliness (e.g., dust, organic debris) of surfaces, which is not a reliable indicator of microbial contamination.[56,57] ATP bioluminescence measures organic debris (each unit has its own reading scale, <250–500 relative light units-RLU) but is not a reliable indicator of microbial contamination.[53] A validation study of ATP, used to audit cleaning of flexible endoscope channels, demonstrated that

an endoscope assessed as clean by ATP (<250 RLU) could be contaminated with a million (10^6) microorganisms.[58] Fluorescent marking is done with a transparent, easily cleaned, environmentally stable marking solution that fluoresces when exposed to an ultraviolet (UV) light. It is applied by the infection preventionist or environmental service manager after the patient is discharged. Its application is unknown to the environmental service staff. After environmental service cleaning, the markings are reassessed by the infection preventionist or environmental service manager and the thoroughness of cleaning monitored is provided via immediate feedback to the person(s) cleaning/disinfecting the room (e.g., 4 of 10 marker surfaces wiped, 40% compliance with thoroughness of cleaning/disinfection). Microbiologic methods have also been used to evaluate microbial contamination of surfaces and can quantify microbial burden or be pathogen-specific. These methods however can be costly, have significant turnaround times for results, and require substantial microbiology laboratory resources and personnel. While there are no accepted criteria for defining a surface as "clean" using microbiologic methods, some investigators have suggested that microbial contamination should be 2.5 CFU/cm^2 to <5 CFU/cm^2.[59,60] Studies have shown that this level of contamination may be easily achievable, as the microbial burden of room surfaces in one hospital went from 57 CFU/Rodac (2.3 CFU/cm^2) to 8 CFU/Rodac (0.3 CFU/cm^2) prior to and after cleaning.[61] Based upon surface cleaning/disinfection practices that are used in the United States, a revised stricter pass benchmark may need to be considered (<1 CFU/cm^2).

Studies have demonstrated suboptimal cleaning as measured by aerobic colony counts or by use of ATP bioluminescence and fluorescent markers.[49,57] For example, Carling and colleagues assessed the thoroughness of terminal cleaning in the patient's immediate environment in 23 acute-care hospitals (1,119 patient rooms) by using UV light–visible fluorescent markers.[62] The overall thoroughness of cleaning, expressed as a percent of surfaces evaluated, was 49 percent (range for all hospitals, 35 percent to 81 percent). Using a similar design, Carling and associates assessed the environmental cleaning in intensive care unit rooms in 16 hospitals (2,320 objects) and demonstrated that only 57.1 percent of sites were cleaned following discharge of the room's occupant.[63] A study using ATP bioluminescence assays and aerobic cultures demonstrated that medical equipment frequently had not been disinfected as per protocol.[64]

ATP bioluminescence and fluorescent markers are preferred to aerobic plate counts since they provide an immediate assessment of cleaning effectiveness. Two recent reviews reported ATP as a quick and objective monitoring method; however, it was poorly standardized with low specificity and sensitivity in detecting bacteria.[53,65] In a comparison study of the three methods to assess cleaning, we found that the fluorescent marker was the most useful tool in determining how thoroughly a surface was cleaned, as it demonstrated better correlation with microbiological data compared to ATP. For example, compared to microbiological data (62.5 CFU/Rodac), 72 percent of surfaces were classified as clean with fluorescent markers. In contrast, compared to ATP, 27 percent of surfaces were classified as clean with fluorescent markers (Rutala, Gergen, Sickbert-Bennett, Kanamori, Huslage, Weber, unpublished results, 2015).

Improving Room Cleaning and Disinfection, and Demonstrating the Effectiveness of Surface Decontamination in Reducing Healthcare-Associated Infections

Investigators have reported that interventions aimed at improving surface cleaning and disinfection reduced healthcare-associated infections.[54] Such interventions have generally included multiple components: disinfectant product substitutions; and interventions to improve the effectiveness of cleaning and disinfection (e.g., improved housekeeper education, monitoring the thoroughness of cleaning [e.g., by use of ATP assays or fluorescent markers] with feedback of performance to environmental service staff, and/or use of cleaning checklists).[54,66–68] Healthcare facilities must also allow adequate time for room cleaning and disinfection to ensure adherence to all steps recommended by institutional policies and professional organization guidelines. We have found that collaboration between infection prevention and environmental services staff, nursing, and management is critical to an effective environmental cleaning program. This includes ensuring that environmental services staff recognize the significance and relationship of adhering to proper work procedures to reduction of microbial contamination. The assignment of cleaning responsibility (e.g., medical equipment to be cleaned by nursing; environmental surfaces to be cleaned by environmental service) is also important to ensure all objects and surfaces in a patient room are decontaminated, especially the surfaces of medical equipment (e.g., cardiac monitors). Improved environmental cleaning has been demonstrated to reduce environmental contamination with VRE,[68] MRSA,[69] and *C. difficile*.[70] Further, all studies have only focused improvement on a limited number of "high-risk" objects. Thus, a concern of published studies is that they have only demonstrated improved cleaning of a limited number of "high-risk" objects (or, as commonly referred to in the literature, "high-touch objects") not an improvement in the overall thoroughness of room decontamination, which is the objective.

To our knowledge, only one study has objectively evaluated what constitutes a "high-touch object" in a patient room, and no study has demonstrated epidemiologically what constitutes a "high-risk object." Examples of high-touch objects include bed rails, intravenous (IV) poles, call buttons, door knobs, floors, and bathroom facilities;[53] however, a study demonstrated that "high-touch objects" in an ICU were the bed rail, bed surface, and supply cart, while the "high-touch surfaces" in a patient ward were the bed rail, over-bed-table, IV pump, and bed surface.[71] Importantly, the level of microbial contamination of room surfaces was statistically similar regardless of how often they were touched before and after cleaning. Until research identifies which objects and surfaces pose the greatest risk of pathogen transmission, all noncritical surfaces that are touched must be cleaned/disinfected.[61]

"No-touch" (or Automated) Methods for Room Decontamination

As noted above, multiple studies have demonstrated that environmental surfaces and objects in rooms are frequently not properly cleaned and these surfaces may be important in transmission of healthcare-associated pathogens. Further, while interventions aimed at improving cleaning thoroughness have been demonstrated to be effective, many surfaces remain inadequately cleaned and therefore, potentially contaminated. For this reason, several manufacturers have developed room disinfection units that can decontaminate environmental surfaces and objects. These "no-touch" systems generally use one of two methods; either UV light or hydrogen peroxide vapor/mist.[47] These technologies supplement, but do not replace, standard cleaning and disinfection because surfaces must be physically cleaned of dirt and debris.

Ultraviolet Light for Room Decontamination

UV radiation has been used for the control of pathogenic microorganisms in a variety of applications, such as control of legionellosis, as well as disinfection of air, surfaces, and instruments.[47,72] At certain wavelengths, UV light will break the molecular bonds in DNA, thereby destroying the organism. UV radiation has peak germicidal effectiveness in the wavelength range of 240–280 nm. Mercury gas bulbs emit UV-C at 254 nm, whereas xenon gas bulbs produce a broad spectrum of radiation that encompasses the UV (100–280 nm) and the visible (380–700 nm) electromagnetic spectra.[73] The efficacy of UV radiation is a function of many different parameters such as dose, distance, direct or shaded exposure, exposure time, lamp placement, pathogen, carrier or surface tested, inoculum method, organic load, and orientation of carriers (e.g., parallel vs perpendicular). Data demonstrate that several UV systems have effectiveness (e.g., eliminate >3-$\log_{10}$ vegetative bacteria [MRSA, VRE, *Acinetobacter baumannii*] and >2.4-$\log_{10}$ *C. difficile*) at relatively short exposure times (e.g., 5–25 minutes for bacteria, 10–60 minutes for *C. difficile* spores).[73–75] The studies also demonstrated reduced effectiveness when surfaces were not in direct line-of-sight.[73–77]

Hydrogen Peroxide (HP) Systems for Room Decontamination

Several systems that produce hydrogen peroxide (e.g., HP vapor, aerosolized dry mist HP) have been studied for their ability to decontaminate environmental surfaces and objects in hospital rooms. Hydrogen peroxide vapor (HPV) has been used increasingly for the decontamination of rooms in healthcare.[78–88] Studies have demonstrated that HP systems are a highly effective method for eradicating various pathogens (e.g., MRSA, *M. tuberculosis, Serratia, C. difficile* spores, *C. botulinum* spores) from rooms, furniture, and equipment.

Comparison of UV Irradiation versus Hydrogen Peroxide for Room Decontamination

UV devices and hydrogen peroxide systems have their own advantages and disadvantages[47] and there is now ample evidence that these "no-touch" systems can reduce environmental contamination with healthcare-associated pathogens and reduce HAIs (see Table 8.6).[89] However, each specific system should be studied and its efficacy demonstrated before being introduced into healthcare facilities. The main advantage of both types of units is their ability to achieve substantial reductions in vegetative bacteria. Another advantage is their ability to substantially reduce *C. difficile* spores as low-level disinfectants (such as quaternary ammonium compounds) have only limited or no measurable activity against spore-forming bacteria.[55] Both systems are residual-free, and they decontaminate all exposed surfaces and equipment in the room.

The major disadvantages of both decontamination systems are the substantial capital equipment costs, the need to remove personnel and patients from the room, thus limiting their use to terminal room disinfection (must prevent/minimize exposure to UV and HP), the staff time needed to transport the system to rooms to be decontaminated and monitor its use, the need to physically clean the room of dust and debris, and the sensitivity to use parameters. There are several important differences between the two systems. The UV-C systems offer faster decontamination, which reduces the down time of the room before another patient can be admitted. The HP systems have been demonstrated to be more effective in eliminating spore-forming organisms. Whether this improved sporicidal activity is clinically important is unclear, as studies have demonstrated that although environmental contamination is common in the rooms of patients with *C. difficile* infection, the level of contamination is relatively low (also true for MRSA, VRE). Importantly, the UV and HP systems were demonstrated to reduce the incidence of healthcare-associated infections.[78,90–92] Based on data that demonstrated a reduction in colonization and/or infection with healthcare-associated pathogens with these technologies, we recommend that they should be used for terminal room decontamination of rooms of patients on contact precautions. Since different UV and hydrogen peroxide systems vary substantially, infection preventionists should review the peer-reviewed literature and choose only devices with demonstrated bactericidal capability as assessed by carrier tests and/or the ability to disinfect actual patient rooms. Ultimately, one would select a device that also has demonstrated the ability to reduce HAIs.[89]

Other Disinfection and Sterilization Issues

Assessing Risk to Patients from Disinfection and Sterilization Failures

Disinfection and sterilization are critical components of infection control. Unfortunately, breaches of disinfection and sterilization guidelines are not uncommon. Patient notifications due to improper reprocessing of semicritical (e.g., endoscopes) and critical medical instruments have occurred regularly.[7] This referenced article also provides a method for assessing patient risk for adverse events, especially infection. Use of a 14-step algorithm (Table 8.5) can guide an institution in managing potential disinfection and sterilization failures.[7]

Human Papilloma Virus

Human papilloma virus (HPV) is an extremely common sexually acquired pathogen and is considered the cause of cervical

Table 8.5 Protocol for exposure investigation after failure to follow disinfection and sterilization principles

1. Confirm disinfection or sterilization reprocessing failure
2. Embargo any improperly disinfected or sterilized items
3. Do not use the questionable disinfection or sterilization unit (e.g., sterilizer, automated endoscope reprocessor)
4. Inform key stakeholders
5. Conduct a complete and thorough evaluation of the cause of the disinfection/sterilization failure
6. Prepare a line list of potentially exposed patients
7. Assess whether disinfection or sterilization failure increases patient risk for infection
8. Inform expanded list of stakeholders of the reprocessing issue
9. Develop a hypothesis for the disinfection or sterilization failure and initiate corrective action
10. Develop a method to assess potential adverse patient events
11. Consider notification of state and federal authorities
12. Consider patient notification
13. Develop long-term follow-up plan
14. Perform after-action report

Modified from Rutala.[7]

cancer. A 2014 paper demonstrated that the FDA-cleared high-level disinfectants (i.e., glutaraldehyde, OPA) tested did not inactivate HPV, a non-enveloped virus.[93] These findings are inconsistent with many papers in the peer-reviewed literature, which demonstrates that HLD such as OPA and glutaraldehyde inactivate non-enveloped viruses such as HAV, polio, adenovirus, and norovirus. Since the HLD are commonly used to disinfect endocavitary probes (e.g., vaginal probes, rectal probes), there is an urgency to corroborating these data. In a conversation with CDC staff regarding this issue, it was determined that hospitals should continue to use the FDA-cleared high-level disinfectants consistent with the manufacturers' instructions until the data can be corroborated. Data have demonstrated the activity of a hydrogen peroxide mist device to inactivate HPV.[94]

Do Not Reuse Single-Use Devices

The Department of Justice and the FDA have joined forces in prosecuting healthcare providers that reuse single-use devices. For example, one physician was criminally prosecuted for reusing needle guides meant for single use during prostate procedures. These prosecutions are based on conspiracy to commit adulteration and Medicare fraud. Third-party reprocessing is allowed by the FDA as the reprocessor is considered the device manufacturer as defined under 21 CFR Part 820.

Storage of Semicritical Items

In 2011, The Joint Commission recommended that laryngoscope blades be packaged in a way that prevents recontamination. Examples of compliant storage include, but are not limited to, a peel pouch or a closed plastic bag. Examples of noncompliant storage include unwrapped blades in an anesthesia drawer as well as an unwrapped blade on top of or within a code cart. The packaging not only prevents recontamination but also distinguishes a processed from a nonprocessed semicritical item such as a speculum laryngoscope blade, or endoscope. The use of a tagging system, in both inpatient and outpatient facilities,[95] that separates processed from nonprocessed items minimizes the risk that a nondisinfected, semicritical device would be used and potentially lead to cross-transmission of a pathogen.[7] This could involve a tag (e.g., green tag-patient ready, red tag-requires reprocessing) for GI endoscopes or a plastic sheath or plastic-paper peel pouch (e.g., endocavitary probes). Ideally, hospitals and ambulatory care facilities (as appropriate) should develop a strategy (e.g., tagging, storage covers for patient-ready devices) that prevents patient exposures to contaminated devices.

Immersion vs. Perfusion of Channel Scopes such as Cystoscopes

In the United States, it is estimated that over 4 million cystoscopies are performed each year. Cystoscopy is a diagnostic procedure that uses an endoscope especially designed to examine the bladder, lower urinary tract, and prostate gland or is used to collect urine samples, perform biopsies, and remove small stones. A flexible or rigid scope can be used to carry out the procedure. Since the procedure, and other channeled scopes (e.g., hysteroscopes, some nasopharyngoscopes) involves a medical device in contact with the patient's mucous membranes, it is considered a semicritical device that must minimally be high-level disinfected.

We recently evaluated the disinfection of cystoscopes, and our results demonstrated that disinfection (i.e., a reduction in bacterial load of greater than 7-$\log_{10}$ CFU) did not occur unless the channel was actively perfused with the glutaraldehyde

Table 8.6 Clinical trials using UV or HP devices for terminal room disinfection to reduce healthcare-associated infections

Author, year	Design	Setting	Modality tested	Pathogen(s)	Outcome (HAI)	Assessment of HH compliance	Assessment of EVS cleaning	Other HAI prevention initiatives
Boyce, 2008	Before-after (CDI high incidence wards)	Community hospital	HPV (Bioquell)	CDI	2.28 to 1.28 per 1,000 Pt-days ($p = 0.047$)	No	No	NA
Cooper, 2011	Before-after (2 cycles)	Hospitals	HPV (NS)	CDI	Decreased cases (incidence NS)	No	No	Yes
Levin, 2013	Before-after	Community hospital	UV-PX, Xenex	CDI	9.46 to 4.45 per 10,000 Pt-days ($p = 0.01$)	No	No	Yes
Passaretti, 2013	Prospective cohort (comparison of MDRO acquisition; admitted to rooms with or without HPV decontamination)	Academic center	HPV (Bioquell)	MRSA VRE CDI MDRO-all	2.3 to 1.2 ($p = 0.30$) 7.2 to 2.4 ($p < 0.01$) 2.4 to 1.0 ($p = 0.19$) 12.6 to 6.2 per 1,000 Pt-days ($p < 0.01$)	No	No	No
Manian, 2013	Before-after	Community hospital	HPV (Bioquell)	CDI	0.88 to 0.55 cases per 1,000 Pt-days ($p < 0.0001$)	Yes	No	No
Hass, 2014	Before-after	Academic center	UV-PX, Xenex	CDI MRSA VRE MDRO-GNB Total	0.79 to 0.65 per 1,000 Pt-days ($p = 0.02$) 0.45 to 0.33 per 1,000 Pt-days ($p = 0.007$) 0.90 to 0.73 per 1,000 Pt-days ($p = 0.002$) 0.52 to 0.42 per 1,000 Pt-days ($p = 0.04$) 2.67 to 2.14 per 1,000 Pt-days ($p < 0.001$)	No	Yes	Yes
Mitchell, 2014	Before-after	Acute care hospital	Dry hydrogen vapor (Nocosray)	MRSA (colonization and infection)	9.0 to 5.3 per 10,000 Pt-days ($p < 0.001$)	Yes	No	Yes
Miller, 2015	Before-after	Urban hospital	UV-PX, Xenex	CDI	23.3 to 8.3 per 10,000 Pt-days ($p = 0.02$)	No	No	Yes

Nagaraja, 2015	Before-after	Academic center	UV-PX, Xenex	CDI	1.06 to 0.83 per 1,000 Pt-days (p = 0.06)	No	No	No
Pegues, 2015	Before-after	Academic center	CV-C (Optimum)	CDI	30.34 to 22.85 per 10,000 Pt-days (IRR=0.49, 95% CI 0.26–0.94, p = 0.03)	Yes	Yes	No
Anderson, 2015	RCT	9 hospitals	UV-C (Tru-D)	MRSA, VRE, CDI	51.3 to 33.9 per 10,000 Pt-days (p = 0.036)	Yes	Yes	No

Modified from Weber et al.[89] CDI, *Clostridium difficile* infections; EVS, environmental service; GNB, Gram-negative bacteria; HAI, healthcare-associated infections; HH, hand hygiene; HP, hydrogen peroxide; HPV, hydrogen peroxide vapor; MDRO, multidrug-resistant organism; MRSA, methicillin-resistant *Staphylococcus aureus*; NS, not stated; Pt, patient; UV, ultraviolet light; UV-C, ultraviolet light-C; UV-PX, ultraviolet light, pulsed xenon device; VRE, vancomycin-resistant enterococci

disinfectant. In fact, failure to perfuse the channel led to only minimal, if any, reduction in bacterial contamination. However, complete inactivation of 10^8 CFU of both VRE and CRE was achieved when the channel was actively perfused. It appears that no high-level disinfectant entered the channel unless it was actively perfused, as the level of microbial contamination was not reduced by immersion.[96] This occurs because the air pressure in the channel is stronger than the fluid pressure at the fluid-air interface. Recommendations are provided for cystoscope high-level disinfection and include actively perfusing the device while immersed in the high-level disinfectant.[96] Unfortunately, some cystoscope reprocessing recommendations published in the literature are incorrect. For example, authors have recommended complete immersion of the cystoscope into the high-level disinfectant but did not mention perfusion of the high-level disinfectant into the channel.[97]

Clostridium difficile: Role of the Environment and Prevention Strategies

C. difficile is an enteric bacterial pathogen that may cause an infection ranging from mild diarrhea to life-threatening pseudomembraneous colitis. Although *C. difficile* infection (CDI) has been frequently encountered in hospitals and long-term care facilities for many years, rates in the United States have doubled between 2000 and 2009,[98] and now it is the leading cause of HAIs.[99] This trend has been associated with the emergence of a highly virulent strain of *C. difficile* that produces greater quantities of toxins A and B, and a separate binary toxin. To effectively manage this disease and keep informed of its changing epidemiology, optimal strategies in CDI surveillance, diagnosis, treatment, antibiotic stewardship, and effective infection prevention are warranted.[98,100,101]

C. difficile shares common epidemiologic characteristics with other epidemiologically important pathogens such as MRSA and VRE. Both the skin and environment become contaminated with *C. difficile*, and healthcare personnel hands become contaminated by touching the environment around the patient or the patient directly.[102,103] Since *C. difficile* spores are less susceptible to commonly used disinfectants and antiseptics, there are special prevention strategies employed, such as enhanced environmental cleaning/disinfection of the rooms housing CDI patients (e.g., at least daily disinfection of environmental surfaces).[103,104]

Several factors facilitate the environmental route of transmission of *C. difficile*.[46] First, the organism contaminates the environment of patients colonized or infected with *C. difficile*. Second, the *C. difficile* spore can survive in the hospital environment for up to 5 months.[105] On dry surfaces, vegetative *C. difficile* bacteria die rapidly (within 15 minutes of exposure to room air), due to desiccation, whereas they can remain viable for up to 6 hours on moist surfaces in room air.[106] These data suggest that moist surfaces in hospitals (e.g., toilets, sinks, moist dressings) may provide a suitable environment for vegetative *C. difficile* to persist for several hours.[106] The spore is also more resistant to the effect of the gastric acids in the stomach.[107] Thus, the spore is the bacterial form more likely important in disease transmission and that must be inactivated and/or removed by surface disinfection. Since *C. difficile* spores are more likely involved in disease transmission than are vegetative bacteria, a claim based only on the vegetative bacteria would likely be potentially misleading and be incompletely effective in preventing disease transmission. Thus, the Environmental Protection Agency (EPA) letter preventing claims based on the inactivation of vegetative bacteria is both soundly based in science and judicious public health policy (F. Sanders, EPA, written communication, September 2008). Third, since spores are relatively resistant to inactivation by low-level disinfectants, a higher level of disinfection is needed to prevent environmental spread. At present, there are 34 products registered by the EPA (www.epa.gov/oppad001/list_k_clostridium.pdf) to kill *C. difficile* spores. Most are chlorine-based disinfectants, but some include hydrogen peroxide plus peracetic acid, or peracetic acid with silver.

Role of the Environment. Healthcare personnel are the most likely mode of transmission of *C. difficile* to patients; healthcare personnel's hands may become contaminated by either direct patient contact or contact with a contaminated environment. Additionally, a patient can unintentionally self-inoculate by touching a contaminated surface and bringing their hand to their mouth. *C. difficile* contamination has been found in rooms of patients that are colonized or infected with *C. difficile* at a frequency of 10 to approximately 50 percent but the level of contamination is usually low.[104] For example, *C. difficile* contamination has been found on 49 percent of sites in rooms occupied by patients with *C. difficile* infection and 29 percent of sites in rooms occupied by asymptomatic carriers.[108] Greater hospital room square footage is a significant risk factor for nosocomial CDI, which highlights the importance of the hospital environment in CDI transmission and the need for improved environmental cleaning interventions.[109] Contamination of the environment and patient care equipment occurs through fecal shedding or through the contaminated hands of the patient or healthcare personnel.[107] There are several observations that demonstrate that contaminated environmental surfaces are important in the acquisition of *C. difficile*, including the fact that the incidence of CDI is significantly associated with the proportion of culture-positive environmental sites, and that there is epidemiological evidence that the use of sodium hypochlorite for environmental cleaning may significantly reduce the incidence of CDI.[54] Data also demonstrate that the proportion of positive personnel hand-specimen cultures was strongly correlated with the density of environmental contamination.[110] For example, the proportion of positive hand-specimen cultures was 0 percent when the environmental contamination rate was 0–25 percent, 8 percent when environmental contamination was 25–50 percent, and 36 percent when environmental contamination was >50 percent.[111] Additionally, the use of an effective antimicrobial (e.g., sodium hypochlorite) significantly decreased environmental contamination rates in rooms of patients with *C. difficile*.[54] For example, Eckstein observed 9 of 10 (90 percent) rooms of patients with CDI had one or more positive cultures

prior to cleaning with a 1:10 dilution of bleach versus 2 (20 percent) of the rooms after cleaning.[70] Sitzlar et al. evaluated the impact of sequential cleaning and disinfection interventions that included formation of a dedicated daily disinfection team and implementation of a standardized process for cleaning CDI rooms and showed that they achieved consistent room disinfection.[112] Not only is the product important, but it is essential that the practice of thoroughly cleaning contaminated surfaces be monitored and improved.[49]

Prevention Strategies. With increasing CDI rates, clearly there is a need for more effective infection prevention strategies. Strategies to prevent patient ingestion of spores consist of traditional infection prevention strategies that target the environment, hand hygiene (with soap and water), and barrier precautions, such as contact precautions.[98,113] Two strategies have been shown to be effective at interrupting disease transmission during CDI clusters or epidemic periods: effective room decontamination by surface disinfection with sodium hypochlorite to minimize environmental contamination; and the use of effective barrier precautions (especially gloves) by healthcare personnel during patient contact to prevent transmission.[98,113] More recently, "no-touch" room decontamination systems (both hydrogen peroxide vapor and UV) have also been shown to reduce HAIs in 11 studies.[89]

Studies have shown that admission to a room previously occupied by a patient with *C. difficile*[51] significantly increases the odds of acquiring CDI. These studies demonstrate the importance of effective room disinfection for eliminating the pathogen from the environment. Rutala et al. have shown that wiping with a sporicidal agent provides excellent removal and inactivation of *C. difficile* spores (e.g., 3.90 $\log_{10}$ reduction).[114] Pathogen survival on environmental surfaces or patient care equipment may be attributable to ineffective products (i.e., disinfectants that don't kill the pathogen) or poor practices (i.e., all surfaces are not wiped or a poor technique that does not remove/inactivate the pathogen).[49] For this reason, the practice of thoroughly cleaning contaminated surfaces should be monitored and improved.

Since *C. difficile* is shed in the feces, any surface or device that becomes contaminated by feces or hands can serve as a reservoir for *C. difficile* spores. The frequency of *C. difficile* contamination in patients' rooms may vary from approximately 10 percent to greater than 50 percent.[70,78,104,105,110,111,115–122] The *C. difficile* spore load on environmental surfaces in healthcare facilities is generally low. Several studies have assessed the microbial load of *C. difficile* on environmental surfaces, and most usually found less than 10 colonies of *C. difficile* on sampled surfaces found to be contaminated.[70,78,105,111,115,117,122] Two studies reported more than 100 colonies; one reported a range of "1 to >200" colonies, and one study that sampled several sites with a sponge found 1,300 colonies. The heaviest contamination is found on floors, but other sites frequently found to be contaminated are windowsills, commodes, toilets, call buttons, scales, blood pressure cuffs, toys, bathtubs, tables, light switches, phones, door handles, mops, electronic thermometers, and feeding tube equipment. These spores will remain in the environment for months unless physically removed or inactivated by disinfectants. Most low-level disinfectants used in healthcare (e.g., alcohol, quaternary ammonium compounds, phenolics) are not effective against *C. difficile* spores, although higher-level disinfectants do kill the spores (e.g., glutaraldehyde [not for surface disinfection], chlorine at a concentration of 5,000 ppm)(Unpublished data, WA Rutala, December 2008).[123,124]

The importance of environmental contamination in disease transmission is emphasized by the epidemiological findings that disinfection with sodium hypochlorite (i.e., bleach) has been shown to be effective in reducing environmental contamination in patient rooms and in reducing CDI rates in hospital units where the rate of CDI is high in at least 5 studies.[54] For this reason, the use of bleach (1:10 dilution of concentrated bleach) is recommended by the CDC during outbreaks of CDI and in hyperendemic settings.[13,98] One application of bleach covering all surfaces to allow a sufficient wetness for ≥1 minute contact time is recommended. A dilution of bleach with water normally takes 1 to 3 minutes to dry. At UNC Hospitals, we use bleach and UV disinfection in all rooms of patients with CDI.[89]

In summary, environmental interventions are an important part of a comprehensive strategy in preventing transmission of *C. difficile* in the healthcare setting. The use of chlorine during hyperendemic and epidemic periods has been shown to reduce environmental contamination with *C. difficile* and to reduce the incidence of *C. difficile* infection. Interventions, such as chlorine, aimed at optimizing environmental disinfection are an important component of our infection prevention strategies.

Inactivation of Creutzfeldt-Jakob Disease

Creutzfeldt-Jakob disease (CJD) is a degenerative neurologic disorder of humans with an incidence in the United States of approximately 1 case per 1 million population.[125–127] CJD is caused by a proteinaceous infectious agent or prion. Prion diseases do not elicit an immune response, result in a noninflammatory pathologic process confined to the central nervous system, have an incubation period of years, and usually are fatal within 1 year of diagnosis.

CJD occurs as both a sporadic disease (approximately 85 percent of cases) and as a familial or inherited disease (approximately 15 percent of cases). Fewer than 1 percent of CJD episodes have resulted from healthcare-associated transmission; the majority result from use of contaminated tissues or grafts.[128] Iatrogenic CJD has been described in humans in three circumstances: after use of contaminated medical equipment on patients undergoing intracranial placement of contaminated EEG electrodes (2 cases in Switzerland) and neurosurgical procedures (4 suspected cases; 3 cases in United Kingdom and 1 case in France); in patients who received cadaveric hormone therapy; and in patients who received an implant of contaminated grafts from humans (cornea-2 cases, dura mater >190 cases).[128–131] All known instances of iatrogenic CJD have resulted from exposure to infectious brain, pituitary, or eye tissue. Tissue infectivity studies in experimental animals have determined the infectiousness of different body tissues.[131,132]

The agents of CJD and other transmissible spongiform encephalopathies (TSEs) exhibit an unusual resistance to conventional chemical and physical decontamination methods. In order for a surgical instrument to act as a vehicle of prion transmission, it must come into contact with infective tissue (e.g., brain) during surgery on the infected patient, it must maintain any adhered infectivity after being decontaminated and sterilized, and must have contact with the receptive tissue in the recipient.[133] For a comprehensive review of disinfection and sterilization recommendations for CJD, the reader is referred to the SHEA guideline[134] and a paper by Belay et al.[135]

The three parameters integrated into disinfection and sterilization processing for prion-contaminated medical instruments are as follows: the risk that the patient has a prion disease; the comparative infectivity of different body tissues; and the intended use of the medical device[136–138] (LM Sehulster, written communication, 2000). High-risk patients include: those with known prion disease; rapidly progressive dementia consistent with possible prion disease; familial history of CJD, Gerstmann-Straussler-Scheinker, fatal familial insomnia; patients know to carry a mutation in the PrP gene involved in familial TSEs; a history of dura mater transplantation; EEG findings or laboratory evidence suggestive of a TSE (e.g., real-time quaking-induced conversion [RT-QuIC] assay of cerebral-spinal fluid or markers of neuronal injury such as 14-3-3 protein); or a known history of cadaver-derived pituitary hormone injection. High-risk tissues include brain, spinal cord, pituitary tissue, and posterior eye (that involves the retina or optic nerve). All other tissues are considered low or no risk. Critical devices are defined as devices that enter sterile tissue or the vascular system (e.g., surgical instruments). Semicritical devices are defined as devices that contact nonintact skin or mucous membranes (e.g., GI endoscopes).

Recommendations for disinfection and sterilization of prion-contaminated medical devices are as follows.[139–151] Instruments should be kept wet (e.g., immersed in water or a prionicidal detergent) or damp after use and until they are decontaminated. They should be decontaminated (e.g., in an automated washer-disinfector) as soon as possible after use. Dried films of tissue are more resistant to prion inactivation by steam sterilization compared to tissues that are kept moist. This may relate to the rapid heating that occurs in the film of dried material compared to the bulk of the sample, and the rapid fixation or dehydration of the prion protein in the dried film.[152] It appears that prions in the dried portions of the brain macerates are less efficiently inactivated than undisturbed tissue. In addition, certain disinfectants (e.g., glutaraldehyde, formaldehyde, ethanol) can fix or dehydrate the protein and make it more difficult to inactivate.[153–156] A formalin-formic acid procedure has been recommended for inactivation of prion infectivity in tissue samples obtained from patients with CJD.[155]

The high resistance of prions to standard sterilization methods warrants special procedures in the reprocessing of surgical instruments. Special prion reprocessing is necessary when reprocessing critical or semicritical medical devices that have had contact with high-risk tissues from high-risk patients. After the device has been cleaned, it should be sterilized by either autoclaving (i.e., steam sterilization) or using a combination of sodium hydroxide and autoclaving,[129,135] using one of the four options below:

Option 1 – autoclave at 134°C for 18 minutes in a prevacuum sterilizer;[143,146,147,151,154,157–161] or

Option 2 – autoclave at 132°C for 1 hour in a gravity displacement sterilizer;[155,162–165] or

Option 3 – immerse in 1 N NaOH (1 N NaOH is a solution of 40 g NaOH in 1 liter of water) for 1 hour; remove and rinse in water, then transfer to an open pan and autoclave (121°C gravity displacement or 134°C porous or prevacuum sterilizer) for 1 hour;[146,157,163,164,166] or

Option 4 – immerse instruments in 1 N NaOH for 1 hour and heat in a gravity displacement sterilizer at 121°C for 30 minutes.[167]

The Association of peri-Operative Nurses and the Association for the Advancement of Medical Instrumentation recommended practices for reprocessing surgical instruments exposed to CJD are consistent with the above recommendations.[136,168,169]

It is essential with any sterilization process, and especially prion-contaminated devices, that the instrument be fully accessible to the sterilant (e.g., steam).[147] Prion-contaminated medical devices that are impossible to clean or fully expose to steam and other sterilants should be discarded. Flash sterilization should not be used for reprocessing. Always discard single-use devices. To minimize environmental contamination, noncritical environmental surfaces should be covered with plastic-backed paper and when contaminated with high-risk tissues the paper should be properly discarded. There are no antimicrobial products registered by the EPA specifically for inactivation of prions on environmental surfaces and no sterilization processes cleared by the FDA for sterilization of reusable surgical instruments. However, the EPA has issued quarantine exemptions to several states permitting the temporary use of a phenolic (containing 6.4 percent *o*-benzyl-*p*-chlorophenol, 3.0 percent *p*-tertiary-amylphenol, 0.5 percent *o*-phenyl phenol, 4.9 percent hexylene glycol, 12.6 percent glycoloic acid, 8 percent isopropanol)[170] for inactivation of prions on hard, nonporous surfaces in laboratories that handle contaminated or potentially contaminated animal tissues and wastes. If no EPA-registered or exempted products are available, then noncritical environmental surfaces (e.g., laboratory surfaces) contaminated with high-risk tissues (e.g., brain tissue) should be cleaned and then spot decontaminated with a 1:5 to 1:10 dilution of hypochlorite solutions, ideally, for a contact time of at least 15 minutes.[158,162,165,171–174]

To minimize the possibility of use of neurosurgical instruments that have been potentially contaminated during procedures performed on patients in whom CJD is later diagnosed, healthcare facilities should consider using the sterilization guidelines outlined above for neurosurgical instruments used during brain biopsy done on patients in whom a specific lesion has not been demonstrated (e.g., by magnetic resonance imaging or computerized tomography scans). Alternatively, neurosurgical instruments used in such patients could be

disposable,[136] or instruments could be quarantined until the pathology of the brain biopsy is reviewed and CJD excluded. If disposable instruments are used, they should be of the same quality as reusable devices. Some countries (e.g., France, Switzerland) have implemented enhanced sterilization rules to prevent transmission of CJD via surgical instruments by requiring steam sterilization at 134°C for 18 minutes of all surgical instruments. Other countries (e.g., United Kingdom) discard all surgical instruments used on high-risk tissues from patients known to have CJD.[151,175]

When strictly followed, these recommendations should eliminate the risk of transmitting infection via prion-contaminated medical and surgical instruments. Belay et al., from the CDC, offered alternative options, which involve combining chemicals and sterilization to include: 1) immerse in 1 N NaOH and heat in gravity at ≥121°C for 30 minutes in an appropriate container; 2) immerse in 1 N NaOH or NaOCl 20,000ppm for 1 hour and then transfer into water and autoclave at ≥121°C for 1 hour; 3) immerse in 1 N NaOH or NaOCl 20,000ppm for 1 hour, rinse with water, transfer to pan and autoclave at 121°C (gravity) or 134°C (porous) for 1 hour.[135]

Emerging Pathogens, Antibiotic-Resistant Bacteria, and Bioterrorism Agents

Emerging pathogens are of growing concern to the general public and infection prevention professionals. Relevant pathogens include Ebola virus,[176] multidrug-resistant bacteria such as CRE, Enterovirus D68, Middle East Respiratory Syndrome-Coronavirus (MERS-CoV), multidrug-resistant *M. tuberculosis*, human papilloma virus, norovirus, and nontuberculous mycobacteria (e.g., *M. chelonae*). The susceptibility of each of these pathogens to chemical disinfectants and/or sterilants has been studied and all of these pathogens (or surrogate microbes such as feline-calicivirus for Norwalk virus, vaccinia for variola,[177] and *B. atrophaeus* [formerly *B. subtilis*] for *B. anthracis*), are susceptible to currently available chemical disinfectants and/or sterilants.[20,178] Standard sterilization and disinfection procedures for patient-care equipment (as recommended in this chapter) are adequate to sterilize or disinfect instruments or devices contaminated with blood or other body fluids from persons infected with bloodborne pathogens, emerging pathogens, and bioterrorism agents, with the exception of prions, HPV, and *C. difficile* spores (see above). No changes in procedures for cleaning, disinfecting, or sterilizing need to be made.[13]

Due to the constant evolution of pathogens causing infections (e.g., MERS-CoV), a new or emerging pathogen will likely not have an EPA-registered disinfectant on the market to kill it. Manufacturers may not make claims about any emerging pathogen without EPA approval, and it can take 18 to 24 months for a manufacturer to obtain label claims for new pathogens (see wwwepa.gov/oppad001/disinfection_hier.htm). Until an EPA-approved claim is available, users may need to refer to the hierarchy of microbial susceptibility to select the appropriate disinfectant for the emerging pathogen.-[13] If the microbiologic class of a new microbe is established, the class-specific test organism(s) would serve as a surrogate for evaluating disinfectant efficacy. The label claim (i.e., registration) would be based on the use of a validated EPA-approved test that assessed the efficacy of disinfectants against the class-specific test organism. For example, an EPA-claim against poliovirus or hepatitis A would be used for MERS-CoV as well as data in the peer-reviewed literature that demonstrated the inactivation of coronavirus.[179–181] Until a new or emerging microbe could be placed in a microbiologic class, it is suggested that only disinfectants with a mycobactericidal claim be allowed by the EPA.[180] For example, the Severe Acute Respiratory Syndrome (SARS) agent, prior to isolation and characterization as a coronavirus, would necessitate the use of a disinfectant with a mycobactericidal label claim for surface disinfection. Once the agent is characterized and placed into a microbial class (as a coronavirus or virus) all EPA-products with a label claim against viruses (e.g., test agent, poliovirus) would be acceptable. In the event that there is not a validated test organism in a class, the next-most-resistant class should be used for purposes of registering disinfectants. For example, if a surrogate for an enveloped virus is not validated, then a non-enveloped virus (e.g., poliovirus) could be used instead. Using this accumulated knowledge on microbial susceptibility should discourage unnecessary testing, listing irrelevant organisms on labels, and "bug-of-the-month" testing.[180,182]

In addition, there are no data to show that antibiotic-resistant bacteria (MRSA, VRE, multidrug-resistant *M. tuberculosis*) are less sensitive to the liquid chemical germicides than antibiotic-sensitive bacteria at currently used germicide contact conditions and concentrations.[183–185]

Conclusion

When properly used, disinfection and sterilization can ensure the safe use of invasive and noninvasive medical devices. The method of disinfection and sterilization depends on the intended use of the medical device: critical items (those that contact sterile tissue) must be sterilized prior to use; semicritical items (those that contact mucous membranes or nonintact skin) must be high-level disinfected; and noncritical items (those that contact intact skin) should receive low-level disinfection. Cleaning should always precede high-level disinfection and sterilization. Current disinfection and sterilization guidelines must be strictly followed.

References

1. Centers for Disease Control and Prevention. National hospital discharge survey: 2010 table, Procedures by selected patient characteristics-number by procedure category and age. 2010.
2. Peery AF DE, Lund J, et al. Burden of gastrointestinal disease in the United States: 2012 update. *Gastroenterol* 2012;**143:** 1179–1187.
3. Epstein L, Hunter JC, Arwady MA, et al. New Delhi metallo-beta-lactamase-producing carbapenem-resistant *Escherichia coli* associated with exposure to

duodenoscopes. *JAMA* 2014;**312**: 1447–1455.

4. Wendorf KA, Kay M, Baliga C, et al. Endoscopic retrograde cholangiopancreatography-associated AmpC *Escherichia coli* outbreak. *Infect Control Hosp Epidemiol* 2015;**36**: 634–642.
5. Ofstead CL, Wetzler HP, Snyder AK, Horton RA. Endoscope reprocessing methods: a prospective study on the impact of human factors and automation. *Gastroenterol Nurs* 2010;**33**: 304–311.
6. Kovaleva J, Peters FT, van der Mei HC, Degener JE. Transmission of infection by flexible gastrointestinal endoscopy and bronchoscopy. *Clin Microbiol Rev* 2013;**26**: 231–254.
7. Rutala WA, Weber DJ. How to assess risk of disease transmission to patients when there is a failure to follow recommended disinfection and sterilization guidelines. *Infect Control Hosp Epidemiol* 2007;**28**: 146–155.
8. Weber DJ, Rutala WA. Lessons learned from outbreaks and pseudo-outbreaks associated with bronchoscopy. *Infect Control Hosp Epidemiol* 2012;**33**: 230–234.
9. Centers for Disease Control and Prevention. Immediate need for healthcare facilities to review procedures for cleaning, disinfecting, and sterilizing reusable medical devices. http://emergency.cdc.gov/han/han00382.asp; 2015.
10. Rutala WA, Weber DJ. Disinfection, sterilization and control of hospital waste. In: Bennett JE DR, Blaser MJ, eds. *Principles and Practice of Infectious Diseases*. Philadelphia, PA: Elsevier Saunders; 2015: 3294–309.
11. Rutala WA, Weber DJ. Disinfection and sterilization: an overview. *Am J Infect Control* 2013;**41**: S2–5.
12. Rutala WA, Weber DJ. Cleaning, disinfection and sterilization. In: Grota P, ed. *APIC Text of Infection Control and Epidemiology*. 4th ed. Washington, DC: Association for Professionals in Infection Control and Epidemiology, Inc.; 2014: 31.1–31.15.
13. Rutala WA, Weber DJ, HICPAC. Guideline for disinfection and sterilization in healthcare facilities, 2008. wwwcdc.gov/hicpac/pdf/guidelines/Disinfection_Nov_2008.pdf. Centers for Disease Control and Prevention, 2008.
14. Spaulding EH. Chemical disinfection of medical and surgical materials. In: Lawrence C, Block S. S. ed. *Disinfection, Sterilization, and Preservation*. Philadelphia, PA: Lea & Febiger; 1968: 517–531.
15. Sehulster L, Chinn RYW, Healthcare Infection Control Practices Advisory Committee. Guidelines for environmental infectin control in healthcare facilities. *MMWR Morb Mortal Wkly Rep* 2003;**52**: 1–44.
16. McDonnell G, Burke P. Disinfection: is it time to reconsider Spaulding? *J Hosp Infect* 2011;**78**: 163–170.
17. Food and Drug Administration. Brief summary of the gastroenterology and urology devices panel meeting. 2015. wwwfda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/Gastroenterology-UrologyDevicesPanel/UCM447407.pdf.
18. Rutala WA, Weber DJ. Gastrointestinal endoscopes: a need to shift from disinfection to sterilization? *JAMA* 2014;**312**: 1405–1406.
19. Rutala WA, Weber DJ. ERCP scopes: what can we do to prevent infections? *Infect Control Hosp Epidemiol* 2015;**36**: 643–648.
20. Food and Drug Administration. FDA-cleared sterilants and high level disinfectants with general claims for processing reusable medical and dental devices, March 2015. www.fdagov/MedicalDevices/DeviceRegulationandGuidance/ReprocessingofReusableMedicalDevices/ucm437347htm 2015.
21. Tosh PK, Disbot M, Duffy JM, et al. Outbreak of *Pseudomonas aeruginosa* surgical site infections after arthroscopic procedures: Texas, 2009. *Infect Control Hosp Epidemiol* 2011;**32**: 1179–1186.
22. Rutala WA, Gergen MF, Weber DJ. Microbial contamination on used surgical instruments. *Infect Control Hosp Epidemiol* 2014;**35**: 1068–1070.
23. Rutala WA, Gergen MF, Weber DJ. Efficacy of a washer-disinfector in eliminating healthcare-associated pathogens from surgical instruments. *Infect Control Hosp Epidemiol* 2014;**35**: 883–885.
24. Rutala WA, Gergen MF, Weber DJ. Disinfection of a probe used in ultrasound-guided prostate biopsy. *Infect Control Hosp Epidemiol* 2007;**28**: 916–919.
25. Rutala WA GM, Sickbert-Bennett EE. Effectiveness of a hydrogen peroxide mist (Trophon®) system in inactivating healthcare pathogens on surface and endocavitary probes. *Infect Control Hosp Epidemiol*; In press.
26. Weber DJ, Rutala WA. Role of environmental contamination in the transmission of vancomycin-resistant enterococci. *Infect Control Hosp Epidemiol* 1997;**18**: 306–309.
27. Weber DJ, Rutala WA, Miller MB, Huslage K, Sickbert-Bennett E. Role of hospital surfaces in the transmission of emerging health care-associated pathogens: norovirus, *Clostridium difficile*, and *Acinetobacter* species. *Am J Infect Control* 2010;**38**:S25–S33.
28. Schembre DB. Infectious complications associated with gastrointestinal endoscopy. *Gastrointest Endosc Clin N Am* 2000;**10**: 215–232.
29. Petersen BT, Chennat J, Cohen J, et al. Multisociety guideline on reprocessing flexible GI endoscopes: 2011. *Infect Control Hosp Epidemiol* 2011;**32**: 527–537.
30. Society of Gastroenterology Nurses and Associates I. Standards of infection control and reprocessing of flexible gastrointestinal endoscopes. *Gastroenterol Nurs* 2013;**36**: 293–303.
31. Muscarella LF. Risk of transmission of carbapenem-resistant *Enterobacteriaceae* and related "superbugs" during gastrointestinal endoscopy. *World J Gastrointest Endosc* 2014;**6**: 457–474.
32. Ofstead CL, Wetzler HP, Doyle EM, et al. Persistent contamination on colonoscopes and gastroscopes detected by biologic cultures and rapid indicators despite reprocessing performed in accordance with guidelines. *Am J Infect Control* 2015;**43**: 794–801.
33. Rutala WA, Weber DJ. FDA labeling requirements for disinfection of endoscopes: a counterpoint. *Infect Control Hosp Epidemiol* 1995;**16**: 231–235.
34. Carbonne A, Thiolet JM, Fournier S, et al. Control of a multi-hospital outbreak of KPC-producing *Klebsiella pneumoniae* type 2 in France, September to October 2009. *Euro Surveill* 2010;15.
35. Roberts CG. Studies on the bioburden on medical devices and the importance of cleaning. In: Rutala WA, ed. *Disinfection, Sterilization and Antisepsis: Principles and Practices in*

Healthcare Facilities. Washington, DC: Association for Professionals in Infection Control and Epidemiology; 2000: 63–69.

36. Alfa MJ, Degagne P, Olson N. Worst-case soiling levels for patient-used flexible endoscopes before and after cleaning. *Am J Infect Control* 1999;**27**: 392–401.
37. Food and Drug Administration. Brief summary of the gastroeneterology and urology devices panel meeting, May 14–15, 2015. Food and Drug Administration.
38. Pajkos A, Vickery K, Cossart Y. Is biofilm accumulation on endoscope tubing a contributor to the failure of cleaning and decontamination. *J Hosp Infect* 2004;**58**: 224.
39. Roberts CG. The role of biofilms in reprocessing medical devices. In: Rutala WA, ed. *Disinfection, Sterilization and Antisepsis: Principles, Practices, Current Issues, New Research, and New Technologies*. Washington, DC: Association for Professionals in Infection Control and Epidemiology; 2010: 223–229.
40. Neves MS, daSilva MG, Ventura GM, Cortes PB, Duarte RS, deSouza HS. Effectiveness of current disinfection procedures against biofilm on contaminated GI endoscopes. *Gastrointest Endosc* 2015.
41. Ren-Pei W H-JX, Ke Q, Dong W, Xing N, Zhao-Shen L,. Correlation between the growth of bacterial biofilm in flexible endoscopes and endoscope reprocessing methods. *Am J Infect Control* 2014;**42**: 1203–1206.
42. Agrawal D, Muscarella LF. Delayed reprocessing of endoscopes. *Gastrointest Endosc* 2011;**73**: 853–854.
43. Rutala WA WD. Outbreaks of carbapenem-resistant *Enteriobacteriaceae* infections associated with duodenoscopes: what can we do to prevent infections? *Am J Infect Control*;In press.
44. Otter JA, Yezli S, French GL. The role played by contaminated surfaces in the transmission of nosocomial pathogens. *Infect Control Hosp Epidemiol* 2011;**32**: 687–699.
45. Boyce JM. Environmental contamination makes an important contribution to hospital infection. *J Hosp Infect* 2007;**65** Suppl 2: 50–54.
46. Weber DJ, Anderson DJ, Sexton DJ, Rutala WA. Role of the environment in the transmission of *Clostridium difficile* in health care facilities. *Am J Infect Control* 2013;**41**:S105–S110.
47. Rutala WA, Weber DJ. Disinfectants used for environmental disinfection and new room decontamination technology. *Am J Infect Control* 2013;**41**:S36–S41.
48. Stiefel U, Cadnum JL, Eckstein BC, Guerrero DM, Tima MA, Donskey CJ. Contamination of hands with methicillin-resistant *Staphylococcus aureus* after contact with environmental surfaces and after contact with the skin of colonized patients. *Infect Control Hosp Epidemiol* 2011;**32**: 185–187.
49. Carling P. Methods for assessing the adequacy of practice and improving room disinfection. *Am J Infect Control* 2013;**41**:S20–S25.
50. Huang SS, Datta R, Platt R. Risk of acquiring antibiotic-resistant bacteria from prior room occupants. *Arch Intern Med* 2006;**166**: 1945–1951.
51. Shaughnessy MK, Micielli RL, DePestel DD, et al. Evaluation of hospital room assignment and acquisition of *Clostridium difficile* infection. *Infect Control Hosp Epidemiol* 2011;**32**: 201–206.
52. Han JH SN, Leas BF, Pegues DA, Kaczmarek JL, Umscheid CA. Cleaning hospital room surfaces to prevent health care-associated infections. *Ann Intern Med* 2015;**163**: 598–607.
53. Leas BF SN, Han JH, Pegues DA, Kaczmarek JL, Umscheid CA. Environmental cleaning for the prevention of healthcare-associated infection. Technical brief No. 22 (prepared by the ECRI Institute – Penn Agency for Healthcare Research and Quality). www.effectivehealthcare.ahrq.gov/ehc/products/592/2103/healthcare-infections-report-150810.pdf2015.
54. Donskey CJ. Does improving surface cleaning and disinfection reduce health care-associated infections? *Am J Infect Control* 2013;**41**:S12–S19.
55. Rutala WA, Weber DJ. Selection of the ideal disinfectant. *Infect Control Hosp Epidemiol* 2014;**35**: 855–865.
56. Cooper RA, Griffith CJ, Malik RE, Obee P, Looker N. Monitoring the effectiveness of cleaning in four British hospitals. *Am J Infect Control* 2007;**35**: 338–341.
57. Guh A CP. Options for evaluating environmental cleaning. wwwcdc.gov/HAI/toolkits/Environ-Cleaning-Eval-Toolkit-10–6-2010.pdf2010.
58. Alfa MJ, Fatima I, Olson N. Validation of adenosine triphosphate to audit manual cleaning of flexible endoscope channels. *Am J Infect Control* 2013;**41**: 245–248.
59. Dancer SJ. How do we assess hospital cleaning? A proposal for microbiological standards for surface hygiene in hospitals. *J Hosp Infect* 2004;**56**: 10–15.
60. Lewis T, Griffith C, Gallo M, Weinbren M. A modified ATP benchmark for evaluating the cleaning of some hospital environmental surfaces. *J Hosp Infect* 2008;**69**: 156–163.
61. Huslage K, Rutala WA, Gergen MF, Sickbert-Bennett EE, Weber DJ. Microbial assessment of high-, medium-, and low-touch hospital room surfaces. *Infect Control Hosp Epidemiol* 2013;**34**: 211–212.
62. Carling PC, Parry MF, Von Beheren SM, Healthcare Environmental Hygiene Group. Identifying opportunities to enhance environmental cleaning in 23 acute care hospitals. *Infect Control Hosp Epidemiol* 2008;**29**: 1–7.
63. Carling PC, Von Beheren S, Kim P, Woods C, Healthcare Environmental Hygiene Study Group. Intensive care unit environmental cleaning: an evaluation in sixteen hospitals using a novel assessment tool. *J Hosp Infect* 2008;**68**: 39–44.
64. Havill NL, Havill HL, Mangione E, Dumigan DG, Boyce JM. Cleanliness of portable medical equipment disinfected by nursing staff. *Am J Infect Control* 2011;**39**: 602–604.
65. Mitchell BG, Dancer SJ, Shaban RZ, Graves N. Moving forward with hospital cleaning. *Am J Infect Control* 2013;**41**: 1138–1139.
66. Carling PC, Bartley JM. Evaluating hygienic cleaning in health care settings: what you do not know can harm your patients. *Am J Infect Control* 2010;**38**:S41–S50.
67. Boyce JM, Havill NL, Dumigan DG, Golebiewski M, Balogun O, Rizvani R. Monitoring the effectiveness of hospital cleaning practices by use of an adenosine triphosphate bioluminescence assay. *Infect Control Hosp Epidemiol* 2009;**30**: 678–684.
68. Hota B BD, Lyle EA, Weinstein RA, Hayden MK. Interventional evaluation of environmental contamination by vancomycin-resistant enterococci: failure of personnel, product or procedure? *J Hosp Infect* 2009;**71**: 123–131.
69. Goodman ER, Platt R, Bass R, Onderdonk AB, Yokoe DS, Huang SS. Impact of an environmental cleaning

intervention on the presence of methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci on surfaces in intensive care unit rooms. *Infect Control Hosp Epidemiol* 2008;**29**: 593–599.

70. Eckstein BC, Adams DA, Eckstein EC, et al. Reduction of *Clostridium difficile* and vancomycin-resistant *Enterococcus* contamination of environmental surfaces after an intervention to improve cleaning methods. *BMC Infect Dis* 2007;**7**: 61.
71. Huslage K, Rutala WA, Sickbert-Bennett E, Weber DJ. A quantitative approach to defining "high-touch" surfaces in hospitals. *Infect Control Hosp Epidemiol* 2010;**31**: 850–853.
72. Memarzadeh F, Olmsted RN, Bartley JM. Applications of ultraviolet germicidal irradiation disinfection in health care facilities: effective adjunct, but not stand-alone technology. *Am J Infect Control* 2010;**38**:S13–S24.
73. Nerandzic MM, Thota P, Sankar CT, et al. Evaluation of a pulsed xenon ultraviolet disinfection system for reduction of healthcare-associated pathogens in hospital rooms. *Infect Control Hosp Epidemiol* 2015;**36**: 192–197.
74. Rutala WA, Gergen MF, Weber DJ. Room decontamination with UV radiation. *Infect Control Hosp Epidemiol* 2010;**31**: 1025–1029.
75. Rutala WA, Gergen MF, Tande BM, Weber DJ. Room decontamination using an ultraviolet-C device with short ultraviolet exposure time. *Infect Control Hosp Epidemiol* 2014;**35**: 1070–1072.
76. Nerandzic MM, Cadnum JL, Pultz MJ, Donskey CJ. Evaluation of an automated ultraviolet radiation device for decontamination of *Clostridium difficile* and other healthcare-associated pathogens in hospital rooms. *BMC Infect Dis* 2010;**10**: 197.
77. Boyce JM, Havill NL, Moore BA. Terminal decontamination of patient rooms using an automated mobile UV light unit. *Infect Control Hosp Epidemiol* 2011;**32**: 737–742.
78. Boyce JM, Havill NL, Otter JA, et al. Impact of hydrogen peroxide vapor room decontamination on *Clostridium difficile* environmental contamination and transmission in a healthcare setting. *Infect Control Hosp Epidemiol* 2008;**29**: 723–729.
79. French GL, Otter JA, Shannon KP, Adams NM, Watling D, Parks MJ. Tackling contamination of the hospital environment by methicillin-resistant *Staphylococcus aureus* (MRSA): a comparison between conventional terminal cleaning and hydrogen peroxide vapour decontamination. *J Hosp Infect* 2004;**57**: 31–37.
80. Bartels MD, Kristoffersen K, Slotsbjerg T, Rohde SM, Lundgren B, Westh H. Environmental methicillin-resistant *Staphylococcus aureus* (MRSA) disinfection using dry-mist-generated hydrogen peroxide. *J Hosp Infect* 2008;**70**: 35–41.
81. Hall L, Otter JA, Chewins J, Wengenack NL. Use of hydrogen peroxide vapor for deactivation of *Mycobacterium tuberculosis* in a biological safety cabinet and a room. *J Clin Microbiol* 2007;**45**: 810–815.
82. Hardy KJ, Gossain S, Henderson N, et al. Rapid recontamination with MRSA of the environment of an intensive care unit after decontamination with hydrogen peroxide vapour. *J Hosp Infect* 2007;**66**: 360–368.
83. Johnston MD, Lawson S, Otter JA. Evaluation of hydrogen peroxide vapour as a method for the decontamination of surfaces contaminated with *Clostridium botulinum* spores. *J Microbiol Methods* 2005;**60**: 403–411.
84. Heckert RA, Best M, Jordan LT, Dulac GC, Eddington DL, Sterritt WG. Efficacy of vaporized hydrogen peroxide against exotic animal viruses. *Appl Environ Microbiol* 1997;**63**: 3916–3918.
85. Klapes NA, Vesley D. Vapor-phase hydrogen peroxide as a surface decontaminant and sterilant. *Appl Environ Microbiol* 1990;**56**: 503–506.
86. Bates CJ, Pearse R. Use of hydrogen peroxide vapour for environmental control during a *Serratia* outbreak in a neonatal intensive care unit. *J Hosp Infect* 2005;**61**: 364–366.
87. Shapey S, Machin K, Levi K, Boswell TC. Activity of a dry mist hydrogen peroxide system against environmental *Clostridium difficile* contamination in elderly care wards. *J Hosp Infect* 2008;**70**: 136–141.
88. Falagas ME, Thomaidis PC, Kotsantis IK, Sgouros K, Samonis G, Karageorgopoulos DE. Airborne hydrogen peroxide for disinfection of the hospital environment and infection control: a systematic review. *J Hosp Infect* 2011;**78**: 171–177.
89. Weber DJ RW, Anderson DJ, Chen LF, Sickbert-Bennett EE, Boyce JM. Effectiveness of UV devices and hydrogen peroxide systems for terminal room decontamination: focus on clinical trials. *Am J Infect Control*. In press.
90. Passaretti CL, Otter JA, Reich NG, et al. An evaluation of environmental decontamination with hydrogen peroxide vapor for reducing the risk of patient acquisition of multidrug-resistant organisms. *Clin Infect Dis* 2013;**56**: 27–35.
91. Levin J RL, Parrish C, English D, Ahn S. The effect of portable pulsed xenon ultraviolet light after terminal cleaning on hospital-associated *Clostridium difficile* infection in a community hospital. *Am J Infect Control* 2013;**42**: 586–590.
92. Haas JP MJ, Dusza S, Montecalvo MA. Implementation and impact of ultraviolet environmental disinfection in an acute care setting. *Am J Infect Control* 2014;**42**: 586–590.
93. Meyers J RE, Conway MJ, Meyers C, Robison R,. Susceptibility of high-risk human papillomavirus type 16 to clinical disinfectants. *J Antimicrob Chemother 2014*;Epub February 2014.
94. Ryndock E RR, Meyers C. Susceptibility of HPV 16 and 18 to high-level disinfectants indicated for semi-critical ultrasound probes. *J Med Virol* 2015;Epub ahead of print.
95. Bringhurst J. Disinfection and sterilization in physician practices and specialty clinics. *Am J Infect Control*; In press.
96. Rutala WA GM, Bringhurst J, Weber DJ. Effective high-level disinfection pf cystoscopes: is perfusion of channels required? *Infect Control Hosp Epidemiol*; In press.
97. Wendelboe AM BJ, Blossom DB, Frank P, Srinivasan A, Sewell CM. Outbreak of cystoscopy related infections with *Pseudomonas aeurginosa*: New Mexico, 2007. *J Urology* 2008;**180**: 588–592.
98. Dubberke ER, Carling P, Carrico R, et al. Strategies to prevent *Clostridium difficile* infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014;**35** Suppl 2:S48–S65.
99. Magill SS EJ, Bamberg W, et al. Multistate point-prevalence survey of health care-associated infections. *N Engl J Med* 2014;**370**: 1198–1208.
100. Khanafer N, Voirin N, Barbut F, Kuijper E, Vanhems P. Hospital management of *Clostridium difficile* infection: a review of the literature. *J Hosp Infect* 2015;**90**: 91–101.

101. Bartlett JG. Narrative review: the new epidemic of *Clostridium difficile*-associated enteric disease. *Ann Intern Med* 2006;**145**: 758–764.

102. Guerrero DM, Nerandzic MM, Jury LA, Jinno S, Chang S, Donskey CJ. Acquisition of spores on gloved hands after contact with the skin of patients with *Clostridium difficile* infection and with environmental surfaces in their rooms. *Am J Infect Control* 2012;**40**: 556–558.

103. Kundrapu S, Sunkesula V, Jury LA, Sitzlar BM, Donskey CJ. Daily disinfection of high-touch surfaces in isolation rooms to reduce contamination of healthcare workers' hands. *Infect Control Hosp Epidemiol* 2012;**33**: 1039–1042.

104. Barbut F. How to eradicate *Clostridium difficile* from the environment. *J Hosp Infect* 2015;**89**: 287–295.

105. Kim KH, Fekety R, Batts DH, et al. Isolation of *Clostridium difficile* from the environment and contacts of patients with antibiotic-associated colitis. *J Infect Dis* 1981;**143**: 42–50.

106. Jump RL, Pultz MJ, Donskey CJ. Vegetative *Clostridium difficile* survives in room air on moist surfaces and in gastric contents with reduced acidity: a potential mechanism to explain the association between proton pump inhibitors and *C. difficile*-associated diarrhea? *Antimicrob Agents Chemother* 2007;**51:** 2883–2887.

107. Association for Professionals in Infection Control and Epidemiology. *Guide to the Elimination of Clostridium difficile in Healthcare Settings*. Washington DC: APIC; 2008.

108. McFarland LV, Mulligan ME, Kwok RY, Stamm WE. Nosocomial acquisition of *Clostridium difficile* infection. *N Engl J Med* 1989;**320**: 204–210.

109. Jou J, Ebrahim J, Shofer FS, et al. Environmental transmission of *Clostridium difficile*: association between hospital room size and *C. difficile* infection. *Infect Control Hosp Epidemiol* 2015;**36**: 564–568.

110. Wilcox MH, Fawley WN, Wigglesworth N, Parnell P, Verity P, Freeman J. Comparison of the effect of detergent versus hypochlorite cleaning on environmental contamination and incidence of *Clostridium difficile* infection. *J Hosp Infect* 2003;**54**: 109–114.

111. Samore MH, Venkataraman L, DeGirolami PC, Arbeit RD, Karchmer AW. Clinical and molecular epidemiology of sporadic and clustered cases of nosocomial *Clostridium difficile* diarrhea. *Am J Med* 1996;**100**: 32–40.

112. Sitzlar B, Deshpande A, Fertelli D, Kundrapu S, Sethi AK, Donskey CJ. An environmental disinfection odyssey: evaluation of sequential interventions to improve disinfection of *Clostridium difficile* isolation rooms. *Infect Control Hosp Epidemiol* 2013;**34**: 459–465.

113. Gerding DN, Muto CA, Owens RC, Jr. Measures to control and prevent *Clostridium difficile* infection. *Clin Infect Dis* 2008;**46** Suppl 1:S43–S49.

114. Rutala WA, Gergen MF, Weber DJ. Efficacy of different cleaning and disinfection methods against *Clostridium difficile* spores: importance of physical removal versus sporicidal inactivation. *Infect Control Hosp Epidemiol* 2012;**33**: 1255–1258.

115. Kaatz GW, Gitlin SD, Schaberg DR, et al. Acquisition of *Clostridium difficile* from the hospital environment. *Am J Epidemiol* 1988;**127**: 1289–1294.

116. Cohen SH, Tang YJ, Rahmani D, Silva J, Jr. Persistence of an endemic (toxigenic) isolate of *Clostridium difficile* in the environment of a general medicine ward. *Clin Infect Dis* 2000;**30**: 952–954.

117. Fekety R, Kim KH, Brown D, Batts DH, Cudmore M, Silva J, Jr. Epidemiology of antibiotic-associated colitis; isolation of *Clostridium difficile* from the hospital environment. *Am J Med* 1981;**70**: 906–908.

118. Mayfield JL, Leet T, Miller J, Mundy LM. Environmental control to reduce transmission of *Clostridium difficile*. *Clin Infect Dis* 2000;**31**: 995–1000.

119. Cohen SH, Tang YJ, Muenzer J, Gumerlock PH, Silva J, Jr. Isolation of various genotypes of *Clostridium difficile* from patients and the environment in an oncology ward. *Clin Infect Dis* 1997;**24**: 889–893.

120. Dubberke ER, Reske KA, Noble-Wang J, et al. Prevalence of *Clostridium difficile* environmental contamination and strain variability in multiple health care facilities. *Am J Infect Control* 2007;**35**: 315–318.

121. Verity P, Wilcox MH, Fawley W, Parnell P. Prospective evaluation of environmental contamination by *Clostridium difficile* in isolation side rooms. *J Hosp Infect* 2001;**49**: 204–209.

122. Mulligan ME, George WL, Rolfe RD, Finegold SM. Epidemiological aspects of *Clostridium difficile*-induced diarrhea and colitis. *Am J Clin Nutr* 1980;**33**: 2533–2538.

123. Perez J, Springthorpe VS, Sattar SA. Activity of selected oxidizing microbicides against the spores of *Clostridium difficile*: relevance to environmental control. *Am J Infect Control* 2005;**33**: 320–325.

124. Rutala WA, Gergen MF, Weber DJ. Inactivation of *Clostridium difficile* spores by disinfectants. *Infect Control Hosp Epidemiol* 1993;**14**: 36–39.

125. Centers for Disease C, Prevention. Surveillance for Creutzfeldt-Jakob disease–United States. *MMWR Morb Mortal Wkly Rep* 1996;**45:** 665–668.

126. Johnson RT, Gibbs CJ, Jr. Creutzfeldt-Jakob disease and related transmissible spongiform encephalopathies. *N Engl J Med* 1998;**339**:1994–2004.

127. Collins SJ, Lawson VA, Masters CL. Transmissible spongiform encephalopathies. *Lancet* 2004;**363**: 51–61.

128. Brown P, Brandel JP, Preece M, Sato T. Iatrogenic Creutzfeldt-Jakob disease: the waning of an era. *Neurology* 2006;**67**: 389–393.

129. WHO infection control guidelines for transmissible spongiform encephalopathies. 2003. at wwwwho .int/csr/resources/publications/bse /whocdscsraph2003.pdf.

130. Brown P, Preece M, Brandel JP, et al. Iatrogenic Creutzfeldt-Jakob disease at the millennium. *Neurology* 2000;**55**: 1075–1081.

131. Brown P. Environmental causes of human spongiform encephalopathy. In: Baker HR, R. M., eds., *Methods in Molecular Medicine: Prion Diseases*. Totowa, NJ: Humana Press Inc.; 1996: 139–154.

132. Brown P, Gibbs CJ, Jr., Rodgers-Johnson P, et al. Human spongiform encephalopathy: the National Institutes of Health series of 300 cases of experimentally transmitted disease. *Ann Neurol* 1994;**35**: 513–529.

133. Rabano AdP-C, J, Pedro-Cuesta J, Molbak,K. et al. Tissue classification for the epidemiological assessment of surgical transmission of sporadic Creutzfeldt-Jakob disease: a proposal on hypothetical risk levels. *BMC Public Health* 2005;5.

134. Rutala WA, Weber DJ, Society for Healthcare Epidemiology of

A. Guideline for disinfection and sterilization of prion-contaminated medical instruments. *Infect Control Hosp Epidemiol* 2010;**31**: 107–117.

135. Belay ED, Blase J, Sehulster LM, Maddox RA, Schonberger LB. Management of neurosurgical instruments and patients exposed to Creutzfeldt-Jakob disease. *Infect Control Hosp Epidemiol* 2013;**34**: 1272–1280.
136. Rutala WA, Weber DJ. Creutzfeldt-Jakob disease: recommendations for disinfection and sterilization. *Clin Infect Dis* 2001;**32**: 1348–1356.
137. Favero MS. Current issues in hospital hygiene and sterilization technology. *J Infect Control* (Asia Pacific Edition) 1998;**1**: 8–10.
138. Favero MS BW. Chemical disinfection of medical and surgical materials. In: SS B, ed. *Disinfection, Sterilization, and Preservation*. Philadelphia, PA: Lea & Febiger; 2001: 881–917.
139. Jacobs P. Cleaning: principles, methods and benefits. In: WA R, ed. *Disinfection, Sterilization, and Antisepsis in Healthcare*. Champlain, NY: Polyscience Publications; 1998: 165–181.
140. Merritt K HV, Brown SA. Safety and cleaning of medical materials and devices. *Journal of Biomedical Materials Research* 2000;**53**: 131–136.
141. Alfa MJ, Jackson M. A new hydrogen peroxide–based medical-device detergent with germicidal properties: comparison with enzymatic cleaners. *Am J Infect Control* 2001;**29**: 168–177.
142. Lipscomb IP, Pinchin H, Collin R, Keevil CW. Effect of drying time, ambient temperature and pre-soaks on prion-infected tissue contamination levels on surgical stainless steel: concerns over prolonged transportation of instruments from theatre to central sterile service departments. *J Hosp Infect* 2007;**65**: 72–77.
143. Fichet G, Comoy E, Duval C, et al. Novel methods for disinfection of prion-contaminated medical devices. *Lancet* 2004;**364**: 521–526.
144. Baier M, Schwarz A, Mielke M. Activity of an alkaline "cleaner" in the inactivation of the scrapie agent. *J Hosp Infect* 2004;**57**: 80–84.
145. Yoshioka M, Murayama Y, Miwa T, et al. Assessment of prion inactivation by combined use of *Bacillus*-derived protease and SDS. *Biosci Biotechnol Biochem* 2007;**71**: 2565–2658.
146. Yan ZXS L; Heeg P, Roth K, Mauz P-S. Low-temperature inactivation of prion-protein on surgical steel surfaces with hydrogen peroxide gas plasma sterilization. *Zentr Steril* 2008;**16**: 26–34.
147. Jackson GS, McKintosh E, Flechsig E, et al. An enzyme-detergent method for effective prion decontamination of surgical steel. *J Gen Virol* 2005;**86**: 869–878.
148. Lawson VA, Stewart JD, Masters CL. Enzymatic detergent treatment protocol that reduces protease-resistant prion protein load and infectivity from surgical-steel monofilaments contaminated with a human-derived prion strain. *J Gen Virol* 2007;**88**: 2905–2914.
149. McDonnell G. Prion disease transmission: can we apply standard precautions to prevent or reduce risks? *Healthcare Challenges* 2008;**18**: 298–304.
150. United Kingdom Department of Health. *New Technologies Working Group Report on Prion Inactivating Agents*. London: 2008.
151. Fichet, GH, Harrison J, McDonnell G. Reduction of risk of prion transmission on surgical devices with effective cleaning processes. *Zentr Steril* 2007;**15**: 418–437.
152. Taylor DM. Inactivation of transmissible degenerative encephalopathy agents: a review. *Veterinary J* 2000;**159**: 10–17.
153. Kampf G, Bloss R, Martiny H. Surface fixation of dried blood by glutaraldehyde and peracetic acid. *J Hosp Infect* 2004;**57**: 139–143.
154. Taylor DM, McConnell I. Autoclaving does not decontaminate formol-fixed scrapie tissues. *Lancet* 1988;**1**: 1463–1464.
155. Brown P, Liberski PP, Wolff A, Gajdusek DC. Resistance of scrapie infectivity to steam autoclaving after formaldehyde fixation and limited survival after ashing at 360 degrees C: practical and theoretical implications. *J Infect Dis* 1990;**161**: 467–472.
156. Fernie K, Steele PJ, Taylor DM, Somerville RA. Comparative studies on the thermostability of five strains of transmissible-spongiform-encephalopathy agent. *Biotechnol Appl Biochem* 2007;**47**: 175–183.
157. Yan ZX SL, Heeg P, Pfaff E, Roth K. Infectivity of prion protein bound to stainless steel wires: a model for testing decontamination procedures for transmissible spongiform encephalopathies. *Infect Control Hosp Epidemiol* 2004;**25**: 280–283.
158. Taylor DM, Fraser H, McConnell I, et al. Decontamination studies with the agents of bovine spongiform encephalopathy and scrapie. *Arch Virol* 1994;**139**: 313–326.
159. Vadrot C, Darbord JC. Quantitative evaluation of prion inactivation comparing steam sterilization and chemical sterilants: proposed method for test standardization. *J Hosp Infect* 2006;**64**: 143–148.
160. Taylor DM. Inactivation of prions by physical and chemical means. *J Hosp Infect* 1999;**43** Suppl:S69–S76.
161. Peretz D, Supattapone S, Giles K, et al. Inactivation of prions by acidic sodium dodecyl sulfate. *J Virol* 2006;**80**: 322–331.
162. Kimberlin RH, Walker CA, Millson GC, et al. Disinfection studies with two strains of mouse-passaged scrapie agent: guidelines for Creutzfeldt-Jakob and related agents. *J Neurol Sci* 1983;**59**: 355–369.
163. Taguchi F, Tamai Y, Uchida K, et al. Proposal for a procedure for complete inactivation of the Creutzfeldt-Jakob disease agent. *Arch Virol* 1991;**119**: 297–301.
164. Ernst DR, Race RE. Comparative analysis of scrapie agent inactivation methods. *J Virol Methods* 1993;**41**: 193–201.
165. Brown P, Rohwer RG, Gajdusek DC. Newer data on the inactivation of scrapie virus or Creutzfeldt-Jakob disease virus in brain tissue. *J Infect Dis* 1986;**153**: 1145–1148.
166. Taylor DM, Fernie K, McConnell I. Inactivation of the 22A strain of scrapie agent by autoclaving in sodium hydroxide. *Vet Microbiol* 1997;**58**: 87–91.
167. Brown SA, Merritt K. Use of containment pans and lids for autoclaving caustic solutions. *Am J Infect Control* 2003;**31**: 257–260.
168. Association of periOperative Registered Nurses. Recommended practices for cleaning and care of surgical instruments and powered equipment. In: Nurses Aop-OR, ed. *Perioperative Standards and Recommended Practices* 2014: 555–563. Available at www.aornstandards.org/.
169. Association for the Advancement of Medical Instrumentation ANSI. *Comprehensive Guide to Steam Sterilization and Sterility Assurance in Health Care Facilities*. Arlington, VA:

Association for the Advancement of Medical Instrumentation, 2010.

170. Race RE, Raymond GJ. Inactivation of transmissible spongiform encephalopathy (prion) agents by environ LpH. *J Virol* 2004;**78**: 2164–2165.
171. Brown P, Rohwer RG, Green EM, Gajdusek DC. Effect of chemicals, heat, and histopathologic processing on high-infectivity hamster-adapted scrapie virus. *J Infect Dis* 1982;**145**: 683–687.
172. Brown P, Gibbs CJ, Jr., Amyx HL, et al. Chemical disinfection of Creutzfeldt-Jakob disease virus. *N Engl J Med* 1982;**306**: 1279–1282.
173. Lemmer K, Mielke M, Pauli G, Beekes M. Decontamination of surgical instruments from prion proteins: in vitro studies on the detachment, destabilization and degradation of PrPSc bound to steel surfaces. *J Gen Virol* 2004;**85**: 3805–3816.
174. Clinical and Laboratory Standards Institute. Protection of laboratory workers from occupationally acquired infections: Approved guideline. 2005.
175. Fichet G CE, Dehen C, Challier L, Antloga K, Deslys JP, McDonnell G,. Investigations of a prion infectivity assay to evaluate methods of decontamination. *J Microbiol Methods* 2007;**70**: 511–518.
176. Cook BWM CT, Nikiforuk AM, Poliquin PG, Court DA, Strong JE, Theriault SS. Evaluating environmental persistence and disinfection of the Ebola Virus Makona Variant. *Viruses* 2015;**7**: 1975–1986.
177. Klein M DA. The inactivation of viruses by germicides. *Chem Specialists Manuf Assoc Proc* 1963;**49**: 116–118.
178. Rutala WA, Gergen MF, Weber DJ. Sporicidal activity of a new low-temperature sterilization technology: the Sterrad 50 sterilizer. *Infect Control Hosp Epidemiol* 1999;**20**: 514–516.
179. Sattar SA. Hierarchy of susceptibility of viruses to environmental surface disinfectants: a predictor of activity against new and emerging viral pathogens. *J AOAC Int* 2007;**90**: 1655–1658.
180. Rutala WA, Weber DJ. Registration of disinfectants based on relative microbicidal activity. *Infect Control Hosp Epidemiol* 2004;**25**: 333–341.
181. Hulkower RL, Casanova LM, Rutala WA, Weber DJ, Sobsey MD. Inactivation of surrogate coronaviruses on hard surfaces by health care germicides. *Am J Infect Control* 2011;**39**: 401–407.
182. Sattar SA, Springthorpe VS, Karim Y, Loro P. Chemical disinfection of non-porous inanimate surfaces experimentally contaminated with four human pathogenic viruses. *Epidemiol Infect* 1989;**102**: 493–505.
183. Rutala WA, Stiegel MM, Sarubbi FA, Weber DJ. Susceptibility of antibiotic-susceptible and antibiotic-resistant hospital bacteria to disinfectants. *Infect Control Hosp Epidemiol* 1997;**18**: 417–421.
184. Anderson RL, Carr JH, Bond WW, Favero MS. Susceptibility of vancomycin-resistant enterococci to environmental disinfectants. *Infect Control Hosp Epidemiol* 1997;**18**: 195–199.
185. Rutala WA, Barbee SL, Aguiar NC, Sobsey MD, Weber DJ. Antimicrobial activity of home disinfectants and natural products against potential human pathogens. *Infect Control Hosp Epidemiol* 2000;**21**: 33–38.
186. Kohn WG, Collins AS, Cleveland JL, et al. Guidelines for infection control in dental healthcare settings – 2003. *MMWR Recomm Rep* 2003;**52**: 1–61.
187. Rutala WA, Weber DJ Disinfection and sterilization of prion-contaminated medical instruments, Reply to Belay. *Infect Control Hosp Epidemiol* 2010;**31**: 1306–1307.
188. Weber DJ, Rutala WA, Sickbert-Bennett EE. Outbreaks associated with contaminated antiseptics and disinfectants. *Antimicrob Agents Chemother* 2007;**51**: 4217–4224.
189. Rutala WA, Cole EC, Thomann CA, Weber DJ. Stability and bactericidal activity of chlorine solutions. *Infect Control Hosp Epidemiol* 1998;**19**: 323–327.

Chapter 9

Improving Hand Hygiene in Healthcare Settings

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Introduction

The association between Healthcare workers, (HCW) hand hygiene and prevention of healthcare-associated infections (HAI) was established over 150 years ago and continues to be reinforced by scientific studies around the world.[1–5] Because HAI are multifactorial, some studies fail to show an association between adherence and decreased HAI. However, there is evidence to support the link between hand hygiene and infection outcome from studies across a wide spectrum of care. In recent history, hand hygiene has become a foundational component of HAI prevention and has been promoted through local initiatives, accrediting bodies, professional societies, and global campaigns. In particular, the proliferation and widespread use of alcohol-based hand sanitizers has improved HCW's ability to conveniently sanitize hands at frequent intervals.[6,7] The importance of hand hygiene in healthcare is especially critical in today's healthcare environment, where the spread of multidrug-resistant organisms is an increasing threat to patient safety.

Despite enhanced awareness and technological advancements, hand hygiene practices among HCW remain suboptimal; a recent systematic review of hand hygiene studies in industrialized nations revealed an overall adherence rate of less than 50 percent.[8] An arbitrary goal of 90 percent had been set by some facilities and accrediting agencies; however, Pittet and colleagues realized a decrease in MRSA in their three-year study, which culminated with a final hand hygiene adherence of 66 percent.[4] Current guidance is to assess weak points in individual units or facilities and focus on targeted improvements. Healthcare workers report myriad reasons for lack of adherence, including: lack of access to sinks or hand hygiene product, understaffing or busy work setting, and skin irritation, as well as cultural issues such as lack of role models and inattention to guidelines.[9–11] In this chapter, we review existing guidelines for hand hygiene in healthcare settings, highlight current issues in measurement and product selection, and summarize recommendations for effective implementation of hand hygiene programs.

Guidelines

The Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO), and the Society for Healthcare Epidemiology of America (SHEA) have published broadly distributed evidence-based recommendations and guidance for implementation of HCW hand hygiene programs in 2002, 2009, and 2014, respectively.[12–14] The WHO guidelines are rooted in a global perspective and address unique aspects of hand hygiene, including religious and cultural issues, promotion on a national scale, social marketing, safety issues, infrastructure required for hand hygiene, and implementation of programs in under-resourced settings. The 2014 SHEA compendium on hand hygiene highlights practical guidance for hand hygiene program implementation and updated recommendations based on studies published since the release of the CDC and WHO guidelines.

When to Perform Hand Hygiene

The most commonly recognized framework for characterizing hand hygiene opportunities is the WHO's "My 5 moments for hand hygiene" (Figure 9.1), which is featured in the 2009 guideline and accompanying implementation guide.[15] The 5 moments include: 1) before touching the patient; 2) before a clean/aseptic procedure; 3) after body fluid exposure; 4) after touching the patient; and 5) after touching patient surroundings. Indications for hand hygiene that are not encompassed explicitly by the "5 Moments" include: before handling medication; before or after handling respiratory devices, urinary catheters, and intravascular catheters; after removing gloves; and when moving from a contaminated body site to a clean body site regardless of body fluid exposure.[14] It is not uncommon for institutions to teach the concepts of the 5 moments but simplify measurement by observing hand hygiene before entering and upon

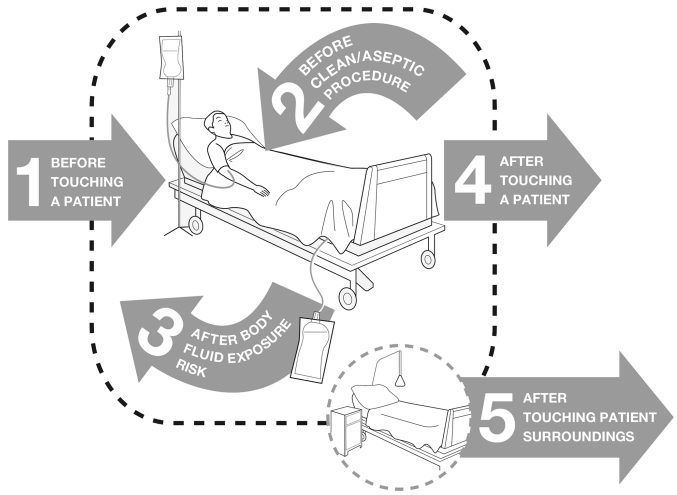

Figure 9.1 My 5 Moments for Hand Hygiene, reproduced with permission from www.who.int/gpsc/5may/background/5moments/en/ (accessed 21 June 2017)

exiting a patient care area; some measure adherence upon exit only.[16] It is important to note that clinical role, increased activity and poor role modeling are some of the factors associated with decreased rates of compliance.[1–3] During physician rounds or other busy times, facilities may wish to target interventions to improve adherence.

Methods for Hand Hygiene Measurement

Monitoring hand hygiene performance is an essential element of hand hygiene promotion. However, there is no standard method for measuring hand hygiene performance, in part because the optimal methods for measurement are still evolving. Further, many technological innovations to facilitate and standardize hand hygiene adherence monitoring are still under evaluation in terms of validity and acceptability.[17] Wide variation in hand hygiene observation methods makes it difficult to compare adherence rates across organizations. The main hand hygiene measurement methods are direct observation, indirect volume or event count measurement, and advanced technologies for automated adherence monitoring. Each method has strengths and weaknesses (Table 9.1).[18] Using multiple methods to measure hand hygiene is a way to address the strengths and limitations associated with a single measurement approach.[19,20]

Direct observation, which has long been considered the gold standard of hand hygiene adherence monitoring, involves in-person monitoring of hand hygiene behavior. To enhance validity and reliability of direct observation, it is crucial that observers be trained, and their observations validated initially and at intervals to assure accuracy; a suite of tools was developed by the WHO to help standardize the observation process.[21] The "Hawthorne effect," or behavior change based on the awareness of subjects that they are being observed, is a well described effect of direct observation. When the desired outcome is improved adherence, with less focus on the true rate of hand hygiene, having known observers may be a potent intervention. However, for more accurate measurement of hand hygiene, some facilities have used covert observers, or "secret shoppers."[22] Although use of covert observers may improve the validity of the measurement and be appropriate for quality improvement initiatives, some experts have raised ethical concerns about avoiding informed consent of those being observed, and it is unlikely that the covert nature of the observations can be sustained.[23] Two studies have found that limiting observation periods to 15 minutes in one location can both minimize the Hawthorne effect and maximize the number and diversity of HCW observed.[24,25]

Technology-assisted direct observation includes use of mobile devices or video monitoring to document hand hygiene monitoring. In-person, direct observation can be streamlined using a mobile hand-held device rather than paper and pen to capture adherence data.[26,27] Another variation on technology-assisted direct observation is video monitoring, in which recording equipment is covertly aimed at a sink or alcohol-based hand rub (ABHR) dispenser and continuously records opportunities for hand hygiene across all shifts and classes of healthcare workers.[28] The video is later reviewed by trained auditors to assess hand hygiene in the same manner as in-person directly observed hand hygiene surveillance. A third-party remote video auditing service can utilize web-based applications to provide adherence feedback, although there is no opportunity for immediate feedback when the review takes place remotely, and patient privacy can be impacted by these systems even with narrow-focus cameras trained on sinks.[29]

Measurement of hand hygiene product (soap, ABHR) consumption or dispenser activation frequency can be used to indirectly assess hand hygiene adherence. This form of measurement can be used to monitor trends over time or by type of care unit.[30] Volume of product used can be compared with the industry-average volume of a single dose of product to approximate hand hygiene adherence rates at a low cost.[31] However, product measurement can be hampered by unreliable usage data from distribution or materials management, or intentional tampering with dispensers or deliberate waste of product. A more reliable, but more expensive mechanism for indirect measurement is the use of dispenser-based counters that create a date and time stamp each time the dispenser is used.[32] Whether these forms of indirect measurement are adequate proxies for hand hygiene adherence (as measured by direct observation) remains unresolved.[33]

"Intelligent" hand hygiene systems are being developed with the idea that the system should use advanced automated technologies to record all hand hygiene opportunities, provide a feedback or reminder system, and, ideally, respond to healthcare workers' behavior and actions.[34] Sensor networks are designed to sense when healthcare workers enter a patient care area such as a room or bedside, detect when hand hygiene is performed, and, if hand hygiene is not performed, remind the healthcare worker to do so.[35,36] Newer systems use personal wearable electronic monitors that communicate with ceiling-mounted infrared emitters, or use WIFI or radio frequency signals to establish defined zones around patient beds or at the threshold of patient rooms. These systems usually capture entry and exit into a patient zone, comparable to WHO moments 1 and 4, but are less successful at capturing WHO moments 2 and 3 within the patient care episode. They cannot distinguish whether the healthcare provider touched the patient or only touched the environment (WHO moment 5).[37] Since the late 2000s, many studies have been published on the introduction and pilot testing of new technologies, but no single system has been endorsed due to cost, complications in implementation, and lack of rigorous evaluation methods.[17,38]

Hand Hygiene Technique

Most studies on hand hygiene adherence assume that healthcare workers adhere to appropriate technique, and studies are lacking on adequacy of hand hygiene technique in general. The minimum time required per most hand hygiene product manufacturers is generally 15–20 seconds, with the volume required changing based on the size of the hands to meet the time requirement. Recent studies suggest that 15 seconds is insufficient for meeting standards for high-quality hand disinfection (EN 1500)[39] and that physical coverage of

Table 9.1 Summary of observations for hand hygiene adherence measurement, including strengths and weaknesses. Reproduced with permission from (14).

Observation method	Strengths	Weaknesses
Direct observation	• Gold standard for hand hygiene adherence • Only method that can discern all opportunities for hand hygiene within patient care encounter, and assess hand hygiene technique • Allows for immediate corrective feedback.	• Labor intensive and costly • Observers must be trained and validated • Subject to Hawthorne effect • Subject to selection and observer bias
Direct observation with technology assistance	• Use of technology (e.g., tablet) to save data entry step, or to assist observer in standardizing measurement (i.e., removing subjectivity) • Video-assisted observations can provide assessment of all or most opportunities to be analyzed at remote location • Less time-consuming and costly than direct observation	• Requires investment and maintenance of infrastructure. • Video monitoring requires trained observers and has limited opportunity for immediate feedback, and has potential to impact on patient privacy
Product volume or event count measurement	• Not subject to Hawthorne effect, selection or observer bias • Unobtrusive, and encompasses all opportunities • Counters can detect changes in frequency of use according to time of day or patterns of use in a hospital unit • May assist in optimal location of dispensers	• Relies on accurate usage data, which may be compromised by system gaps or intentional tampering • Cannot distinguish hand hygiene opportunities (no denominator), or who used the product • Cannot assess adequacy of technique • There are significant costs associated with event-counting systems, and there is ongoing maintenance required
Automated monitoring systems	• Systems with wearable components can provide positive feedback or just-in-time reminders to perform hand hygiene, and individual level monitoring • Captures all episodes entering and leaving a patient zone (eliminating selection and observer bias) and associated adherence	• Expensive to implement and requires ongoing maintenance (e.g., battery replacement or recharging) for all devices • Difficult to detect opportunities within the patient encounter, or assess technique • Concerns about healthcare worker privacy • Limited data outside of research settings
Self report	• Can raise individuals' awareness of their practice.	• Unreliable as healthcare workers overestimate their performance, and should not be used for hand hygiene monitoring data

hands with hand hygiene product in clinical settings is often substandard.[40]

In 2009, the WHO published guidance on a standardized multistep technique to promote coverage of all surfaces of the hands with hand hygiene product, estimating 20–30 seconds for handrubbing (www.who.int/gpsc/5may/How_To_HandRub_Poster.pdf, Figure 9.2) and 40–60 seconds for hand washing with soap and water (www.who.int/gpsc/5may/How_To_HandWash_Poster.pdf). A 2015 study in a hospital with extremely high adherence (>90 percent) found that only 8.5 percent of hand hygiene events complied with the six key steps in the WHO-recommended technique.[41] Assuring that providers are using appropriate technique to reduce microbial burden through hand hygiene is critical; this can be achieved through training staff on standardized technique, or by instructing providers simply to cover their hands with enough hand hygiene product (i.e., the "reasonable application" approach) regardless of technique used. Importantly, the studies finding "reasonable application" equivalent to a standardized technique had protocols using 3 mL of product, and it is unclear how often this volume is used in clinical practice[42] (due to longer drying times associated with use of higher volumes). The standard dispenser actuation for alcohol-based handrubs is 1.1 mL, although recent studies showed variability from 0.6 mL to 1.3 mL of product dispensed with each actuation,[25] and that the 1.1 mL amount is less effective than higher volumes across a range of products.[43] Because technique is an important but often neglected component of hand hygiene programs, assessing and providing feedback on technique is critical.

Figure 9.2 WHO Six Steps for Hand Rubbing. Reproduced with permission from www.who.int/gpsc/5may/How_To_HandRub_Poster.pdf (accessed June 21, 2017)

Selecting Hand Hygiene Products

Four key factors that are relevant to the selection of hand hygiene products for use in healthcare include: efficacy, tolerability, acceptance, and cost. Infection prevention teams must assess efficacy of various products to start the selection process. Alcohol-based handrubs (ABHR) with alcohol concentrations between 62 and 95 percent perform better than either antimicrobial or plain soaps against bacteria over a broad range of testing conditions.[44–46] Alcohol-

based hand rubs also have good activity against viruses; in most cases they perform better than both plain and antimicrobial soaps and water.[47–49]

There is some concern, however, about the efficacy of ABHR against non-enveloped viruses such as norovirus,[50] and against spore-forming organisms like *C. difficile*.[51] Conflicting studies regarding the efficacy of ABHR against norovirus have led the CDC to recommend use of soap and water for the care of patients with known, suspected, or proven norovirus infection during outbreaks, although this is based on "very low-quality evidence."[52] Regarding *C. difficile*, recent evidence suggests that, while ABHR may not effectively remove spores from hands, soap and water is also not optimal and does not achieve the log reductions seen with other bacteria and viruses.[53] The 2009 WHO guidelines recommend preferential use of soap and water in settings with outbreak or hyperendemic *C. difficile* infection. A recent CDC report and the 2014 SHEA hand hygiene compendium recommend consideration of preferential soap and water use in *C. difficile* outbreak settings, but emphasize shifting the focus to appropriate use of gloves to reduce *C. difficile* transmission rather than focusing on use of a particular hand hygiene product.[14,54]

Requirements for surgical hand preparations include rapid action to kill microorganisms as well as persistence for hours. Alcohol-based surgical hand preparations, which are often combined with another agent with persistent action, provide superior reductions in microorganisms compared to traditional scrub products.[55] Alcohol-based preparations are less damaging to skin, and are at least equivalent in preventing surgical site infections.[56,57] Surgical healthcare workers should apply ABHR for surgical skin prep in accordance with the manufacturer's instructions, since misapplication of product can increase the risk of surgical site infection.[58] Traditional hand scrubbing for surgical procedures is typically performed with either chlorhexidine gluconate or povidone iodine on a sponge or brush. Traditional surgical scrubs also require clean water, which may not be available in some settings. Surgical personnel who opt for scrubbing should use the sponge side of the applicator rather than the brush, since the brush is damaging to skin and may promote skin shedding.[59]

Once a range of products with appropriate efficacy have been selected, clinical staff should be involved in the evaluation of products for use. Acceptance and tolerability of hand hygiene products are key to a successful hand hygiene program. Product acceptance is affected by personal preferences for scent, appearance, and texture. In addition, dispensing modality (foam vs. gel vs. rub or wipe) for ABHR may impact acceptance by staff, and this may vary by healthcare setting.[60] Environmental impact and effects of long-term exposure to hand hygiene products are also important considerations. Triclosan, an antiseptic agent used widely in commercial soaps and body washes as well as healthcare soap products, has undergone increasing scrutiny. Concerns persist about triclosan exposure levels and potential health effects in humans. Triclosan was detected in 75 percent of urine samples from US adults and children involved in the 2003–2004 CDC National Health and Nutrition Examination Survey (NHANES); this survey also revealed positive associations between triclosan levels in individuals and poor health indicators such as altered thyroid hormone levels, elevated body mass index, and allergies.[61–63] Given that there is no evidence of the superiority of triclosan as a hand hygiene agent,[64] combined with growing health and environmental concerns,[65] this product is likely to be a less acceptable option for hand hygiene.

Tolerability is an important aspect of product selection. Since the expectation is that staff will perform hand hygiene many times each day they work, it is important to ensure that the product is mild or has sufficient emollients to reduce the risk of dermatitis. Irritant contact dermatitis is the most frequently occurring adverse reaction to hand hygiene products. Symptoms include dryness, irritation, itching, cracking, and bleeding of the skin, and most nurses have reported experiencing this condition at some time in their careers.[66] It can be exacerbated by seasonal dryness in winter and by product formulation. Risk reduction strategies include promoting use of ABHR over soap and water unless hands are visibly soiled.[67] When soap and water are indicated, hot water should be avoided.[68] Healthcare workers should be encouraged to use gloves, for extensive patient care or tasks that involve contact with liquids, such as bathing patients.[69] Finally, healthcare facilities should provide lotion for use in the workplace and encourage its use.[70]

Institutions should involve a group of healthcare workers to try hand hygiene products before committing to their use. In addition, employee health services should keep track of the number of healthcare workers who report for evaluation of contact dermatitis, and the severity of their skin condition. Products found to be particularly irritating should be replaced with less irritating alternatives. Although cost is an issue for all healthcare facilities, cost alone should not determine selection of hand hygiene products. Tolerability and acceptance should primarily determine which products staff will use daily in their work environment.

Once the products have been selected, care must be taken to place dispensers in locations convenient to healthcare workers. Soaps should obviously be located at sinks, but ABHR can be located throughout healthcare facilities. There are several considerations in placement of ABHR dispensers. Dispensers must be installed and product must be stored in accordance with local fire regulations; ABHRs are widely used, and can be used with minimal fire risk if these regulations and guidelines are followed.[71] Toxicity from ingestion is a concern when ABHR are used in settings that serve cognitively impaired, behavioral health and substance abuse patients. A local risk assessment can guide placement of dispensers in these settings. The WHO recommends placing dispensers at the point of care, and dispensing pocket containers to be carried by healthcare workers, to maximize adherence to hand hygiene practices in healthcare.[21]

Implementation

Although most studies evaluating the impact of implementing hand hygiene programs are not of rigorous scientific

quality,[72] two recent meta-analyses include collated results from multiple studies to enhance power and generalizability of the results.[73,74] A 2014 meta-analysis evaluated several bundle combinations and found that hand hygiene improvement bundles that included enhanced access to ABHR, education, reminders, feedback, and administrative support had a significant collective impact on hand hygiene adherence; of note, these are the same key elements included in the WHO's implementation guide.[73] A 2015 meta-analysis concluded that the WHO bundle was effective in improving hand hygiene adherence, but that rates were even further improved with addition of goal setting, incentives, and accountability.[74] Recent studies have reinforced the importance of sustained feedback of hand hygiene rates for sustained improvement, linking incentives with unit-specific goals, and feedback delivered both verbally and in writing.[75,76] Feedback should be used to engage HCW in identifying problems at the individual hospital or unit level, and to tailor ongoing interventions.[73,74]

There are free materials available such as WHO observation forms at www.who.int/entity/gpsc/5may/Observation_Form.doc.27 2, and in The Joint Commission's hand hygiene monograph at www.jointcommission.org/topics/hai_hand_hygiene.aspx.17. The Joint Commission Center for Transforming Healthcare's targeted solutions tool for hand hygiene (www.centerfortransforminghealthcare.org/tst_hh.aspx) is available for free to organizations accredited by The Joint Commission.

In today's dynamic healthcare environment, where the composition of healthcare workers, procedures performed, and products used constantly evolves, the importance of continuing hand hygiene education cannot be overemphasized. Healthcare workers should be educated on indications for hand hygiene, and on hand hygiene technique, with specific attention to the products available at a particular institution. Interactive methods, such as using ink, fluorescent gels or powders, and UV light boxes can enhance staff engagement in hand hygiene education. Targeting education to specific groups based on their care activities or knowledge gaps or misconceptions (e.g., as determined by surveys) can address local issues in a tailored fashion. Education of healthcare workers upon hire and at least annually is critical for maintaining and documenting competency. Competency can be assessed with tests of didactic knowledge, demonstration of adherence to recommended practices through audits, and demonstration of proper hand hygiene technique.

Recommended Hand Hygiene Improvement Strategies

The following recommendations are adapted from the SHEA/IDSA compendium of strategies to decrease infections:

Recommendations below are categorized as either basic practices that should be adopted by all acute care settings, practices that should not be adopted, and unresolved issues. Each recommendation is given a quality of evidence ranking based on the GRADE system and the Canadian Task Force on Preventive Healthcare. None of the hand hygiene recommendations listed below achieve a category I ranking, which is defined as having high degree of evidence. This requires a wide range of studies demonstrating a similar size and direction of effect with narrow confidence intervals. Grade II recommendations are considered to have moderate evidence to support them. The true effect is likely to be close to the estimated size and direction of the effect, but there is a possibility that it is substantially different. Evidence is rated as moderate quality when there are only a few studies and some have limitations but not major flaws, there is some variation between studies, or the confidence interval of the summary estimate is wide. Level III recommendations have a low level of evidence. The true effect may be substantially different from the estimated size and direction of the effect. Evidence is rated as low quality when supporting studies have major flaws, there is important variation between studies, the confidence interval of the summary estimate is very wide, or there are no rigorous studies, only expert consensus. The lack of randomized trials to test recommendations for hand hygiene indications that have become standard of care is likely to persist, largely due to ethical concerns. However, optimizing methods for hand hygiene measurement, multisite studies on implementation of hand hygiene programs, and studies of hand hygiene in non–acute care settings are needed. Establishing consistent methods for assessing the efficacy of various products relative to volume and technique used in clinical settings is critical.

A. Recommended for all acute hospitals

1. **Select appropriate products (II).**
   a. For routine hand hygiene choose alcohol-based hand rub with at least 62 percent alcohol.
   b. Antimicrobial or non-antimicrobial soap should be available and accessible for routine hand hygiene in all patient care areas.
   c. For surgical antisepsis, use an ABHR that is specially formulated for surgical use containing alcohol for rapid action against microorganisms, and another antimicrobial for persistence or use an antimicrobial soap and water; scrub brushes should be avoided because they damage skin.

2. **Provide convenient access to hand hygiene equipment and products by placing them strategically and assuring that they are refilled routinely as often as required (III).**
   a. Sinks should be located conveniently and in accordance with the local applicable guidelines.
   b. Dispenser location may be determined by assessing staff work flow patterns or use of a more formal framework such as the Toyota Production Systems shop floor management; counters in product dispensers can show which dispensers are frequently used, and those that are rarely used.
      i. It is important to place hand hygiene products in the flow of work to promote adherence.

ii. Location of dispensers and storage of ABHR should be in compliance with fire codes.

3. **Involve healthcare workers in choosing products (III).**

Various components of hand hygiene products can cause irritation, and products that are not well accepted by healthcare workers can negatively impact hand hygiene adherence.

4. **Perform hand hygiene with an alcohol-based hand rub or, alternatively, an antimicrobial or nonantimicrobial soap, for the following indications (II).**
   a. Before direct patient contact.
   b. Before preparing or handling medication in anticipation of patient care (e.g. in medication room or at medication cart before patient encounter).
   c. Before inserting an invasive device.
   d. Before and after handling an invasive device, including before accessing intravenous devices for medication administration.
   e. Before moving from a contaminated body site to a clean body site on the same patient.
   f. After direct patient contact.
   g. After removing gloves.
   h. After contact with blood or bodily fluids.
   i. After contact with the patient environment.

5. **Perform hand hygiene with antimicrobial or nonantimicrobial soap when hands are visibly soiled (II).**
6. **Assess unit or institution-specific barriers to hand hygiene with front-line healthcare workers for the purpose of identifying interventions that will be locally relevant (III).**
7. **Implement a multimodal strategy (or "bundle") for improving hand hygiene adherence to directly address the organization's most significant barriers (II).**
   a. Use a bundled approach including enhanced access to ABHR, education, reminders, feedback, and administrative support; this combination of interventions had a significant collective impact on hand hygiene adherence.
   b. At a minimum, use a bundled approach including education, reminders, and feedback.

8. **Educate, motivate, and assure competency of healthcare workers (anyone caring for the patient on the institution's behalf) about proper hand hygiene (III).**
   a. Educate healthcare workers through regular sessions at hire, when job functions change, and at least annually.
      i. When possible, use interactive means such as fluorescing indicators to simulate hand contamination and subsequent removal, visual reminders such as culture plates of hands or audience response systems to keep the audience engaged.
   b. Assure competency of healthcare workers by testing knowledge of the indications for hand hygiene and requiring demonstration of appropriate hand hygiene technique.
   c. Educate patients and families about hand hygiene on admission to healthcare facilities and when changes in circumstances warrant; encourage patients and families to remind healthcare workers to clean their hands before care episodes.
   d. Motivate healthcare workers to perform hand hygiene using positive message framing for hand hygiene messaging and posters.
   e. Use behavioral frameworks and recognized behavioral techniques to plan and execute interventions.

9. **Measure HH adherence via direct observation (human observers), product volume measurement, or automated monitoring (II).**
   a. Decide upon type of measurement system based on resources available and commitment to using the data collected productively; consider advantages and limitations of each type of monitoring.
      i. Use direct observation to elucidate contextual barriers and facilitators to hand hygiene, and to provide corrective feedback to individuals.
      ii. Use product volume measurement for large-scale benchmarking but complement with direct observation when possible.
      iii. Use automated systems to provide real-time reminders, and generate feedback for quality improvement; be aware that such systems have been mainly used in research settings; they may be limited in their capacity to accurately measure opportunities within each patient care encounter; these systems can, however, measure a large sample of hand hygiene opportunities and can be useful for measuring trends over time and generating real-time displays for feedback.

10. **Provide feedback to healthcare workers on hand hygiene performance (III).**
    a. Provide feedback in multiple formats and on more than one occasion.
    b. Provide meaningful data with clear targets and an action plan in place for improving adherence.
       i. Meaningful data may include unit- or role-based adherence data rather than overall performance.
       ii. Real-time displays of hand hygiene adherence may provide some incentive for improvement on a shift-by-shift basis.

B. Approaches that should not be considered part of routine hand hygiene

1. Do not use hot water for hand washing because it can irritate the skin.

2. Do not use ABHR hand rub when hands are visibly soiled.
3. Do not use triclosan-containing soaps: given concerns about the potential human and environmental impacts of this chemical combined with its potential to promote resistance, triclosan-containing soaps should be avoided until the benefits versus risks can be adequately characterized.
4. Do not use self-report as the primary method of hand hygiene adherence measurement.

C. Unresolved Issues

1. There is no national standard for measuring hand hygiene adherence: this includes the optimal number of observations, which indications should be monitored, whether technique should be considered and the best method to assess adherence.
2. There is conflicting evidence as to whether soap and water should be used preferentially to ABHR during care for patients with known or suspected norovirus or *C. difficile* infection: current guidelines recommend preferential use of soap and water in outbreak settings, but these recommendations are based on conflicting studies and low-quality evidence in general.
3. Prohibition or allowance of shellac (gel) nails and nail enhancements on healthcare workers: if institutions consider these nail adherents artificial, then they should be prohibited among healthcare workers caring for high-risk patients per existing CDC and WHO guidance. Whether shellac (gel) nails are "artificial," however, is controversial.
4. More research is needed to assess whether donning nonsterile gloves without prior hand hygiene is safe for patient care and whether it leads to significant increases in contamination of unused gloves in glove boxes. Additionally engineering solutions that could reduce potential contamination of unused gloves during removal from the box should be pursued.
5. Policies requiring hand washing or scrubbing upon entry to high-risk areas, such as neonatal intensive care units or burn units, are common, but there are no data to support or refute these practices. Hand hygiene before patient contact in these settings is recommended, but it is unclear whether additional benefit is conferred by washing or scrubbing upon entry and before reaching the patient care area.
6. Although many manufacturers of surgical hand preparation products stipulate use of picks and brushes, two recent studies show no benefit when using picks or brushes.

References

1. Lane HJ, Blum N, Fee E. Oliver Wendell Holmes (1809–1894) and Ignaz Philipp Semmelweis (1818–1865): preventing the transmission of puerperal fever. *Am J Public Health*. 2010;**100**(6): 1008–1009.
2. Mortimer EA, Jr., Lipsitz PJ, Wolinsky E, Gonzaga AJ, Rammelkamp CH, Jr. Transmission of staphylococci between newborns. Importance of the hands to personnel. *Am J Dis Child*. 1962;**104**: 289–295.
3. Allegranzi B, Pittet D. Role of hand hygiene in healthcare-associated infection prevention. *J Hosp Infect*. 2009;**73**(4): 305–315.
4. Pittet D, Hugonnet S, Harbarth S, et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene: Infection Control Programme. *Lancet*. 2000;**356**(9238): 1307–1312.
5. Backman C, Zoutman DE, Marck PB. An integrative review of the current evidence on the relationship between hand hygiene interventions and the incidence of health care-associated infections. *Am J Infect Control*. 2008;**36** (5): 333–348.
6. Mody L, Saint S, Kaufman SR, Kowalski C, Krein SL. Adoption of alcohol-based handrub by United States hospitals: a national survey. *Infect Control Hosp Epidemiol*. 2008;**29** (12): 1177–1180.
7. Voss A, Widmer AF. No time for handwashing!? Handwashing versus alcoholic rub: can we afford 100 percent compliance? *Infect Control Hosp Epidemiol*. 1997;**18**(3): 205–208.
8. Erasmus V, Brouwer W, van Beeck EF, et al. A qualitative exploration of reasons for poor hand hygiene among hospital workers: lack of positive role models and of convincing evidence that hand hygiene prevents cross-infection. *Infect Control Hosp Epidemiol*. 2009;**30** (5): 415–419.
9. Larson E, Killien M. Factors influencing handwashing behavior of patient care personnel. *Am J Infect Control*. 1982;**10** (3): 93–99.
10. Harris AD, Samore MH, Nafziger R, DiRosario K, Roghmann MC, Carmeli Y. A survey on handwashing practices and opinions of healthcare workers. *J Hosp Infect*. 2000;**45**(4): 318–321.
11. Lankford MG, Zembower TR, Trick WE, Hacek DM, Noskin GA, Peterson LR. Influence of role models and hospital design on hand hygiene of healthcare workers. *Emerg Infect Dis*. 2003;**9**(2): 217–223.
12. Boyce JM, Pittet D. Guideline for Hand Hygiene in Health-Care Settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HIPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *Am J Infect Control*. 2002;**30**(8):S1–S46.
13. Pittet D, Allegranzi B, Boyce J. The World Health Organization Guidelines on Hand Hygiene in Health Care and their consensus recommendations. *Infect Control Hosp Epidemiol*. 2009;**30**(7): 611–622.
14. Ellingson K, Haas JP, Aiello AE, et al. Strategies to prevent healthcare-associated infections through hand hygiene. *Infect Control Hosp Epidemiol*. 2014;**35** Suppl 2: S155–S178.
15. World Health Organization. A Guide to the Implementation of the WHO Multimodal Hand Hygiene Improvement Strategy. 2009.
16. Sunkesula VC, Meranda D, Kundrapu S, et al. Comparison of hand hygiene monitoring using the 5 Moments for Hand Hygiene method versus a wash in-wash out method. *Am J Infect Control*. 2015;**43**(1): 16–19.
17. Boyce JM. Measuring healthcare worker hand hygiene activity: current practices and emerging technologies. *Infect Control Hosp Epidemiol*. 2011;**32**(10): 1016–1028.

18. The Joint Commission. Measuring Hand Hygiene Adherence: Overcoming the Challenges: www.jointcommission.org/assets/1/18/hh_monograph.pdf. Published 2009. Accessed May 18, 2013.
19. Boyce JM. Hand hygiene compliance monitoring: current perspectives from the USA. *J Hosp Infect*. 2008;**70** Suppl 1: 2–7.
20. Gould DJ, Drey NS, Creedon S. Routine hand hygiene audit by direct observation: has nemesis arrived? *J Hosp Infect*. 2011;**77**(4): 290–293.
21. World Health Organization. SAVE LIVES Clean Your Hands, Tools and Resources for Evaluation and Feedback: www.who.int/gpsc/5may/tools/evaluation_feedback/en/. Accessed May 18, 2013.
22. Pan SC, Tien KL, Hung IC, et al. Compliance of health care workers with hand hygiene practices: independent advantages of overt and covert observers. *PloS one*. 2013;**8**(1): e53746.
23. Larson EL, Aiello AE, Cimiotti JP. Assessing nurses' hand hygiene practices by direct observation or self-report. *J Nurs Meas*. 2004;**12**(1): 77–85.
24. Fries J, Segre AM, Thomas G, Herman T, Ellingson K, Polgreen PM. Monitoring hand hygiene via human observers: how should we be sampling? *Infect Control Hosp Epidemiol*. 2012;**33**(7): 689–695.
25. Yin J, Reisinger HS, Vander Weg M, et al. Establishing evidence-based criteria for directly observed hand hygiene compliance monitoring programs: a prospective, multicenter cohort study. *Infect Control Hosp Epidemiol*. 2014;**35**(9): 1163–1168.
26. Hlady CS, Severson MA, Segre AM, Polgreen PM. A mobile handheld computing application for recording hand hygiene observations. *Infect Control Hosp Epidemiol*. 2010;**31**(9): 975–977.
27. Chen LF, Carriker C, Staheli R, et al. Observing and improving hand hygiene compliance: implementation and refinement of an electronic-assisted direct-observer hand hygiene audit program. *Infect Control Hosp Epidemiol*. 2013;**34**(2): 207–210.
28. Armellino D, Hussain E, Schilling ME, et al. Using high-technology to enforce low-technology safety measures: the use of third-party remote video auditing and real-time feedback in healthcare. *Clin Infect Dis*. 2012;**54**(1): 1–7.
29. Palmore TN, Henderson DK. Big brother is washing . . . video surveillance for hand hygiene adherence, through the lenses of efficacy and privacy. *Clin Infect Dis*. 2012;**54**(1): 8–9.
30. McGuckin M, Govednik J. Hand hygiene product volume measurement: an integral part of a multiple-method program. *Infect Control Hosp Epidemiol*. 2010;**31**(9): 980–981; author reply 981.
31. McGuckin M, Waterman R, Govednik J. Hand hygiene compliance rates in the United States–a one-year multicenter collaboration using product/volume usage measurement and feedback. *Am J Med Qual*. 2009;**24**(3): 205–213.
32. Morgan DJ, Pineles L, Shardell M, et al. Automated hand hygiene count devices may better measure compliance than human observation. *Am J Infect Control*. 2012;**40**(10): 955–959.
33. Marra AR, Moura DF, Jr., Paes AT, dos Santos OF, Edmond MB. Measuring rates of hand hygiene adherence in the intensive care setting: a comparative study of direct observation, product usage, and electronic counting devices. *Infect Control Hosp Epidemiol*. 2010;**31**(8): 796–801.
34. Boscart VM, Gorski S, Holliday PJ, et al. Advanced technologies to curb healthcare-associated infections. *HealthcarePapers*. 2009;**9**(3): 51–55 discussion 60–52.
35. Swoboda SM, Earsing K, Strauss K, Lane S, Lipsett PA. Isolation status and voice prompts improve hand hygiene. *Am J Infect Control*. 2007;**35**(7): 470–476.
36. Venkatesh AK, Lankford MG, Rooney DM, Blachford T, Watts CM, Noskin GA. Use of electronic alerts to enhance hand hygiene compliance and decrease transmission of vancomycin-resistant *Enterococcus* in a hematology unit. *Am J Infect Control*. 2008;**36**(3): 199–205.
37. Cheng VC, Tai JW, Ho SK, et al. Introduction of an electronic monitoring system for monitoring compliance with Moments 1 and 4 of the WHO "My 5 Moments for Hand Hygiene" methodology. *BMC Infect Dis*. 2011;**11**: 151.
38. Srigley JA, Gardam M, Fernie G, Lightfoot D, Lebovic G, Muller MP. Hand hygiene monitoring technology: a systematic review of efficacy. *J Hosp Infect*. 2015;**89**(1): 51–60.
39. Kampf G, Reichel M, Feil Y, Eggerstedt S, Kaulfers PM. Influence of rub-in technique on required application time and hand coverage in hygienic hand disinfection. *BMC Infect Dis*. 2008;**8**: 149.
40. Widmer AF, Conzelmann M, Tomic M, Frei R, Stranden AM. Introducing alcohol-based hand rub for hand hygiene: the critical need for training. *Infect Control Hosp Epidemiol*. 2007;**28**(1): 50–54.
41. Tschudin-Sutter S, Sepulcri D, Dangel M, Schuhmacher H, Widmer AF. Compliance with the World Health Organization hand hygiene technique: a prospective observational study. *Infect Control Hosp Epidemiol*. 2015;**36**(4): 482–483.
42. Macinga DR, Edmonds SL, Campbell E, Shumaker DJ, Arbogast JW. Efficacy of novel alcohol-based hand rub products at typical in-use volumes. *Infect Control Hosp Epidemiol*. 2013;**34**(3): 299–301.
43. Kampf G, Ruselack S, Eggerstedt S, Nowak N, Bashir M. Less and less-influence of volume on hand coverage and bactericidal efficacy in hand disinfection. *BMC Infect Dis*. 2013;**13**: 472.
44. Zaragoza M, Salles M, Gomez J, Bayas JM, Trilla A. Handwashing with soap or alcoholic solutions? A randomized clinical trial of its effectiveness. *Am J Infect Control*. 1999;**27**(3): 258–261.
45. Girou E, Loyeau S, Legrand P, Oppein F, Brun-Buisson C. Efficacy of handrubbing with alcohol based solution versus standard handwashing with antiseptic soap: randomised clinical trial. *BMJ (Clinical research ed.)*. 2002;**325**(7360): 362.
46. Chow A, Arah OA, Chan SP, et al. Alcohol handrubbing and chlorhexidine handwashing protocols for routine hospital practice: a randomized clinical trial of protocol efficacy and time effectiveness. *Am J Infect Control*. 2012;**40**(9): 800–805.
47. Turner RB, Fuls JL, Rodgers ND. Effectiveness of hand sanitizers with and without organic acids for removal of rhinovirus from hands. *Antimicrob Agents Chemother*. 2010;**54**(3): 1363–1364.
48. Steinmann J, Paulmann D, Becker B, Bischoff B, Steinmann E, Steinmann J. Comparison of virucidal activity of alcohol-based hand sanitizers versus antimicrobial hand soaps in vitro and in vivo. *J Hosp Infect*. 2012;**82**(4): 277–280.

49. Grayson ML, Melvani S, Druce J, et al. Efficacy of soap and water and alcohol-based hand-rub preparations against live H1N1 influenza virus on the hands of human volunteers. *Clin Infect Dis*. 2009;**48**(3): 285–291.
50. Lages SL, Ramakrishnan MA, Goyal SM. In-vivo efficacy of hand sanitisers against feline calicivirus: a surrogate for norovirus. *J Hosp Infect*. 2008;**68**(2): 159–163.
51. Oughton MT, Loo VG, Dendukuri N, Fenn S, Libman MD. Hand hygiene with soap and water is superior to alcohol rub and antiseptic wipes for removal of *Clostridium difficile*. *Infect Control Hosp Epidemiol*. 2009;**30**(10): 939–944.
52. MacCannell T, Umscheid CA, Agarwal RK, Lee I, Kuntz G, Stevenson KB. Guideline for the prevention and control of norovirus gastroenteritis outbreaks in healthcare settings. *Infect Control Hosp Epidemiol*. 2011;**32**(10): 939–969.
53. Edmonds SL, Zapka C, Kasper D, et al. Effectiveness of hand hygiene for removal of Clostridium difficile spores from hands. *Infect Control Hosp Epidemiol*. 2013;**34**(3): 302–305.
54. CDC Vital Signs: www.cdc.gov/VitalSigns/Hai/StoppingCdifficile/. 2012.
55. Shen NJ, Pan SC, Sheng WH, et al. Comparative antimicrobial efficacy of alcohol-based hand rub and conventional surgical scrub in a medical center. *J Microbiol Immunol Infect = Wei mian yu gan ran za zhi*. 2015;**48**(3): 322–328.
56. Parienti JJ, Thibon P, Heller R, et al. Hand-rubbing with an aqueous alcoholic solution vs traditional surgical hand-scrubbing and 30-day surgical site infection rates: a randomized equivalence study. *JAMA*. 2002;**288**(6): 722–727.
57. Tanner J, Swarbrook S, Stuart J. Surgical hand antisepsis to reduce surgical site infection. *The Cochrane Database of Systematic Reviews*. 2008 (1): CD004288.
58. Haessler S, Connelly NR, Kanter G, et al. A surgical site infection cluster: the process and outcome of an investigation – the impact of an alcohol-based surgical antisepsis product and human behavior. *Anesth Analg*. 2010;**110**(4): 1044–1048.
59. Blanchard JBR BN, Bolyard E, Graves P. Recommended practices for hand hygiene in the perioperative setting in perioperative standards and recommended practices, 2013 edition. *AORN*. 2013: 66–67.
60. Larson EL, Cohen B, Baxter KA. Analysis of alcohol-based hand sanitizer delivery systems: efficacy of foam, gel, and wipes against influenza A (H1N1) virus on hands. *Am J Infect Control*. 2012;**40**(9): 806–809.
61. Koeppe ES, Ferguson KK, Colacino JA, Meeker JD. Relationship between urinary triclosan and paraben concentrations and serum thyroid measures in NHANES 2007–2008. *Sci Total Envirom*. 2013;**445**–446: 299–305.
62. Lankester J, Patel C, Cullen MR, Ley C, Parsonnet J. Urinary triclosan is associated with elevated body mass index in NHANES. *PloS one*. 2013;**8**(11): e80057.
63. Clayton EM, Todd M, Dowd JB, Aiello AE. The impact of bisphenol A and triclosan on immune parameters in the U.S. population, NHANES 2003–2006. *Environ Health Perspect*. 2011;**119**(3): 390–396.
64. Aiello AE, Larson EL, Levy SB. Consumer antibacterial soaps: effective or just risky? *Clin Infect Dis*. 2007;**45** Suppl 2:S137–S147.
65. Syed AK, Ghosh S, Love NG, Boles BR. Triclosan promotes *Staphylococcus aureus* nasal colonization. *mBio*. 2014;**5** (2).
66. Larson E, Girard R, Pessoa-Silva CL, Boyce J, Donaldson L, Pittet D. Skin reactions related to hand hygiene and selection of hand hygiene products. *Am J Infect Control*. 2006;**34**(10): 627–635.
67. Ahmed-Lecheheb D, Cunat L, Hartemann P, Hautemaniere A. Prospective observational study to assess hand skin condition after application of alcohol-based hand rub solutions. *Am J Infect Control*. 2012;**40**(2): 160–164.
68. Ohlenschlaeger J, Friberg J, Ramsing D, Agner T. Temperature dependency of skin susceptibility to water and detergents. *Acta Derm Venereol*. 1996;**76**(4): 274–276.
69. Ibler KS, Jemec GB, Diepgen TL, et al. Skin care education and individual counselling versus treatment as usual in healthcare workers with hand eczema: randomised clinical trial. *BMJ (Clinical research ed.)*. 2012;**345**: e7822.
70. Williams C, Wilkinson SM, McShane P, et al. A double-blind, randomized study to assess the effectiveness of different moisturizers in preventing dermatitis induced by hand washing to simulate healthcare use. *Brit J Dermatol*. 2010;**162**(5): 1088–1092.
71. Boyce JM, Pearson ML. Low frequency of fires from alcohol-based hand rub dispensers in healthcare facilities. *Infect Control Hosp Epidemiol*. 2003;**24**(8): 618–619.
72. Gould DJ, Moralejo D, Drey N, Chudleigh JH. Interventions to improve hand hygiene compliance in patient care. *Cochrane Database of Systematic Reviews (Online)*. 2010(9): CD005186.
73. Schweizer ML, Reisinger HS, Ohl M, et al. Searching for an optimal hand hygiene bundle: a meta-analysis. *Clin Infect Dis*. 2014;**58**(2): 248–259.
74. Luangasanatip N, Hongsuwan M, Limmathurotsakul D, et al. Comparative efficacy of interventions to promote hand hygiene in hospital: systematic review and network meta-analysis. *BMJ (Clinical research ed.)*. 2015;**351**: h3728.
75. Talbot TR, Johnson JG, Fergus C, et al. Sustained improvement in hand hygiene adherence: utilizing shared accountability and financial incentives. *Infect Control Hosp Epidemiol*. 2013;**34**(11): 1129–1136.
76. Larson EL, Patel SJ, Evans D, Saiman L. Feedback as a strategy to change behaviour: the devil is in the details. *J Eval Clin Pract*. 2013;**19**(2): 230–234.

Chapter 10

Surveillance: An Overview

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A good surveillance system does not guarantee that you make the right decisions but it reduces the chance of making the wrong ones.
–Alexander Langmuir[1]

Introduction

The cornerstone of any clinical outcomes program, including one responsible for healthcare epidemiology (HE) and infection prevention (IP) and antimicrobial stewardship (ASP), is surveillance for complications of medical care. Because of the changing paradigm of healthcare, infections that have been labeled "nosocomial" in the past are now called "healthcare-associated." The term "healthcare-associated infection" (HAI) describes an infection that is neither present nor incubating at the time the patient is admitted to the healthcare institution. We refer to surveillance systems that collect information about HAIs, colonization or infection with epidemiologically significant organisms, antimicrobial use, and the related processes of care. For simplicity, we use the term "HAI" to encompass areas of interest to the healthcare epidemiologist. Although we focus on surveillance as it applies to HAIs, the methods we discuss in this chapter are well established and can also be applied to noninfectious complications. Surveillance in ASP overlaps with surveillance for HAIs. When tracking multidrug-resistant organisms (MDROs), some of which are HAIs, resistance patterns are important. In some areas, the surveillance for ASP is being developed, and the discussion may not apply.

This chapter reviews basic principles of surveillance for HAIs and colonization or infection with epidemiologically important organisms. Additionally, with IP, ASP, and other elements of patient safety being elevated from the dark corners of hospitals into the public, regulatory, and legislative realms, we will also briefly discuss surveillance in the current era of emphasis on patient safety. The focus has now expanded to health systems and the population served by the larger medical community including nonacute healthcare settings (e.g., .long-term care facilities, rehabilitation units, and home healthcare).

In this chapter we describe the components of a surveillance system, methods for surveillance, methods for finding HAI events of interest and of public health importance, use of antimicrobial agents and data sources. We describe methods used to stratify patients by their risk of developing an HAI or acquiring an epidemiologically significant organism and methods to risk-adjust use of antimicrobials in hospitals and other healthcare settings. We also discuss the importance of calculating rates or ratios of infection, colonization, antimicrobial resistance, antimicrobial use, and other outcomes in a standardized fashion to ensure that appropriate comparisons can be made.

Finally, we review the importance of using computers and information technology, which are becoming integral to efficient and effective surveillance. We encourage HE, IP, and ASP teams to use this information as they design surveillance systems or integrate informatics systems into their daily activities so that they meet the goals of their program. The information in this chapter should be supplemented with the training and resources needed to provide healthcare institutions with accurate collection and analysis of these complex data.

Background

In 1847, Ignaz Semmelweis reported on an unusual difference in mortality rates among mothers delivering babies at the Allgemeines Krankenhaus der Stadt Wien, in Austria (the Vienna Lying-In Hospital). Semmelweis had made the general observation that mothers delivering in the hospital's First Obstetrical Clinic were more likely to develop puerperal fever than were those delivering in the Second Obstetrical Clinic. This difference was so pronounced that it was common knowledge on the streets, and women admitted to the hospital would plead for admission to the "Second Clinic," believing they would die if they gave birth in the "First Clinic." Troubled by this seemingly inexplicable disparity, Semmelweis documented the mortality rates from puerperal fever in the two clinics and began to collect data on the differences in patients and practices. He examined numerous variables without identifying a possible cause, until he noted that women in the First Clinic were treated by interns, who began the morning examining cadavers. Midwives, who were not involved in cadaver dissections, treated women in the Second Clinic. Hypothesizing that some element transferred from cadavers to the interns' hands and then to the pregnant women was responsible for the puerperal fever, Semmelweis instituted the practice of having all interns wash their hands with a chlorinated lime solution after dissection and prior to examining patients. With this single intervention, rates of puerperal fever in the First Clinic declined dramatically, until they generally equaled those in the Second Clinic.

Semmelweis's observation of the difference in rates of death due to puerperal fever was a basic form of surveillance. Surveillance can be described as the process of identifying rates of complications and ultimately intervening to reduce those rates. Surveillance is a dynamic process for collecting, concatenating, analyzing, and disseminating data concerning specific healthcare events that occur in a specific population.[2]

Findings from surveillance are commonly linked to or should result in actions or decisions, often at the level of hospital policy. As the cornerstone of HE and IP programs, surveillance provides data that are used to determine baseline rates of HAIs, and to detect changes in previously measured rates or distributions of events. The changes that have been found may lead to investigations of each case, including the determination of whether such events or significantly increased rates were clustered in time and/or space, the generation of hypotheses about risk factors, the institution of prevention and control measures, and, ultimately, the determination of whether the interventions instituted were effective. Appropriately performed surveillance requires defined events and systematic case-finding, and appropriate risk stratification to identify trends and to evaluate the impact of interventions over time. Surveillance data should also be used to determine the risk factors for the outcome of interest, to monitor compliance with established hospital policies and practices, to evaluate changes in practice, and to identify topics for further study. Importantly, such processes are critical to ensure that appropriate data are generated for interhospital comparisons.

Historically, in the United States, it was accepted by the Centers for Disease Control and Prevention (CDC), accrediting agencies, and hospital administrators that surveillance for nosocomial infections (now called healthcare-associated infections) was an important element of an infection prevention and control program. In 1974, the CDC initiated the Study on the Efficacy of Nosocomial Infection Control (SENIC) to determine the magnitude of the problem with HAIs, to evaluate the extent to which hospitals had adopted surveillance and control programs, and to examine whether infection prevention and control programs reduced rates of surgical site infection (SSI), ventilator-associated pneumonia (VAP), urinary tract infection (UTI), and bloodstream infection (BSI).[3] The SENIC investigators found that different combinations of infection control practices helped reduce the incidence of each of these types of infections.[3] However, surveillance was the only component found essential to reduce all four types of infection. Of note, this study examined the rates of the four most common infections, and these data suggest that the incidences of other types of HAIs are also reduced with comprehensive surveillance activities.[3–5] In addition, the SENIC project concluded that effective programs included surveillance for HAIs, adequate numbers of infection control practitioners or infection preventionist's, feedback of data to healthcare providers, and a trained hospital epidemiologist (a physician trained in epidemiologic methods and infection control and prevention strategies).

Since the SENIC study was published, surveillance for HAIs, including those resistant to antimicrobial agents, has taken on even greater importance in facilitating the prevention of transmission among an increasingly ill population of patients. Although much of the experience with surveillance for HAIs has taken place in North America, European and other international groups have recently developed large surveillance programs for HAIs and antimicrobial-resistant organisms that have supported the fundamental findings of the SENIC project and have enhanced our understanding of the expanding roles of surveillance.[6–10] Such sophisticated surveillance programs that involve large numbers of hospitals have proven extremely effective in identifying new trends in the spread of antimicrobial-resistant organisms and in measuring the impact of interventions.

Several other new trends in surveillance should be mentioned. "Syndromic surveillance" uses health-related data to track events of potential public health significance, such as infection with an agent of bioterrorism or newly emerging diseases (e.g., severe acute respiratory syndrome [SARS], Ebola [EBV]).[11] Data that can be captured in these systems include admission diagnoses, emergency department chief complaints, prescriptions written or filled, and test utilization patterns. Such data, once concatenated, are processed using sophisticated algorithms to identify syndromes (e.g., respiratory syndromes, rash-associated illness, febrile influenza-like illness, or gastroenteritis) that mimic significant infectious and noninfectious diseases. Such data would be routinely transmitted to the public health authorities, as an "early warning" system for a bioterrorism event or to alert clinicians and, over time, assess the effectiveness of interventions. These efforts have been most studied with influenza using social media and publically available data and appear to be valid and effective. Several recent examples of these strategies have been important in early identification of patients with "high-impact" pathogens such as Ebola and Middle East Respiratory Syndrome (MERS-CoV). However, the integration of social media is associated with cautionary notes of "overcalling" potential infectious events. The utility of this type of surveillance is that it detects outbreaks early and tracks disease trends and patterns. Hence, its potential application in HE and IP programs is being investigated, and it is being incorporated more frequently.[12]

Because of the impact and importance of HAIs and MDROs, transparency about frequency and trends is being called for increasingly in the United States and other developed nations. Furthermore, France, the United Kingdom, and many states in the United States and Canadian provinces have passed legislation requiring healthcare facilities to report HAIs, detection of MDROs, and/or process-of-care measures to public health authorities for review and verification. Data are then made available by the agencies to the public and may affect reimbursement for acute care and other healthcare facilities. The intended goal of this new regulatory role is to release these data to the public and encourage improvements in the quality of healthcare and patient safety.[13–15] With increasing requirements for public reporting of HAIs, the importance of using standardized definitions, identifying cases systematically, and appropriately assigning risk factors is paramount.[16]

What Does Surveillance Entail?

Surveillance requires that relevant information be collected systematically. This includes the careful collection and validation of both numerator and denominator data regardless if this is for HAIs or antimicrobial use. The purpose of, and time frame for, data collection should be specific. Data need to be analyzed and displayed to enhance interpretation and facilitate

any necessary interventions. This chapter focuses on surveillance for HAIs, MDROs, and relevant processes of care. We also consider some unique aspects of ASP, commonly linked with HAI and MDRO surveillance although with some unique features. These principles can also be applied to non-infectious adverse outcomes of medical care, such as falls and medication errors. This process and its epidemiologic aspects are important to maintain given the increasing pressure to publicly report these data and to reimburse healthcare providers for their ability to provide safe care. Additionally, although we recognize that an increasing number of patients receive medical care and surgical procedures in the outpatient setting, this chapter primarily describes surveillance in acute care hospitals. The principles set out here, however, can be used in any healthcare setting.

Why Conduct Surveillance?

Surveillance is conducted for a myriad of reasons. Some are more important than others. Conducting surveillance or establishing a surveillance program allows an IP program to achieve multiple goals:

- To establish baseline rates for comparison;
- To detect clustering in time and space of infections or healthcare-related events (e.g., outbreaks);
- To convince clinicians and administrators that there is a potential problem (that may require additional resources to address);
- To generate hypotheses concerning risk factors for infection;
- To identify a source of cases with which to test hypotheses concerning risk factors;
- To assess the impact of prevention and control measures (e.g., interventions);
- To guide treatment (e.g., the choice of antimicrobial agents) and/or prevention strategies (e.g., administration of vaccine or chemoprophylaxis);
- To reinforce practices and procedures;
- To satisfy patient-care standards, guidelines, and/or regulatory requirements;
- To defend lawsuits;
- To conduct research;
- To reduce the incidence of HAIs;
- To make comparisons within and between hospitals or healthcare systems; and
- To drive interventions that will improve patient safety.

What Is Necessary to Plan for, and Conduct, Surveillance for HAIs, MDROs, and ASP?

Many IP programs establish surveillance systems based on recommendations from the CDC or another federal agency, legislative directives, regulatory agency requirements, or other external pressure, such as competition from hospitals in the community that have already established programs. Commonly the surveillance systems for HAIs and MDROs house data needed for ASP programs, and the surveillance activities are linked. Hospitals and health systems that have established programs under such circumstances may not have established their own goals and priorities prior to undertaking surveillance. Consequently, data collection becomes an end unto itself.

Unfortunately, in these instances, the surveillance data have little influence on the infection rates because clarity as to their purpose and practical application is lacking. On the other hand, HE and IP programs with defined objectives and goals can effectively use data to motivate clinicians and enhance quality improvement efforts.

There are a number of requirements for successful surveillance programs that are generally multidisciplinary efforts with physician, HE, IP, pharmacy, laboratory, and other stakeholder involvement (Table 10.1). Chief among them is a set of clear and specific primary objectives. When developing a new surveillance system or revising an existing system, the staff must first define the priorities of the IP/ASP program(s). By outlining program priorities, staff can clarify both the type of surveillance they should conduct and the types of data they should collect. After the HE, IP, and ASP staff have analyzed preliminary data from their own institution (i.e., data obtained either through the previous surveillance system or through a hospital-wide/health system–wide prevalence survey), they can custom design a surveillance system specific for their own facility. National

Table 10.1 System requirements for surveillance programs

Programmatic
Leadership support
Access to data
Multidisciplinary approach
Human resources
• Trained personnel
◦ Infection prevention
◦ Hospital epidemiology
◦ Data management
Financial resources
• Equipment
◦ Computer hardware and software
• Supplies for interventions
Components
Statement of primary objective(s) and goal(s)
Standardized application of case definitions and collection methods
Measurable metrics of success
Numerator and denominator data
Data to stratify by risk
Mechanism to report results broadly and efficiently

and state (or provincial) regulatory issues, national guidelines, and local patient care standards that may dictate special surveillance needs must be considered. For example, some states require environmental surveillance for *Legionella* species, while others require reporting of specific organisms and or HAI rates.

When developing a surveillance program, HE, IP, and ASP personnel should consider characteristics of the institution, including the size, hospital type (e.g., private, university, or federal, and teaching or nonteaching), patient populations served, procedures and treatments offered, and proportion of inpatient care and outpatient care provided at that facility. These staff also should consider the resources available to the IP program, including the budget, the number of personnel and their level of training and experience, and the available technology resources that can be used by the staff. A surveillance system should be designed in a manner that supports accomplishing the stated objectives with the most efficient use of resources, keeping in mind that additional resources must remain available to appropriately utilize the surveillance data gathered (e.g., for analysis, reporting, developing interventions, and monitoring efficacy). Because of the trend toward increasing transparency and public reporting of these data, verification of numerators and denominators has become increasingly important to administrators, which requires additional resources.

As the surveillance system is designed, the staff should consider the advantages and disadvantages of different surveillance methods (Table 10.2) and the sensitivity of different case- finding methods or surveillance strategies (Table 10.3). Identifying which events to study and the data sources available in their hospital when they choose the case-finding methods is crucial. Definitions must be standard and applied in the same fashion using appropriate numerators and denominators. In general, in the United States, definitions promoted by the CDC are used.[17] These definitions, although not perfect, have been used for years, and their utility is well understood by the healthcare epidemiology community. They are discussed in more detail below (in the discussion of how to target outcomes and populations).

Similarly for ASP, identifying conditions to monitor in a standard fashion facilitates interventions. However, definitions may be less clear as commonly infections and syndromes are targeted for surveillance activities including community-acquired pneumonia, urinary tract infections, skin and soft tissue infections. Basic information should be collected on all patients with HAIs and MDROs or who are receiving antimicrobials (Table 10.4). For some infections, one may want to collect additional data (e.g., on central venous catheter–associated BSIs, specific antimicrobials, doses, duration) or collect information during certain time periods (e.g., when conducting a study to evaluate the prevalence of certain infections and to identify risk factors for those infections). Additionally, for surveillance for ASP, data may be collected on antimicrobial choices for certain types of infections such as perioperative prophylaxis for cardiac surgery or treatment of *Staphylococcus aureus* bacteremia.

Ideally, IP and ASP staff should focus on infections or transmission of organisms that can be prevented, occur frequently, cause serious morbidity, increased mortality, are costly to treat, or are caused by organisms resistant to multiple antimicrobial agents. For example, because infections associated with medical devices are preventable, consider surveying those UTIs associated with indwelling catheters or those infections caused by antimicrobial-resistant organisms. Another strategy would be to limit this type of surveillance to device-related infections in intensive care units or limit it to step-down units where such devices are commonly used. HAIs caused by *Legionella* species or *Aspergillus* species occur infrequently, but cause substantial morbidity and mortality, and most can be prevented with environmental controls. Similarly, for ASP efforts, staff may focus on areas where antimicrobials are commonly misused such as in the perioperative setting or the treatment of asymptomatic bacteruria. Therefore, IP and ASP staff may want to use available data sources to identify all of these cases.

Vancomycin-resistant enterococci (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA), *Clostridium difficile* (CDI), multidrug-resistant *Pseudomonas aeruginosa* or *Acinetobacter* species, carbapenem-resistant enterobacteraciae (CRE) and other organisms resistant to multiple antimicrobials can spread rapidly within healthcare settings. Colonization or infection caused by these organisms can be very costly to treat or may not be treatable. Therefore, microbiology laboratory data can be used to perform surveillance for patients who are infected or colonized with MDROs. IP personnel may choose to study infections that are relatively minor but occur frequently, because these infections will increase the total cost to the healthcare system substantially. For example, saphenous vein harvest site infections are less severe than sternal wound infections after coronary artery bypass graft procedures. However, at least two-thirds of SSIs that occur after coronary artery bypass graft are harvest site infections, with an attributable cost of nearly $7,000 per infection.[18] Because harvest site infections occur much more frequently than do serious sternal wound infections, the total cost to a healthcare system of the former approximates that of the latter. Furthermore, harvest site infections may be caused by problems with surgical technique and thus could be prevented if surgical technique was improved. Therefore, IP personnel might want to develop a surveillance system that is able to detect harvest site infections instead of focusing on the more serious but less common sternal wound infections.

Strategies that are similar can be used for ASP programs. While infections after colorectal surgery may not be the most common, if expensive antimicrobials such as ertapenem or meropenem are used, a targeted intervention by the ASP staff may improve treatment and save costs. On the other hand, if aminoglycosides are being used inappropriately, an ASP intervention to appropriately monitor the agents or switch to a less toxic agent may enhance patient safety. The challenge, therefore, is to determine how a program can get the most from the resources that it has to use – that is, should the surveillance focus on serious infections that are rare or more common infections that are less serious? Or the focus could be to appropriately use expensive antibiotics and minimize the use of agents associated with expensive toxicities.

Table 10.2 Advantages and disadvantages of basic surveillance strategies

Strategy	Advantages	Disadvantages
Health system or hospital-wide surveillance	Provides data on all organisms and infection types Identifies clusters, recognizes outbreaks early Establishes accurate baseline rates Identifies risk factors	Expensive and labor intensive Time dedicated to data collection decreases the amount of time for analysis No defined prevention objectives making it difficult to develop interventions Identifies infections that may not be preventable
Prevalence survey	Inexpensive Time-efficient; can be completed periodically Provides snapshot of rates in a population	Overestimates rates Does not capture important differences in infections Does not provide information about variation within rates
Targeted surveillance (i.e., site or unit specific; rotating)	Flexible, easy to combine with other strategies Can include postdischarge component Identifies risk factors Easily adaptable to interventions Allows focus on patients at greater risk Requires fewer resources and simplifies surveillance effort Cost effective	May miss clusters Denominator may be inadequate to make comparisons Risk stratification may be difficult Rates may be unreliable or not generalizable
Objective/priority based	Adaptable to specific patient populations and interventions Can be tailored based on resources Focus on specific problems Identifies risk factors Can include a postdischarge component	May miss clusters Unable to provide baseline or comparison data for other infections
Threshold (outbreak or periodic)	Increases efficiency of surveillance, allowing IP to perform other activities Institution specific; valuable as long as rates are below national benchmarks at baseline Decreases possibility of missing a significant problem	Does not provide ongoing surveillance data Institution specific; will not identify rates that are above national benchmarks at baseline May miss clusters

As medical care moves from the hospital to outpatient and alternative care settings, healthcare practitioners will be challenged with how to identify HAIs that develop in the ambulatory care or nontraditional setting.[19,20] Unless HE and IP teams expand their boundaries and develop innovative surveillance strategies, they will underestimate the frequency of infections associated with medical care. At present some IP programs that monitor patients who develop SSI after ambulatory operative procedures remain in a quandary about how to best find them.[20] These efforts are equally challenging for ASP programs that are working to improve the appropriateness of use of antimicrobial agents and minimize adverse events in these alternate settings. In addition, IP and ASP staff might consider using surveillance to identify patients who acquire infections associated with outpatient treatments, such as dialysis, chemotherapy, and intravenous therapy (e.g., antimicrobial or antiviral therapy, or parenteral

Table 10.3 Sensitivities and time demands of various case finding methods used for healthcare-associated Infection surveillance

Method	Estimated time required for surveillance	
	Sensitivity	(hours)/500 beds/wk*
Physician self-report forms	0.14–0.34	3
Fever	0.47–0.56**	8
Antibiotic use	0.48–0.81**	13.8
Fever and antibiotic use	0.70**	13.4
Microbiology reports	0.33–0.84**	23.2
Gold Standard	0.94–1.00	35.7–45
Selective chart review using "Kardex clues"	0.82–0.94**	35.7
Chart review		
Prospective	0.76–0.94	53.6
Retrospective (Univ. of Virginia)	0.79	35.7
Retrospective (SENIC)	0.74–0.96	not specified
Infection Control Sentinel Sheet Survey	0.73–0.87	1 minute/chart
(For ICUs or unit-based surveillance)		
Ward liaison surveillance	0.62	17.6
Laboratory-based ward liaison	0.76–0.89	32.0
Risk factor-based surveillance	0.50–0.89	32.4
Selective surveillance based on	0.74	not specified
physician reports		
Automated computer algothrithm review of antibiotic exposure and ICD-9 codes for surgical site infection	0.88–0.91	not specified
Administrative Coding Data***	0.02–0.89	not specified
Clostridium difficile infection	overall 0.76	not specified
Surgical site infection	0.81	not specified
Ventilator associated pneumonia	0.42–0.72	not specified
Catheter associated urinary tract infection	0.50–0.52	not specified
Methicillin-resistant *Staphylococcus aureus*	0.24–0.59	not specified

* Time required for an infection control practitioner to perform surveillance in a 500-bed, acute care hospital
** The Gold Standard for healthcare-associated infection surveillance was determined by a trained physician who examined each patient, each medical record, all "Kardexes" and who verified microbiologic data.
*** Sensitivity of administrative coding data improves with algorithms that use data from electronic health records (Goto et al. Clin Infect Dis 2014;58 688–96).

nutrition) or associated with programs such as hospital-based home care. These latter areas of treatment remain of interest not only because increasingly-ill patients are receiving care in these areas but also because recently there have been incidents of use of contaminated products or poor IP practices at home that have put patients at risk.

How Do You Assess the Surveillance System and Develop Priorities?

At a minimum, an HE and IP program should include an annual evaluation of its surveillance system to determine if it provided meaningful and actionable data. The staff should ask themselves a series of questions:

Table 10.4 Information to collect about patients who have a healthcare-associated infection or colonization with an epidemiologically significant organism, and or process of care or disease syndrome

General information for all sites of infection, infections with epidemiologically important organisms
Patient name
Patient identification number
Patient age
Patient gender
Nursing unit
Service
Bed trace
Admission date
Date of infection onset and/or date specimen for culture was obtained
Site of infection
Organism(s) isolated
Antimicrobial susceptibility pattern of isolates
Admitted from (home, long-term care . . .)
Additional information
Presence of a risk factor (e.g., CVC, urinary catheter, or endotracheal tube, dialysis catheter)
Date of exposure or risk factor[a]
Primary diagnosis[a]
Comorbidities present, if any
Medications received (antibiotics, steroids, immunosuppressive agents, and/or chemotherapeutic agents)[a]
Exposure or risk factor (e.g., immunosuppression, instrumentation, and/or procedure[s])[a]
Antimicrobial therapy (agents and dose) and duration of antimicrobial therapy
History of colonization with another multidrug resistant organism (MDRO)
Travel
Comments
General information for infection with resistant or epidemiologically important organisms
Date culture specimen was obtained
Site from which culture specimen was obtained
Current and/or previous roommates
Previous rooms during current hospitalization
Previous hospitalization(s) in this hospital
Intensive care unit stay
Additional information
Underlying disease(s) or condition(s)
History of antimicrobial use
Previous hospitalization(s) in another hospital/institution

Table 10.4 (cont.)

Previous stay in a long-term care facility
Previous vaccinations or history of infectious disease(s)[a]
Results of molecular typing of isolate(s) including next generation sequencing
General information for syndromic surveillance and some process measures
Patient name
Patient identification number Patient age
Service date
Chief complaint (with or without *ICD-/10* code[s])
Laboratory and radiologic tests ordered and their results and findings
Prescriptions/vaccinations
Compliance with process measures including hand hygiene, isolation precautions, cleaning protocols
Other
General information for infection site–specific surveillance and some process measures
Surgical site infection
Operation and operation CPT or other code
Operation date
Surgeons (attending and resident) and other relevant personnel
Patient's ASA score
Wound classification
Time of incision
Time procedure finished
Antibiotic(s) administered peri-operatively including dose, redosing, timing[a]
Intraoperative oxygenation and/or glucose administered; patient lowest temperature
Operating room number
Bloodstream infection
Intravascular catheters present (yes or no)
Number of catheters, placement circumstances, and time in place
Compliance with insertion and maintenance care bundles
Type of intravascular catheter (central placement, PICC vs. peripheral)
Location of intravascular catheter insertion site
Number of days catheter in place
Person(s) who inserted catheters
Any secondary source of infection
Checklist completed (yes or no)
Infection-related ventilator-associated complication or possible ventilator-associated pneumonia
Positive cultured respiratory specimen or other diagnostic criterion such as test for legionella, influenza, etc.
Endotracheal intubation (yes or no)
Ventilation (yes or no)

Table 10.4 (cont.)

Number of ventilator days
Date patient intubated
FIO_2
PEEP
Checklist completed (yes or no)
Urinary tract infection
Urethral catheter present (yes or no)
External catheter present (yes or no)
Number of days catheter in place
Person(s) who inserted catheter[a]
Other urinary tract instrumentation[a]
Checklist completed (yes or no)
General information for processes of care
Process was performed (yes or no)
There was an opportunity to perform the process (yes or no) Aspects of or steps in process being surveyed
General information for antimicrobial stewardship
Appropriate selection of empiric antimicrobials
Timing for initiation of antimicrobial agents
Descalation appropriately
Dosing and interval for "targeted antimicrobials"
Antimicrobial-related adverse events (e.g., renal dysfunction, hematologic abnormalities, prolonged Q-T intervals)
Prevalence of antimicrobial-resistant pathogens
Incidence of *C. difficile* infection
Costs of antimicrobials (to pharmacy)
Additional information
Compliance with antimicrobial stewardship recommendations
Rate of de-escalation

NOTE: ASA, American Society of Anesthesiologists; CVC, central venous catheter; *ICD-9, International Classification of Diseases, Ninth Revision;* PICC, peripherally inserted central catheter.
[a] Information to be collected under particular circumstances, such as during an outbreak.

- Did the surveillance system measure meaningful outcomes or proxies of best practice? Are these outcomes relevant to the hospital/health system population and infectious diseases or MDROs that are prevalent or emerging in the community?
- Did the surveillance system detect clusters or outbreaks?
- How successful was the system in identifying events of interest (i.e., the sensitivity, specificity, and/or positive and negative predictive values)?
- How representative was the system, if it was not 100 percent sensitive? Could the findings be generalized to other patient populations or institutions?
- Were patient-care practices changed on the basis of the surveillance data?
- Were data used to develop and implement interventions to decrease the endemic rate of infection or inappropriate antibiotic use?

- Were surveillance results communicated and distributed to the administrative and clinical staff? Were data made available in a timely fashion?
- Were data used to encourage interventions or to assess their efficacy?
- Were data used to ensure that rates of infection or colonization did not increase when procedures were changed, new products were introduced, etc.?
- What was the burden of data collection (i.e., the time required to collect valid data, given the importance of the outcome)? Are appropriate resources (IP and other groups within the institution) allocated to perform the necessary data collection?
- How flexible was the surveillance system?
- Does the system provide data to meet regulatory needs?
- Can the system transfer information electronically to public health authorities?

If no one, including the IP or ASP staff, uses the data to alter practice, one must conclude that the current system is ineffective. At this point, it may be more fruitful to abandon the surveillance system and devise a new strategic approach with surveillance goals and objectives in mind. This plan should clearly identify HE and IP objectives, outline the surveillance data needed to address those objectives, and include specific actions that use the collected data to achieve those goals. The goals should focus on infections that are truly preventable and cause harm, antimicrobials that are being used inappropriately, or those HAIs and MDROs for which surveillance is required because of legislative mandates. If appropriate, one could develop interventions on the basis of currently available data. The staff could then plan how they will use the revised surveillance system to monitor the efficacy of the proposed interventions.

To determine the surveillance needs, strategic thinking is necessary. The IP/ASP teams should meet off-site for a day and discuss issues and priorities and should use documents to accomplish the goals. As part of this, each institution should assess their "risk." This process should occur annually and allows the HE and IP team to think critically about where problems and vulnerabilities lie, what regulatory requirements they must fulfill, and which areas have the greatest chance of being improved (Figure 10.1). The institution's risk can include the frequency of healthcare-related events of interest and the risk of patient harm and/or its severity. Also included in the risk assessment is an evaluation of the institution's response to a situation. For example, the IP/ASP team may consider a problem differently if the hospital leadership and hospital units are engaged in solving the problem than if they deny a problem exists.

Validation of data enhances the credibility of the IP/ASP team. Periodically, the team must verify that the surveillance system is actually capturing the data the staff believe they are receiving. Hospital departments that provide data for the surveillance program may change their procedures and thereby cause what appears to be a change in rates. Surveillance systems that use data from information systems are particularly vulnerable to this. This issue is becoming an increasingly important problem for systems in which both numerator and denominator data are generated by computer queries from administrative data systems. If the departments that provide data notify IP/ASP staff about procedural changes, system upgrades, or coding changes, the staff must validate the new data and modify surveillance appropriately. However, departments often change important procedures without informing staff in other departments. These changes could affect relevant rates of infection or antimicrobial use substantially. Other changes do not affect the infection rates or drug use directly but alter the surveillance system's ability to obtain the necessary data. Because changes in procedures instituted by other departments can be invisible and can affect rates of infection or colonization substantially, IP/ASP personnel must investigate and verify changes in the rates or other important results before assuming that there is an outbreak or that an intervention has been very successful (Table 10.5).

For example, you calculate the proportion of *S. aureus* isolates that are resistant to methicillin and find that it has dropped precipitously from 34 percent to 0 percent. However, you suspect that the decrease is not real. Historically, most of the MRSA isolates were recovered from surgical wounds, so you check to see whether the surgeons had changed their management of infected wounds. You discover that the surgeons are now treating SSI empirically without first sending a wound specimen to be cultured. Upon further investigation, you find that the laboratory has changed the criteria for culturing wound specimens: laboratory personnel no longer plate the specimen if the Gram stain does not show any white blood cells. The two unrelated changes artificially reduced the proportion of *S. aureus* isolates that are resistant to methicillin.

Another example: the overall infection rate (or drug utilization) in another hospital suddenly decreases (Table 10.5). Ever skeptical of numbers that seem too good to be true, the HE team searches for a possible artificial cause for this rapid decline. They eventually discover that the fiscal department had changed the bed-count procedure so that an admission was counted each time a patient was transferred to another unit. Thus, the denominator was inflated, and the resulting infection rate (or drug utilization) appeared low.

How Should the Outcomes of Interest and Targeted Populations Be Determined?

Infection prevention and ASP programs that have bountiful resources may want to continue doing hospital-wide or even health system–wide surveillance so they can detect HAIs/MDROs in all patient populations. In some cases they may adopt electronic surveillance strategies to facilitate this activity. However, programs that find themselves in this enviable position should develop innovative methods for conducting hospital-wide surveillance and not just use the traditional labor-intensive method of total chart review. The more likely scenario is one of IP and ASP programs having severely limited budgets; thus the staff must prioritize how to use these precious resources to their greatest possible advantage. We believe that

Your Medical Center

Review Date:
Reviewed By: XXX Committee

Hazard Identification	Risk Assessment: Probability					Risk Assessment: Outcome Severity						Assessment Score		Level of Preparedness *: Needed*				Level of Preparedness *: Achieved				Preparedness Score
	High	Med	Low	None		Very High	High Disrup	Mod Disrup	Low Disrup	None				High	Med	Low		High	Med	Low		
Score	3	2	1	0	X	4	3	2	1	0	=			3	2	1	X	1	2	3	=	
Healthcare-Associated Infections (examples)																						
Surgical site infection examples**																						
CABG																						
Laminectomy/fusion																						
Craniotomy																						
C-section																						
Colon																						
Outpatient																						
Hysterectomy																						
Other																						
MDRO																						
MRSA																						
C. difficile																						
VRE																						
GNRs-MDR																						
Device related infections																						
Central line-associated BSI																						
VAP																						
Catheter-associated UTI																						
Organisms																						
TB																						
Ebola																						
MERS CoV																						
Influenza																						
Other Infection Prevention/ASP Issues																						
Process Measures																						
Hand Hygiene Non-Compliance																						
Environmental Cleaning																						
Surveillance of Employee Illness																						
Isolation Policy Non-Compliance																						
Construction Related Issues																						
Staff Influenza Vaccination Rates																						
Endoscope cleaning and disinfection																						
Contamination of cardiac surgery bypass machines																						
Outbreaks																						
Influx/Surge of Patients or pandemic influenza																						
Endoscopy suite																						
Respiratory protection																						
OR Guideline/Standard Non-Compliance																						
- Skin preparation																						
- Surgical attire																						
- Antibiotic prophylaxis																						
- Flash sterilization																						
- Traffic control																						
- Room cleaning																						

*__Level of Preparedness Needed__: Based on the **Assessment Score** determine the level of preparedness needed utilizing the following guidelines:

Score	Rating
≤2	Low
3 to 5	Med
>6	High

Note: All HCA infections are scored a minimum of 2 on **Level of Preparedness Needed**
I: Infection Control Plan Risk assessment template 2 8 08

Figure 10.1 Example of an Infection Prevention Risk Assessment 20xx

Based on the risk assessment, XXX institution has identified those items scoring 6 or greater in **Preparedness Score** in the risk assessment as priority focus areas for IP. They are prioritized below in descending order.	
Priority	**Risk**
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	

Figure 10.1 (cont.)

most IP and ASP programs should not conduct hospital-wide surveillance. Instead, they should limit their surveillance to specific infections, pathogens, patient populations, or medications.

To begin collecting surveillance data, the HE and IP/ASP staff first must identify the outcomes and the population they will study. An outcome of interest should be identified on the basis of the impact of the event on patients (i.e., the associated morbidity and/or mortality), its frequency, its impact on the institution (financial and other resource burden), and any regulatory requirements. For example, healthcare facilities with only oncology, pediatric, ophthalmology, or trauma patients may prioritize outcomes of interest differently than general hospitals.

Next, the staff should develop written definitions that are precise, concise, and unambiguous. For example, the IP may be faced with cultured blood growing coagulase negative staphylococci and must be able to differentiate between a potential contaminant and infection. This requires evaluating risk factors (premature or with a catheter, etc.) and other factors. Because of these clinically real situations, the CDC developed definitions for HAIs that were introduced in 1988 and revised more recently and are used widely and accepted as a standard.[21,22] The National Healthcare Safety Network (NHSN; formerly the National Nosocomial Infection Survey [NNIS]), supported by the CDC, maintains a database that accepts surveillance data on HAIs, infection and colonization with multidrug-resistant organisms, infections in healthcare workers, and antimicrobial use and resistance (AUR) data that are collected in a systematic fashion from hospitals and other healthcare facilities.[23] Having a large repository of data that have been collected in a similar fashion allows for comparisons of some rates between institutions ("benchmarking"), so that IP and ASP programs can determine whether their rates are similar to those at other institutions with similar patient mixes, bed size, and missions, and can evaluate the success of IP or ASP interventions.

The NHSN recently updated the previously proposed definitions for HAIs, and these definitions should be used if IP or administrative personnel wish to compare their institution's infection rates to those published by the NHSN.[21,22] It is also of note that although these definitions are currently being used for reimbursement in some settings, they have not been validated for this purpose. More recently, with the interest in multidrug-resistant and epidemiologically significant organisms, such as MRSA, VRE, CRE, and CDI, refined definitions have been proposed to stratify according to the place of acquisition, as community-acquired, healthcare-associated, or healthcare-acquired.[24–27] For some events, such as SSI in a solid transplant recipient or BSI in a hematopoietic transplant recipient, the NHSN definitions need to be studied and may need to be further modified.[22]

In other cases, hospitals may need to slightly modify or develop their own definitions. Some larger institutions, or those with large volumes, can use control charts or 95 percent confidence intervals to compare rates.[28] The advantage of using internal rates for comparison over time is that the patient population is likely similarly heterogeneous with respect to underlying illnesses. The major disadvantage is that one cannot discern whether the rates (e.g., rates of HAI or infection with multidrug-resistant organisms) are higher or lower than they should be, in comparison with other institutions, because of the differences in definitions.

Table 10.5 Examples of practices that affect observed rates of infection

Changes in practice	Apparent effect on infection rate
Locus of treatment is shifted from the hospital to the outpatient setting	Decrease in the overall infection rate, because surveillance rarely is performed in the outpatient setting
Patients are discharged earlier, and the length of stay in the hospital decreases	Decrease in the overall infection rate
Patients are discharged earlier after operative procedures, and the length of stay in the hospital decreases	Decrease in the rate of surgical site infection, because surveillance is rarely performed in the outpatient setting
Low-risk operative procedures are performed in a separate ambulatory surgery facility rather than the hospital	Increase in the rate of surgical site infection, because patients who have a higher risk of infection have operative procedures performed in the hospital
Patients residing on a boarding unit are not counted toward the hospital's denominator (i.e., the number of patients hospitalized)	Increased infection rate, if surveillance is performed on these admitted patients, because the denominator appears to decrease
The accounting department changes procedure and counts an admission each time a patient is transferred to another unit	Decreased rate of central line–associated infection, because the denominator (i.e., the number of CVCs inserted) appears to increase
The business office assigns each surgical procedure to the admitting physician, regardless of that physician's specialty, rather than to the surgeon who performs the procedure	Inaccurate surgeon-specific infection rates, because some surgical site infections will be assigned to the wrong physician
Microbiology laboratory changes screening criteria for processing specimens	Decreased rates of infection, if case-finding relies solely on microbiology laboratory reports
Microbiology laboratory implements PCR-based technology to identify a laboratory-based healthcare-associated infection	Increased rates of "colonization/infection" due to capture of "live and dead" organism genetic material
Microbiology laboratory-based surveillance for healthcare-associated infection	Increased infection rates as laboratory-based surveillance may not capture present on admission infections
Definitions of infection are used inconsistently and/or written definitions are absent	Inaccurate infection rates
ICD-9/ICD-10 codes are used to identify patients with healthcare-associated infections	Inaccurate infection rates
A new electronic medical record counts catheter days	Inaccurate infection rates dues to an overestimated or underestimated number of catheter days

NOTE: CVC, central venous catheter; *ICD-9, International Classification of Diseases, Ninth Revision*.

To collect meaningful data, IP and ASP personnel not only must use clear definitions but also must apply the definitions consistently. Training HE and IP personnel enhances their ability to identify infections appropriately and consistently, as has been shown by Cardo and colleagues.[29,30] These investigators demonstrated that, with training, the sensitivity and specificity of surveillance for SSI increased from approximately 84 percent to greater than 93 percent. This training is critical to ensure that appropriate definitions, sources of information, and case-finding strategies are used.

Infections should be considered healthcare-associated if they are related to procedures, treatments, or other events that occur immediately after the patient is admitted to the hospital or if they are related to the same in an alternative healthcare setting, such as a surgical center. In general, infections with onset that occurs more than 48–72 hours after admission and within 7–30 days after hospital discharge are defined as healthcare associated. The time frame is modified for infections that have incubation periods of less than 48–72 hours (e.g., gastroenteritis caused by norovirus) or more than 10 days (e.g., hepatitis A or hepatitis C). An SSI is considered healthcare associated if the onset of infection occurs within 30 days after the operative procedure, or within 90 days after the procedure if a device or foreign material is implanted.

Additionally, within the term "HAI," IP professionals can include infections or pathogen transmission resulting from a surgical or medical procedure that did not require hospitalization. For example, if a patient has a surgical procedure in the outpatient surgical suite and develops an SSI, it is considered healthcare-associated. Or, for another example, because bone marrow transplantation, chemotherapy, and other procedures are now being performed in the outpatient setting, high-risk patients treated in such alternative settings develop BSIs; these infections are almost always related to indwelling intravenous catheters and are therefore considered HAIs.

On the other hand, if a patient admitted with shortness of breath and fever has a chest radiograph that reveals consolidation in the left lower lobe of the lung on day 4 after admission and has a positive result of a test for *Legionella* antigen on day 6 after admission, the infection is not healthcare-associated, because it was incubating when the patient was admitted. Because of these situations, IP will need to refine and validate definitions in order to accurately capture infectious complications in new healthcare delivery settings.

Fortunately, Lessler and colleagues have proposed a systematic method to determine whether an infection was likely acquired in the hospital or in the community. Using the incubation period and the incidence rate ratio of infection, one can obtain a quantitative result that allows for mathematical estimation of the likelihood that an infection was acquired in a certain setting.[31] One can select disease-specific cut-off values to distinguish community-acquired from hospital-acquired infections that perform well for important illnesses. For example, patients who develop influenza symptoms in the first 1.5 days of their hospital stay are classified as having acquired infection in the community. If patients develop symptoms later in their hospital stay, then the likelihood that the infection was acquired in the hospital is 87 percent. Methods of this type will improve the application of HAI definitions.

Antimicrobial use monitoring uses defined measures that require less interpretation. Days of therapy (DOT) is an aggregate sum of the days a given patient receives a specific antimicrobial agent. The patient is considered the numerator and a standardized denominator is used such as patient days or admissions. The defined daily dose (DDD), on the other hand, estimates antimicrobial use in healthcare settings by aggregating the number of grams of each antimicrobial agent purchased, dispensed, or administered divided by time (i.e., the period of interest).

Collecting Data

One of the first mantras of surveillance is that its purpose is to determine the burden of disease, to identify trends and potential problems, and to establish the epidemiologic features of the illness or event of interest. Hence, only the information needed to adequately analyze and interpret the data should be collected. If these data suggest a potential problem, the HE and IP or ASP teams can design a more comprehensive study. Data can be collected prospectively, retrospectively, or using both strategies. In prospective or concurrent surveillance, data are collected at the time the event occurs or shortly thereafter. Concurrent surveillance requires the IP or ASP staff to review the medical record or electronic databases, to assess the patient(s) affected, and to discuss the event with caregivers at the time of the event. Because the data are obtained close to the time the event occurs, additional information not normally a part of the medical record may be available, such as daily management boards and nursing reports. Lack of availability of records becomes less of a barrier as electronic medical record implementation grows. The advantage of this form of data collection is that clusters of the event of interest can be identified as they occur. Importantly, providing feedback about any adverse event as it is occurring helps healthcare workers appreciate the significance of the event; it becomes "real" and less theoretical, and helps them identify other potential prevention strategies. If data are collected after the patient is discharged or retrospectively, clusters or potential outbreaks are not identified as promptly. In some cases, the "distance" of the event in time sometimes impedes interest and interventions. Nonetheless, both methods have similar sensitivities, but retrospective surveillance depends on the completeness, accuracy, and quality of the medical records[32] (Table 10.3). Commonly, programs mix and match data collection strategies to ensure the most complete data collection.

To identify cases, highly sensitive methods for case-finding are preferred, so that important cases are not missed. Commonly, infection preventionists employ several case-finding methods simultaneously. The practice of using information collected from different sources has increased with the shift to early patient discharge and to provision of care in the outpatient setting. However, with this method, one must identify strategies to increase the specificity of the surveillance process and thus reduce the time wasted collecting irrelevant data. If one uses currently available computer systems that can identify patients who may have an HAI or may have acquired an epidemiologically important organism, the time spent in reviewing charts can be reduced; thus, computer-based surveillance strategies are rapidly emerging as important adjuncts to surveillance.[19,20,33,34] As computer hardware and software become more sophisticated and as computer-based decision algorithms are developed and validated, these can be integrated into surveillance systems to streamline data collection and improve identification of HAIs.[19,20,33,34]

Semi-automated surveillance has been well described. These decision support tools filter data from laboratory, pharmacy, and admission, discharge, and transfer systems to identify the surgical procedures that are most likely to have an SSI as a complication.[17,35] Combinations of data such as administrative codes for SSI, readmission with antibiotic administration, or extended length of stay are known to improve case finding for SSI.[19–22,36–39] Chart review and user input are still required, but semiautomated surveillance is valuable in reducing the amount of time IP staff need to spend on surveillance.

Fully automated electronic systems, particularly for SSI identification, are not yet well developed. A piece of the surveillance process that can be automated is the acquisition of denominator data. SSI surveillance requires that specific data elements be gathered at the individual patient level for all patients undergoing surgery to allow for risk adjustment.[12,24,40,41]

When beginning a new surveillance project, the staff should periodically look for flaws in the data, the collection tool, the data sources, and the surveillance process. Validation needs to be done for numerators and denominators, and is increasingly important now that many of these data are commonly reported publicly. Validation is also used to ensure that practitioners apply the definitions systematically and uniformly.[42] In this manner, problems or errors can be identified and corrected before reaching the end of the study or providing data to

stakeholders. The surveillance project's sensitivity and specificity should be determined by examining a random subset of medical records for a defined time period and comparing the number of events identified by this manual review with the number identified by the usual surveillance system. In addition, changes in the surveillance system – such as identifying a new data source or a new item, modifying definitions, or changing the personnel who collect the data – can impact the integrity of the surveillance process. Such changes require validation to ensure that the data are high quality.

Managing Data

Managing surveillance data and organizing them in a meaningful fashion are necessary for identifying patterns and trends. While much of this discussion relates to IP, the strategy for ASP is similar. One of the first organizational processes is for the "cases" identified to be catalogued systematically on a flow sheet or in a computer spreadsheet. This is called a line-listing and will include data pertinent to the problem being examined (see Chapter 11, on outbreak investigations). For example, a line listing may include, in a single row, the patient name, hospital or medical record number, the admission data, type or site of infection, date of infection onset, organism(s), and surgical procedure, if relevant. Many of the IP/ASP software vendors provide this feature. Once the data are in a database, IP/ASP personnel can easily plot numbers or rates over time so they can identify possible trends. Queries of these relational databases can be developed to present data to staff and facilitate workflow.

Programs that are embedded into the electronic medical record allow more end users access and can integrate information from various hospital computer systems. These systems can provide data that are concatenated and presented in epidemiologic terms that facilitate identifying root causes or systematic issues that require further investigation. These electronic IP/ASP software programs facilitate obtaining the information needed for surveillance and can allow electronic labeling of patients with HAIs or antimicrobial use outside of institutional guidelines. Queries can automatically examine specific hospital units or geographic areas, looking for important time-and-space relationships or clusters of cases. In some cases, such as with ASP, they can look at individual cases. The power of these programs is increasingly being used to identify cases of interest.

Analyzing Data

If the IP or ASP teams do not analyze their data, they have wasted the time, money, and effort they spent collecting and recording the data. The purpose of surveillance is not merely to count and record infections/antimicrobial use but to identify problems quickly and to intervene so that the risk of infection or antimicrobial overuse is reduced. The time factor inherent in this process requires that the data be analyzed promptly. The frequency of data analysis is based on the nature and frequency of the healthcare event of interest and the purpose of surveillance. The goal is to strike a balance between analyzing the data frequently enough to detect clusters or events of interest promptly and collecting data for a long enough period of time to ensure that variations in rates are real. Informatics facilitates data collection over a long period of time, since standard analyses can be generated automatically. Queries can be built to identify singular events such as if a patient is receiving a restricted antimicrobial agent. In addition, the IP and in some cases the ASP team must ensure that an adequate sample of cases is reviewed, so that the data are meaningful. For example, if three patients had a procedure performed by a particular surgeon in one month, and one of the patients develops an SSI, it is difficult to interpret the infection rate because there are so few cases. In general, data should be collected for 50 procedures or processes for analysis to be useful and significant.

Infection prevention and ASP personnel may choose to report only the number of events that occur in a specified time period (i.e., the numerator). While there is merit to providing units or individuals with immediate feedback during an intervention or outbreak, to compare data over time one must calculate the incidence, or the proportion of patients being studied who have a new instance of the event of interest. This calculation requires both the number of events studied in the defined population (the numerator) and the number of patients at risk during the same time period (the denominator). Consider the following example:

Ten (10) patients in a hospital develop MRSA BSI in May. If the hospital discharged 1,000 patients that month, the incidence rate of new MRSA BSI acquired in the hospital would be 1 percent. However, if all 10 patients were hospitalized on the medical service, which discharged 600 patients that month, the incidence rate of patients with MRSA BSI on the medical service would be 1.7 percent. If 8 of the 10 patients developed MRSA BSI while in the medical intensive care unit, which discharged 90 patients that month, the incidence rate in the medical intensive care unit would be 9 percent. If, however, the number of admissions in the medical intensive care unit drops to 45 patients for the month, the incidence of MRSA BSI is 18 percent. Thus, the true incidence of an event can only be assessed if the denominator in a defined population accurately represents the patients who are at risk of experiencing the event for a defined period of time. Such issues with denominators when calculating days of therapy or daily drugs delivered are equally relevant.

Similarly, if only summary reports of microbiology laboratory data are evaluated, important trends in specific units may be missed. Fortunately, in facilities with electronic medical records obtaining data can enhance surveillance activities. Still, the summary reports may obscure the fact that 90 percent of the *Pseudomonas aeruginosa* isolates recovered from patients in the medical intensive care unit are resistant to certain antibiotics. Stratton et al.[43,44] demonstrated that yearly summaries showed little variation in antimicrobial susceptibility patterns within the whole hospital. Focused microbiologic surveillance on specific units, in contrast, demonstrated that the predominant pathogens and their antimicrobial

susceptibility patterns differed among specialty units and between those units and the entire hospital. These examples illustrate the importance of critically examining data and using summary statistics as a guide to further analyze data whether for IP or for an ASP team. Srinivasan and colleagues provide an additional example[45] where they would have missed a doubling of *P. aeruginosa* infection among patients undergoing bronchoalveolar lavage had they calculated the overall hospital rate and not procedure-specific rates. In both instances, the safety and subsequent care of patients is altered by the prompt identification of changes in the microbiology.

Another important surveillance variable to determine is the endemic (baseline) rate of all types of healthcare-associated events of interest, including HAIs. To do so, data must have been historically collected for a sufficiently long period of time in a consistent manner. Subsequently, it is easier to determine whether the current rates are substantially different from the baseline rate. In addition to calculating overall rates for the population of patients in the institution, the HE and IP staff can analyze the data further by calculating attack rates for specific nursing units, services, and/or procedures. These rates enable the staff to identify significant changes and important trends within subgroups of patients that might be missed if the entire population were analyzed as a whole. When comparing data, either within an institution or with another institution, comparable surveillance methods, definitions, and time frames must be used. Statistical tests of differences can then be used to determine whether the rates have changed significantly over time.

Finally, the data must be interpreted. If the incidence of a particular event increases substantially, a more thorough analysis must be completed to determine if a problem really exists. The analysis should include assessing whether the increase is statistically significant. However, even if the increase is not statistically significant, it may be clinically significant and warrant initiation of control measures. Furthermore, the team should assess whether the incidence of an event is acceptable. For example, even if the rate of SSI is stable, the incidence may be higher than that reported by comparable institutions or may be higher than it would be if the process of care was improved. A study by Classen et al.[46] demonstrated that examining the process of care can allow the rate of SSI to be decreased significantly. In their study, the SSI rate among patients who received antibiotic prophylaxis within 2 hours before the start of surgery was significantly lower than it was among patients who received antibiotic prophylaxis either early (2–24 hours before the start of surgery) or after the operation was completed (i.e., more than 3 hours after first incision but less than 24 hours after the end of surgery). Therefore, an IP team that wants to decrease SSI rates in their hospital might want to review the time at which antimicrobial prophylaxis for surgery is given. Such strategies have been implemented in multiple institutions, with similar improvements.[47,48]

Communicating Results

The data must be communicated to the stakeholders, such as the clinical staff, and those who have the power to authorize changes. To ensure that regulatory requirements are met and that results are communicated to the organization's leadership, IP should regularly report to the institution's healthcare epidemiology and infection prevention committee and also to the quality or performance improvement committee. Data to be communicated include appropriate rates and counts, which should be shared with key persons on individual nursing units, in each clinical service, in the nursing administration, and in the hospital administration. For example, as part of an intervention to reduce catheter-related BSI, report BSI data weekly to intensive care unit personnel.[49] In addition, IP personnel may need to report their data to the education service, the intensive care unit committee, the safety committee, or an external agency, such as the local health authority. Commonly, committee reports should include simple but well-labeled graphic displays of trends over time. Changes in rates over months, quarter-years, or years may be important to display. Comparison with national data is helpful to promote ongoing process-improvement activities. When reporting data, in any circumstance, epidemiology personnel must maintain the confidentiality of data related to both patients and employees.

Simple reports that the target audience can understand in a few seconds (the amount of time usually given to a report at a busy committee meeting) are most effective. Graphical or tabular displays of the data can present important trends in pictures and help clinicians and administrative personnel grasp key points quickly as shown in the following examples (www.cdc.gov/healthreport/dashboards/; https://healthcarequality.mhcc.maryland.gov/Article/View/22b69236-d9b7-412e-a500-52820cf6461b). The use of 95 percent confidence intervals, to help in understanding the significance of a variation in rates, or comparison with rates such as those published by the NHSN, can be helpful in comparisons against other groups. Benchmarking rates against an external organization has proven useful. While most North American institutions compare their rates with those published by the NHSN, other groups are using similar methods in other areas of the world, including in the developing world.[50,51,52,53,54] Moreover, individuals who are unfamiliar with issues in IP may not understand the importance of a problem if they are presented only with the data. This is particularly true if the number of cases is small or the etiologic agent has not been discussed in the popular press. Thus, the IP team should include their assessment and conclusions in the report, so that they can persuade clinicians or hospital administrators that corrective action is necessary to reduce the number of cases.

Surveillance for HAIs

Data Sources

Many different sources provide information about patients with infections (Table 10.6). In addition, infection prevention and control personnel can obtain data from databases maintained by other departments, such as medical records,

Table 10.6 General sources of data for surveillance

PATIENT BASED
• Clinical ward rounds including questioning nurses, review of temperature curves
• Electronic medical record including review of notes, vital signs, antimicrobial use, surgical procedure data, radiology and laboratory reports
• Hospital employees
• Laboratory, radiology, pathology reports
• Pharmacy department
• Admissions department and readmission rates
• Emergency rooms and emergency transfer personnel
• Operating room logs
• Outpatient clinics including surgical centers, infusion centers
• Medical records department
• Employee or occupational health department
• Incident and patient safety reports; sentinel events
• Postdischarge, outpatient antimicrobial clinics, wound clinic visits
• Local/state/provincial public health officials
• National public health sources
LABORATORY BASED
• Microbiology, virology, and serology reports
• MMWR
• NHSN and other national databases
• Antimicrobial susceptibility patterns; serology patterns, sequencing data
PHARMACY BASED
• Antimicrobial use including dosing
• Adverse events of interest such as renal injury, hematologic abnormalities

pharmacy, respiratory therapy, admissions, risk, and financial management. However, it must be remembered that these databases are not generally designed for collecting data on infections or multidrug-resistant organisms. Therefore, one must determine whether those databases include complete and accurate data needed for surveillance. As vendors are developing products that collect data for epidemiologic purposes including those that interface with the electronic medical record, this will become less of an issue. Nonetheless, the sources of data must be validated. For instance, an IP professional who conducts surveillance and uses the daily surgery schedule to obtain the number and classification of operative procedures, instead of using the list of completed operative procedures, will not calculate accurate rates, because if surgeons add, cancel, and/or change operative procedures during the day, the denominator for calculating SSI rates will be inaccurate.

Surveillance Methods

A surveillance method that is best suited to the hospital and patient population served should be identified. We describe five surveillance methods here and have summarized their advantages and disadvantages in Table 10.2.

Health System and Hospital-wide Traditional Surveillance

Hospital-wide surveillance, the most comprehensive method, requires the HE and IP team to prospectively and continuously survey all care areas to identify patients who have acquired infections or epidemiologically significant organisms during hospitalization.[55,56] The infection preventionist gathers information from daily microbiology laboratory reports and from the medical records of patients who have fever or cultures growing organisms and of patients who are receiving antibiotics or are placed on isolation precautions. They also garner important information frequently by talking (daily if possible) with nursing staff and occasionally by seeing patients. In addition, the infection preventionist periodically reviews all autopsy reports and employee health records. The team regularly calculates both the overall hospital rate of HAI and infection with multidrug-resistant organisms, as well as the infection rates according to type or site of infection, nursing unit, physician service, pathogen, and operative procedure. These can be calculated monthly, quarterly, or semiannually, depending on the hospital size and number of HAIs or infections with multidrug-resistant organisms.

Traditional hospital-wide surveillance is comprehensive. However, this system is very costly, and it identifies many infections that cannot be prevented. Consequently, many IP programs have developed other surveillance methods that require fewer resources. With access to increasingly sophisticated electronic patient records, it is possible to capture many clinical details that facilitate and enhance surveillance for HAIs and infections with multidrug-resistant organisms. With such improved clinical informatics systems, the time commitment required for surveillance will need to be reevaluated. Importantly, similar strategies are used to collect antimicrobial use data so that the burden of certain microbials can be calculated

Prevalence Survey

A prevalence survey can be hospital-wide or can focus on a specific area of the hospital. In a prevalence survey, the IP professional counts the number of active infections or cases of infection with epidemiologically significant organisms during a specified time period.[57] The total number of active infections is defined as all infections present during the time of the survey, including those that are newly diagnosed and those being treated when the survey begins. This total number is divided by the number of patients present and at risk of the event of interest during the survey.

Because new and existing infections are counted, the rates obtained from prevalence surveys are usually higher than incidence rates, which consider only new cases within a given time

period. Prevalence surveys can focus on particular populations, such as patients with central venous catheters or patients receiving antimicrobials.[58] Prevalence studies also are useful for monitoring the number of patients colonized or infected with epidemiologically important organisms such as CDI, CRE, VRE, or MRSA.

Infection prevention and control programs also can use prevalence studies to assess the risk factors for infection with multidrug-resistant organisms in a particular population. To determine why patients in this population are developing infections, the epidemiology staff could collect additional data about potential risk factors from all patients surveyed. Because prevalence studies assess all patients in the target population, regardless of whether they have an infection, IP personnel can compare the prevalence of infection among patients who have the potential risk factor with the prevalence among patients who do not have the potential risk factor.

Targeted Surveillance

There are several approaches to targeted surveillance. Many HE and IP programs focus their efforts on selected areas of the hospital, such as critical care units, or selected services, such as the cardiothoracic surgery service. Other programs focus surveillance on specific populations, such as patients at high risk of acquiring infection (e.g., patients undergoing transplant or pediatric patients), patients undergoing specific medical interventions (e.g., hemodialysis patients), or patients with specific types or sites of infection (e.g., BSI, UTI, or SSI). Some target surveillance for infections associated with specific devices (e.g., catheter-associated UTI, central line–associated BSI). By limiting the scope of surveillance, IP can collect data on entire patient populations, which allows them to accurately assess the incidence of infection in the surveyed populations.

Some IP and ASP programs use data from the microbiology laboratory to limit the scope of surveillance. For example, the epidemiology team may focus either on specific microorganisms, such as CDI, or on organisms with particular antimicrobial susceptibility patterns, such as VRE or MRSA. This type of surveillance allows programs to focus on patients at increased risk, on areas of the hospital with an elevated rate of infection or MDROs, or on patient populations or procedures where infection rates can be further examined or antimicrobial use can be harmonized with guidelines or identified local problems. Importantly, however, because targeted surveillance requires fewer resources than facility-wide surveillance, these resources can be used to develop interventions to prevent infection or transmission of multidrug-resistant organisms and can assess the impact of these interventions.

Outbreak Thresholds

Some investigators have conducted surveillance to assess baseline infection rates at their institution and, based on their data, developed threshold rates to identify outbreaks. Subsequently, they stopped conducting routine surveillance and evaluated problems only when the number of isolates of a particular species or the number of cultures positive for a pathogen exceeded those outbreak thresholds.[59,60] For example, McGuckin et al.[60] used a threshold of the 80th percentile above the baseline for each bacterial species from a particular nursing ward for a specified time period. Similarly, Schifman et al.[54] established a threshold of double the baseline positive culture rate. Wright et al.[61] used a computer-based program and set a threshold of 3 sigma (i.e., standard deviations from the mean). One of the more interesting applications uses data collected from previous influenza seasons to set a threshold that identifies the "start" of the respiratory virus season. Reich et al. used a novel tool and metric to determine when influenza cases increased over baseline to begin a clinical trial.[62] Automated algorithms that use surveillance data are increasingly being used as tools to identify increases in rates that require additional investigation.[62]

Objective or Priority-Based Surveillance

Objective- or priority-based surveillance is a form of targeted surveillance that is primarily used in hospitals with special populations and resources, such as children's hospitals, ophthalmologic hospitals, orthopedic institutions, or other specialty institutions. These facilities can tailor surveillance programs to assess the problems or events that are specific to their types of institution. For example, many children's hospitals have active programs of surveillance for respiratory virus infections, especially respiratory syncytial virus infection, which can be particularly devastating in children.[5]

Case-Finding Methods

IP personnel should collect data only for infections and/or MDROs that were acquired in their facility or as a consequence of procedures performed or treatments administered in their hospital or clinics. For example, a patient may become infected with CDI while in Hospital A and then be transferred to Hospital B while still infected. Hospital B personnel should not include this infection in their HAI rate, even though it was acquired in a hospital. If such infections are included, it will cause the extent of the problem to be overestimated and the efficacy of the prevention and control programs to be underestimated. Although not included in HAI rates, all patients who on admission are colonized or infected with particular organisms of interest, such as CDI, VRE, MRSA, and respiratory syncytial virus, should be identified. Such data allow HE and IP personnel to estimate the entire population of patients affected by these organisms. By determining the proportion of patients who acquire the organism in the hospital, IP can evaluate the efficacy of their control efforts. However, to improve patient care, notifying an institution about the infection is helpful and, some argue, should be required by regulations.

Investigators have described various methods used to identify patients with HAIs. We review some of these case-finding methods in this section; their sensitivities and the time they require are summarized in Table 10.3. Evaluating institutional resources is a critical first step to determining the optimal case-finding method for an institution.

Total Chart Review

In total chart review, the infection preventionist reviews nurses' and physicians' notes, medication and treatment records, and radiologic and laboratory reports for each patient of interest.[55,56] This strategy remains the goal standard and is viable but is extremely time consuming, limiting its utility with the emergence of powerful computer programs. In addition, many review notes from the specialties of respiratory therapy, physical and occupational therapy, dietetics, and any other specialty service caring for the patient. Because the infection preventionist reviews each individual medical record, this method is time-consuming and costly. As mentioned above, this type of review likely requires less by way of staff resources if electronic patient records can be used to display all the information necessary for surveillance. Clinical information systems typically provide demographic and administrative information, data from the microbiology laboratory and the radiology and pharmacy departments, and, in some instances, physician, physical therapy, respiratory therapy, and nursing notes as well as information about use of intravascular lines. Although many institutions have moved away from using total chart review, new algorithms that use data captured from electronic medical records may change that approach in the next few years.[34,39,63]

Review of Laboratory Reports

Clinical laboratory reports often are a primary source of data for identifying infections, particularly if the infection preventionist reviews virologic and serologic testing reports in addition to bacteriologic test results.[55,64,65] The infection preventionist may directly identify some HAIs from reports that include information about culture-yielding pathogens. A laboratory report might prompt the infection preventionist to review the patient's medical record. While reviewing the medical record, the infection preventionist might identify an HAI for which a culture was not performed. For example, a patient might have a blood culture from which *Klebsiella pneumoniae* was isolated. In the medical record, the infection preventionist might learn that chest radiographs revealed a new pulmonary infiltrate and that Gram stain of a sputum sample revealed many white blood cells and gram-negative rods. This information might lead the infection preventionist to conclude that the patient had pneumonia and secondary bacteremia caused by *K. pneumoniae*. Alternatively, a urine culture result might prompt the infection preventionist to review a patient's medical record; while reviewing the record, the infection preventionist might discover healthcare-associated pneumonia caused by another organism.

Developing a rapport with laboratory staff is key, as they may note outbreaks that were not identified either by standard surveillance techniques or by outbreak detection algorithms using newer electronic databases.[66–68] Nonetheless, laboratory reports have some substantial limitations, and the IP program should not use them as the sole source of data for identifying patients with HAIs. When a clinician empirically treats a patient who has evidence of an infection, but forgoes ordering a culture, laboratory reports will not capture this infection. This commonly occurs with SSI or UTI. In addition, cultures of specimens from some sites of infection may yield negative results. This is particularly true if the patient is receiving antimicrobial therapy or if the organism is fastidious or does not grow on routinely used culture media. Consequently, the sensitivity of laboratory records is directly affected by the number of infections for which culture is performed and by the culture methods used by the laboratory.[69] The sensitivity of using microbiology laboratory reports for case-finding is 33 percent to 84 percent. Of note, with the advent of PCR, the laboratory tests may be overly sensitive. Increased rates of C. difficil have been attributed to improved case identification or false identification of colonization.[69]

Clinical Ward Rounds

Infection preventionists who regularly visit clinical wards can gain excellent information about patients, infections, and other adverse events, because much of this valuable information is not included in the patients' records.[70,71] This method allows the infection preventionist to be highly visible in patient-care areas, to observe infection prevention practices directly, and to talk with the healthcare workers caring for patients. In this manner, the infection preventionist not only can collect data on patients with HAIs but also can assess compliance with isolation precautions, can answer questions on infection prevention issues, and can conduct informal educational sessions. One variation of this method is to use trained personnel who function as liaisons to the HE and IP group. They can notify the infection preventionist of patients with potential HAIs.

Computer Alerts, Smart Phone/Tablet and Computer-Based Automated Surveillance

In attempts to expand the reach of surveillance activities and enhance efficiency, electronically obtained data elements continue to be tested as surrogates for traditional surveillance activities. The goals are to increase the sensitivity of surveillance, to decrease the need for chart review, and to reduce costs. Most of the work has been done with electronic systems that support large healthcare systems providing integrated healthcare. Many organizations have home-grown programs or purchased software in place to facilitate surveillance or identification of patients colonized or infected with epidemiologically important organisms and patterns of antimicrobial use such as use of antimicrobials that do not cover organisms identified in culture (bug-drug mismatch). These tools can be embedded in the electronic medical record, which may provide more powerful approaches to identify infection, MDROs or patterns of antimicrobial use.

Lin and colleagues reported an elegant surveillance strategy to identify bloodstream infections in 20 intensive care units in 4 academic centers. These investigators identified a cautionary note and found significant institutional variability in the application of CDC-based definitions for central line–associated bacteremias and that the correlation between traditional surveillance and algorithm-based surveillance was poor. Although successful implementation of electronic surveillance has been reported in the literature, ips need to determine the utility of these tools specific to their practices. Electronic surveillance should be considered whenever possible as they are likely to decrease the time required to perform surveillance, which will

allow the infection preventionist to spend time with interventions and other activities.

Postdischarge Surveillance

As patients are discharged from hospitals earlier, IP will have increasing difficulty detecting HAIs. One way of obtaining the data is to perform surveillance after patients are discharged. HE and IP teams who do not conduct postdischarge surveillance may report spuriously low HAI rates, because traditional hospital-based surveillance methods identify only events that occur while the patient is in the hospital or institution. In fact, studies have documented that postdischarge surveillance identifies 13 percent to 70 percent more SSIs than do methods that survey only inpatients.[19,72,73]

Most investigators who have studied methods for postdischarge surveillance have not evaluated all discharged patients but have focused on specific populations, such as postoperative patients, postpartum women, or neonates.[19,72,74] Investigators have assessed various methods for identifying HAIs after such patients are discharged, including directly assessing patients, reviewing records of visits to clinics or emergency departments, and contacting physicians or patients by mail or telephone. Although all these methods identify patients who develop infections after discharge, the methods are time consuming and can lack sensitivity. None of these methods have been accepted widely. Sands et al.[19,72] used administrative billing databases from an integrated healthcare system to study the best methods to identify SSIs, 84 percent of which develop after discharge. Unfortunately, most infection prevention and control programs do not have access to such resources.

Which Case-Finding Method Is Best?

Each case-finding method has some merit, but each also has limitations. There is little to no universal agreement about which case-finding method is best. Some experts consider total chart review to be the gold standard (criterion standard) for identifying HAIs. However, in two studies that compared total chart review with combinations of two or more case-finding methods, the former identified only 74 percent to 94 percent of the infections that were identified by the combined methods.[32,55] Investigators were unable to identify all HAIs by reviewing only the medical record, for four reasons:

1. Records did not document all data required to determine whether the patients met the criteria for having specific infections;
2. Laboratory or radiology department reports were missing;
3. Records were not available for review; and/or
4. The reviewer could not examine the patient.

Nettleman and Nelson conducted surveillance to identify adverse events among patients hospitalized on general medical wards.[75] They used numerous data sources and found that no single source identified all adverse occurrences. In fact, the number of adverse events the investigators identified in each category was dependent on which data source they used. Certain data sources efficiently identified specific adverse occurrences. For example, the investigators identified 77 percent of medication-related errors by reviewing the medication administration record, but they detected only 10 percent of these events by reviewing the physicians' progress notes. Conversely, they identified 100 percent of procedure-related adverse occurrences by reviewing the physicians' progress notes, but they did not detect any of these events by reviewing the medication administration record.[75]

Consequently, it is clear that total chart review is no more sensitive than other case-finding methods or combinations of methods. Of note, these issues will change as more sophisticated and complete electronic medical records become available. When selecting a surveillance method, IP staff must consider their objectives and the various sources from which the necessary data may be obtained in order to choose the most effective and efficient identification of the HAIs they choose to study.

National Healthcare Safety Network

In 1970, the CDC enrolled a sample of hospitals, all of which voluntarily agreed to collect data on nosocomial infections, into the NNIS system. Restructured into the NHSN in 2005, it currently has more than 17,000 participating medical facilities, and is the only source of national data on HAIs in the United States.[76] NHSN is a secure, Internet-based surveillance system that integrates patient and healthcare personnel safety surveillance systems. NHSN provides surveillance data on both outcome measures and process measures known to be associated with prevention of HAI, and provides facilities with risk-adjusted data that can be used for interfacility comparisons. NHSN also provides data that can be used by local IP and quality improvement programs to develop methods for timely recognition of patient and healthcare personnel safety problems, and for prompt intervention with appropriate measures. NHSN also has the capacity to allow healthcare facilities to share data in a timely manner with public health agencies, as well as with other facilities. Switzerland, Germany, Spain, the Netherlands, and France have developed remarkable, mostly country-wide surveillance systems for HAIs that have elements of the NNIS/NHSN system.[10,57,77,78,79]

Current participants include acute care hospitals, long-term acute care hospitals, psychiatric hospitals, rehabilitation hospitals, outpatient dialysis centers, ambulatory surgery centers, and nursing homes. Participation is expected to continue to grow in future years. The NHSN program has several goals:

- To estimate the incidence of HAIs and infections with multidrug-resistant organisms;
- To identify changes in the pathogens causing HAIs, the frequency of HAIs of specific types and at specific sites, the predominant risk factors, and the antimicrobial susceptibility patterns;
- To provide data on HAIs with which hospitals can compare their data, including the distribution of HAIs by major types and sites, device-associated infection rates by type of unit, and SSI rates by operative procedure; and
- To develop strategies that infection prevention and control personnel can use for surveillance and assessment of HAIs.

HAI Rates

Frequency measures of HAIs have myriad names but can be categorized as incidence measures and prevalence measures. The merits of these measures and some of the controversies about them are described in this section. Incidence is the number of new events divided by the number of patients at risk during a defined period of interest. Prevalence is the number of events (new and old) that are present during a defined period of interest. Prevalence is usually ascertained by surveys. Typically, prevalence is obtained at a given point in time. It is calculated as the number of active current infections divided by the number of patients at risk or studied. To measure incidence, the most common measures include the crude cumulative incidence (the number of infections per 100 admissions or discharges), the crude incidence density or the adjusted infection rate (the number of infections per 1,000 patient-days), the specific cumulative or incidence density (according to unit, procedure, or provider), and the adjusted cumulative or incidence density (adjusted for intrinsic host factors, such as age). Finally, standardized infection ratios (SIR) are used to compare event frequency;[79] this measure is calculated as the ratio of the observed to the predicted rate of infection (the predicted rate is derived from data from a reference population).

Overall Hospital Infection Rates

Infection prevention and control programs that conduct hospital-wide surveillance sometimes track the overall infection rate for their facility. This rate is calculated by dividing the number of HAIs identified in a given month by the number of patients admitted or discharged during the same month. The overall HAI rate has several inherent disadvantages:

- It treats all infections as though they are of equal importance. Changes in rates of uncommon but epidemiologically important infections (e.g., bacteremia) might be hidden in the larger volume of more common but less important infections (e.g., UTIs).
- It does not distinguish between patients who had a single infection and those who had numerous infections.
- It may not be accurate and may underestimate the true rate, because the infection preventionist often cannot identify all HAIs.
- It does not account for patients who are at increased risk for becoming infected because of underlying diseases or exposure to procedures and medical devices; therefore, it tends to obscure important trends in intensive care units or among high-risk patients.
- It does not adjust for length of stay.
- It is not adjusted for risk, and therefore it cannot be compared with rates from other hospitals.

In short, the accuracy and usefulness of the overall HAI rate is limited. Therefore, we recommend that infection prevention and control personnel avoid calculating their overall infection rate in favor of calculating adjusted infection rates.

Site-Specific Infection Rates

Site-specific infection rates (i.e., rates of infection stratified by type or body site of infection) are a more appropriate measure, because they represent a more homogeneous group of infections. Examples of site-specific infections include BSI, catheter-associated infection, UTI, and VAP. These rates are calculated using the number of specific infections as the numerator and dividing it by an appropriate denominator, usually the number of device-days (e.g., catheter-days or ventilator-days). The most common measure used is the specific cumulative incidence or incidence density ratio (see Chapter 6, on epidemiologic methods).

Adjusting Rates

Hospital epidemiology and IP personnel calculate infection rates so that they can identify problems and assess the effectiveness of their interventions. In addition, they follow rates over time to identify meaningful changes from baseline rates and to assess the efficacy of their program. In addition, to determine whether they actually have a problem, HE personnel often compare their rates with those of other institutions. However, comparisons within a single hospital over time may not be valid, because the patient population or patient care may have changed substantially. Further, comparisons between hospitals may not be valid, because healthcare facilities are not standardized.[80] Patients in different hospitals have different underlying diseases and different severities of illness. In addition, patients who have the same disease and the same severity of illness but who are in different hospitals could undergo different diagnostic and therapeutic interventions and stay in the hospital for different lengths of time. Each hospital has its own unique environment, patient-care practices, and healthcare providers. Infection prevention programs vary substantially in the intensity of surveillance, the methods used for surveillance, the consistent application of definitions of infections used, and the methods used for calculating infection rates. Consequently, IP personnel must use adjusted rates if they want to assess their rates over time or to compare their rates with those in other hospitals. In the following paragraphs, we discuss several methods for adjusting rates.

Adjusting for Length of Stay

Infection rates more accurately reflect the risk of infection when they are adjusted for length of stay. Infection prevention staff attempt to control for the length of stay by calculating the number of HAIs per patient-day. This method uses the total number of HAIs in a month as the numerator and the total number of patient-days in that month (i.e., the sum of the number of days that each patient was on the unit during the month) as the denominator. For example, an obstetrics ward admits many patients who stay in the hospital for a very brief time and whose risk of infection is low, but a rehabilitation ward admits a few patients who stay for long periods of time and whose risk of infection is high. If the number of patients admitted were used as the denominator, the infection rate for the obstetrics ward probably would underestimate the risk of

infection, whereas the rate for the rehabilitation ward most likely would overestimate the risk of infection. By using the number of patient-days as the denominator, IP staff control for the effect of length of stay on the infection rate. However, this method does not control for the effect of other risk factors, such as use of invasive devices or the severity of the patient's underlying illness.

Adjusting for Exposure to Devices

Device-associated infection rates control for the duration of exposure to an invasive device, which is one of the major risk factors for these infections. Therefore, device-associated rates can be compared more reliably over time and between institutions than can overall infection rates. To calculate this rate, the IP team first specifies the type of device (e.g., indwelling urinary catheter) and the population (e.g., patients in the medical intensive care unit) to be studied. Next, the team identifies the cases of device-associated infection (e.g., CAUTI) that occur in the selected population during a specified time period. The number of infections is the numerator. To obtain the denominator, the team sums the number of patients exposed to the device during each day of the specific period. For example, if the team surveyed the medical intensive care unit for 7 days and found that the number of patients who had a urinary catheter on each of those days was 4, 3, 5, 5, 4, 6, and 4, then the number of urinary catheter days would be 31. If the team identified 3 cases of CAUTI during the week, the CAUTI rate would be 3 divided by 31, or 0.097 cases per urinary catheter day; this can be expressed as 97 cases per 1,000 urinary catheter days.

Adjusting for Surgical Site Infection Risk

The amount of data that should be collected depends on the purpose of the surveillance program. Collecting only the required elements for SSI surveillance in the NHSN is likely to be adequate for routine surveillance.[12] However, if an issue is identified that requires further assessment, additional patient and surgical information may be useful. Timing and choice of preoperative antibiotic administration, type of skin prep, patient comorbidities, and surgical staff performing the surgery are a few examples of information that may be useful for an investigation, but are unlikely to add significant value to routine surveillance.

SSI surveillance data is not useful unless it is analyzed, summarized, and reported to key stakeholders, particularly surgeons and surgical staff. In addition to calculating SSI rates, IP staff should utilize the SIR obtained via the NHSN. Stepwise logistic regression was used to develop specific risk models by procedure category.[24] Using these risk models, the NHSN is able to generate predicted numbers of SSI by procedure category. The SIR is then calculated by dividing the number of observed SSI by the calculated number of predicted SSI. An SIR of greater than 1 indicates that more SSI are being identified than predicted, while an SIR of less than 1 would indicate that fewer SSI have been identified than predicted.

IP staff should regularly provide SSI reports to surgeons, surgical staff, and hospital administration. Providing actionable data in a transparent manner will help build the relationships required for successful implementation of interventions. IP staff should engage the surgical team to improve communication and cooperation, reinforcing the importance of preventive measures to reduce SSI risk. Helping hospital administration understand the data may also ensure support for appropriate IP staffing resources.

Surveillance for Process Measures

Surveillance for outcome measures or infection rates has long been used in IP programs. However, there are several limitations to outcome-based surveillance. First, the preventable fraction of HAIs is not known, therefore making it difficult to evaluate if the infection prevention measures are adequate in a given unit. Second, infection rates do not provide information about breaches in infection prevention measures that contribute to the problem, which should become the focus of prevention efforts.[81]

Surveillance for process measures may fill some of the gap. Warren et al.[48] developed a checklist tool as one of several strategies to decrease catheter-related BSI in the intensive care unit. The checklist was used to ensure adherence to infection-control practices and was one component of the intervention to reduce the infection rate.[47,82] This checklist was subsequently adopted by Pronovost and colleagues[82] in a statewide effort to prevent BSI. Other examples of surveillance based on process measures are the vaccination rate among healthcare personnel, the rate of compliance with recommended hand hygiene, the rate of adherence to administration of surgical antibiotic prophylaxis within 1 hour before the first incision, the rate of appropriate indwelling urinary catheter use, and the device utilization ratio (e.g., a central-line utilization ratio).[83,84]

In contrast to outcome-based surveillance, process measure surveillance provides performance targets; for example, adherence to infection prevention procedures for catheter insertion for every single patient. Deviations in adherence are easy to recognize. Infection prevention interventions, therefore, can be implemented early, perhaps even prior to an increase in the infection rate.[81] Process measure surveillance data can be used as performance indicators for adherence to infection prevention guidelines and can be further evaluated for effects on the outcome or infection rate. Surveillance of process measures is deemed essential by the NHSN.[85]

Surveillance in Developing Countries

The rationale for a basic surveillance system for HAIs and infection or colonization with multidrug-resistant organisms in developing countries is not different from the rationale for a surveillance system in developed countries. However, with limited resources, one has to concentrate efforts on the most achievable goals ("low- hanging fruit") and focus on specific areas of the hospital and specific procedures that have high rates of HAI and infection with multidrug-resistant organisms.[86] Benchmarking of rates with those in other

developing countries has been demonstrated by Rosenthal et al.,[51,52,53] who successfully used the NHSN methods in less developed areas of the world.

Use of Surveillance Data to Meet Regulatory Requirements

Public reporting of outcome and process measures to state or national authorities is intended to enable consumers to make more informed choices for safer care. By promoting competition, a public reporting system may influence healthcare facilities to undertake efforts to improve the quality of care and may result in optimal patient outcomes. However, unintended consequences, such as the intention to avoid admission of sicker patients, may occur. The Healthcare Infection Control Practices Advisory Committee (HICPAC) found inconclusive evidence for the effectiveness of public reporting systems in improving healthcare performance.[87] Therefore, HICPAC has not recommended for or against mandatory public reporting of HAIs. HICPAC, however, proposed guidance on public reporting of HAIs in 2005, highlighting the essential elements for public reporting systems, identifying appropriate measures of healthcare performance for both process and outcome measures, and identifying patient populations to be monitored, as well as making recommendations on case-finding methods, data validation, resource and infrastructure requirements, HAI rates and risk adjustment, and production of useful reports and feedback.[14]

The Inpatient Prospective Payment System (IPPS) was enacted as part of the Affordable Care Act (ACA) and includes several programs that require reporting and use of HAI data for reimbursement calculations. These programs include the Inpatient Quality Reporting Program (IQR), the Value-Based Purchasing Program (VBP), and the Hospital-Acquired Conditions Program (HAC). These reporting requirements can be fulfilled by using the NHSN, which then transmits data to the appropriate authority. Data are exported by the Centers for Medicare and Medicaid (CMS) for public display via the Hospital Compare website, and are also used to calculate reimbursement penalties or incentives. The specifics of these programs are beyond the scope for this chapter. However, it is critical that HE and IP staff be familiar with IPPS reporting requirements so that they ensure the appropriate data are collected and submitted.

Moving Forward: Electronic, Automatic, and Computer-Based Surveillance

An essential part of healthcare surveillance in the twenty-first century will be the integration of increasingly important and rapidly developing surveillance technologies. As HE and IP and ASP have come under increasing pressure from the public, as well as from legislative, administrative, and regulatory forces, some of the focus of IP and HE has shifted away from pure prevention efforts. This translates into a need to be more efficient and to spend less time on surveillance. While ASP surveillance is still in its infancy they should be prepared for similar challenges. Computer-based surveillance systems can save some of the time spent performing routine surveillance, facilitate both multicenter comparisons and the exchange of information between facility sites, notify IPs of potential outbreaks and clusters of infection before they would be picked up by manual surveillance, and reduce the occurrence of errors that commonly result from manual methods of surveillance.

At the time of the first SCENIC investigation in 1976, most of the infection preventionists surveyed spent 50 percent or more of their time performing surveillance.[88] A survey conducted by the CDC in 2000 found that an infection preventionist spends 35 percent to 40 percent of work time performing surveillance.[89] One early study found that the use of electronic systems reduced the time spent on surveillance by 65 percent,[90] and more recent studies have found similar results.[91] This may help explain the results of a recent study of over 4,000 infection preventionists that reported about 25 percent of their time being spent on surveillance activities.[92]

The continued development of standardized, instantly recoverable, and easily shared IP data will not only facilitate communication and comparison of infection rates between multiple facility sites and institutions, but also will allow HE and IP programs to easily meet the demands of complying with regulatory mandates. The ability to immediately access electronic records of, for example, infection rates or trends in resistance, for an entire facility greatly eases the process of auditing, accreditation, and regulation performed by bodies such as CMS and the Joint Commission. An effective electronic surveillance program can be integrated with infection prevention–related goals, such as managing antibiotic usage, tracking adverse drug events, and identifying emerging drug-resistant organisms; such integrated systems have already been shown to be cost-effective.[93] Both commercially and independently developed computer-based surveillance systems have the potential to increase efficiency and to reduce economic costs at multiple levels of the healthcare system. Although more studies aimed specifically at analyzing cost-effectiveness are needed, the potential for computer-based surveillance to reduce expenses (both worker hours and infection costs) will be a vital part of its approval and implementation in any healthcare facility.

The use of electronic surveillance is not without its drawbacks and limitations. The introduction of any new system in a hospital is susceptible to a sharp learning curve, but this is especially the case with the introduction of new and complex electronic surveillance systems. Although there is some evidence that investing in an electronic system is ultimately cost-effective, the obvious challenge of initially funding the purchase of an expensive new system must be overcome.[57] The investment in implementing a new system is not only financial; although Wisniewski et al.[94] estimated that using an independently-designed electronic system saved 1,750 worker hours for each 1,500 charts reviewed, they estimated an investment of 4,000 worker-hours to develop such a system. While manual chart review can be error prone, electronic surveillance often has low thresholds and may identify false-positive outbreaks or clusters of infection. Perhaps the most important issue is to recognize

that while electronic methods of surveillance may reduce the need for manual review, they are not a substitute for critical thinking or further analysis. Computer-based surveillance systems should be seen as a valuable tool for the infection preventionist to obtain, analyze, and communicate relevant information, without becoming overwhelmed by the information or overly reliant solely on an electronic system.

Conclusion

Surveillance for HAIs, MDROs, and AUR is a core component of both IP and ASP programs. Surveillance data need to be obtained systematically and should be validated in the current climate with public reporting and its use as a premier quality measure. It is essential that surveillance systems be extremely flexible so that they can be adapted for use with emerging technology advancements to meet the needs of rapidly changing healthcare systems. Moreover, effective HE and IP and now ASP teams will not use a one-size-fits-all approach to surveillance; rather, these teams must be similarly flexible and utilize different case-finding and surveillance methods to create a system that meets the needs not only of their entire healthcare system but also of the individual components (e.g., the intensive care units and the ambulatory-surgery center). The importance of using standardized definitions and standardized approaches for identifying infections and for calculating rates or use is paramount. Infection prevention and ASP personnel must develop or employ the newer electronic surveillance systems that use the computerized databases and the electronic medical records already present in their institution (e.g., databases from the laboratory, surgical services, and financial management). They need to advocate for inclusion of newer information technology including smart phones and tablets into their program so that they can enhance the efficiency of surveillance activities and increase interventions to prevent adverse events. Furthermore, the IP and ASP teams should collaborate with personnel from the information systems department to develop algorithms to identify patients with possible HAIs or excessive or inappropriate antimicrobial use and to determine the thresholds used to identify likely outbreaks. The electronic patient record systems should streamline these processes. Despite these enhancements, trained IP and ASP personnel must lead the process of obtaining, validating, communicating, and interpreting these data. Such data should be used to improve performance using evidence-based interventions.

References

1. Langmuir AD. The surveillance of communicable diseases of national importance. *N Engl J Med* 1963;**268**: 182–192.
2. TM. P. Surveillance, reporting and the use of computers. In: Wenzel RP, ed. *Prevention and Control of Nosocomial Infections*. Baltimore, MD: Williams and Williams; 1997: 127–162.
3. Haley RW, Quade D, Freeman HE, Bennett JV. The SENIC Project: study on the efficacy of nosocomial infection control (SENIC Project) Summary of study design. *Am J Epidemiol* 1980;**111**: 472–485.
4. Haley RW. The "hospital epidemiologist" in U.S. hospitals, 1976–1977: a description of the head of the infection surveillance and control program. Report from the SENIC project. *Infect Control* 1980;**1:** 21–32.
5. Karanfil LV, Conlon M, Lykens K, et al. Reducing the rate of nosocomially transmitted respiratory syncytial virus [published erratum appears in *Am J Infect Control* 1999 Jun;27(3):303].
6. Carlet J, Astagneau P, Brun-Buisson C, et al. French national program for prevention of healthcare-associated infections and antimicrobial resistance, 1992–2008: positive trends, but perseverance needed. *Infect Control Hosp Epidemiol* 2009;**30**: 737–745.
7. Gastmeier P, Kampf G, Wischnewski N, et al. Prevalence of nosocomial infections in representative German hospitals. *J Hosp Infect* 1998;**38**: 37–49.
8. Harbarth S, Ruef C, Francioli P, Widmer A, Pittet D. Nosocomial infections in Swiss university hospitals: a multi-centre survey and review of the published experience Swiss-Noso Network. *Schweizerische medizinische Wochenschrift* 1999;**129**: 1521–1528.
9. Richet H, Wiesel M, Le Gallou F, Andre-Richet B, Espaze E. Methicillin-resistant Staphylococcus aureus control in hospitals: the French experience. Association des Pays de la Loire pour l'Eviction des Infections Nosocomiales. *Infect Control Hosp Epidemiol* 1996;**17**: 509–511.
10. Prevalence of nosocomial infections in France: results of the nationwide survey in 1996: The French Prevalence Survey Study Group. *J Hosp Infect* 2000;**46**: 186–193.
11. Buehler JW, Berkelman RL, Hartley DM, Peters CJ. Syndromic surveillance and bioterrorism-related epidemics. *Emerg Infect Dis* 2003;**9**: 1197–1204.
12. Bravata DM, McDonald KM, Smith WM, et al. Systematic review: surveillance systems for early detection of bioterrorism-related diseases. *Ann Intern Med* 2004;**140**: 910–922.
13. McKibben L, Fowler G, Horan T, Brennan PJ. Ensuring rational public reporting systems for health care–associated infections: systematic literature review and evaluation recommendations. *Am J Infect Control* 2006;**34**: 142–149.
14. McKibben L, Horan T, Tokars JI, et al. Guidance on public reporting of healthcare-associated infections: recommendations of the Healthcare Infection Control Practices Advisory Committee. *Am J Infect Control* 2005;**33**: 217–226.
15. Fraser V, Murphy D, Brennan PJ, et al. Politically incorrect: legislation must not mandate specific healthcare epidemiology and infection prevention and control practices. *Infect Control Hosp Epidemiol* 2007;**28**: 594–595.
16. McKibben L, Horan TC, Tokars JI, et al. Guidance on public reporting of healthcare-associated infections: recommendations of the Healthcare Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 2005;**26**: 580–587.
17. Garner JS. Guideline for isolation precautions in hospitals. The Hospital Infection Control Practices Advisory

Committee. *Infect Control Hosp Epidemiol* 1996;**17**: 53–80.

18. Morales EM HL, Nettleman M, Larson C, Sanford L, Perl t. *Staphylococcus aureus* carriage and saphenous vein harvest site infection (HS) following coronary artery bypass surgery (CABG). *The 34th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC);* 1994; Orlando, FL.
19. Sands KE, Yokoe DS, Hooper DC, et al. Detection of postoperative surgical-site infections: comparison of health plan–based surveillance with hospital-based programs. *Infect Control Hosp Epidemiol* 2003;**24**: 741–743.
20. Sands K, Vineyard G, Livingston J, Christiansen C, Platt R. Efficient identification of postdischarge surgical site infections: use of automated pharmacy dispensing information, administrative data, and medical record information. *J Infect Dis* 1999;**179**: 434–441.
21. https://www.cdc.gov/NHSN/PDFS/pcsmanual/17pscnosinfdef_current.pdf.
22. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008;**36**: 309–332.
23. The National Healthcare Safety Network (NHSN) Patient Safety Component Manual. 2016. Available at: www.cdc.gov/nhsn/pdfs/pscmanual/pcsmanual_current.pdf.
24. Cohen AL, Calfee D, Fridkin SK et al. Recommendations for metrics for multidrug-resistant organisms in healthcare settings: SHEA/HICPAC Position paper. *Infect Control Hosp Epidemiol* 2008;**29**: 901–913.
25. McDonald LC, Coignard B, Dubberke E, Song X, Horan T, Kutty PK. Recommendations for surveillance of Clostridium difficile–associated disease. *Infect Control Hosp Epidemiol* 2007;**28**: 140–145.
26. Dubberke ER, Gerding DN, Classen D, et al. Strategies to prevent Clostridium difficile infections in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;**29** Suppl 1:S81–S92.
27. Calfee DP, Salgado CD, Classen D, et al. Strategies to prevent transmission of methicillin-resistant Staphylococcus aureus in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;**29** Suppl 1:S62–S80.
28. Morrison AJ, Jr., Kaiser DL, Wenzel RP. A measurement of the efficacy of nosocomial infection control using the 95 per cent confidence interval for infection rates. *Am J Epidemiol* 1987;**126**: 292–297.
29. Cardo DM, Falk PS, Mayhall CG. Validation of surgical wound classification in the operating room. *Infect Control Hosp Epidemiol* 1993;**14**: 255–259.
30. Cardo DM, Falk PS, Mayhall CG. Validation of surgical wound surveillance. *Infect Control Hosp Epidemiol* 1993;**14**: 211–215.
31. Lessler J, Brookmeyer R, Perl TM. An evaluation of classification rules based on date of symptom onset to identify health-care associated infections. *Am J Epidemiol* 2007;**166**: 1220–1229.
32. Haley RW, Schaberg DR, McClish DK, et al. The accuracy of retrospective chart review in measuring nosocomial infection rates: results of validation studies in pilot hospitals. *Am J Epidemiol* 1980;**111**: 516–533.
33. Yokoe DS, Anderson J, Chambers R, et al. Simplified surveillance for nosocomial bloodstream infections. *Infect Control Hosp Epidemiol* 1998;**19**: 657–660.
34. Platt R, Yokoe DS, Sands KE. Automated methods for surveillance of surgical site infections. *Emerg Infect Dis* 2001;**7**: 212–216.
35. Woeltje KF, Lin MY, Klompas M, Wright MO, Zuccotti G, Trick WE. Data requirements for electronic surveillance of healthcare-associated infections. *Infect Control Hosp Epidemiol* 2014;**35**: 1083–1091.
36. Calderwood MS, Ma A, Khan YM, et al. Use of Medicare diagnosis and procedure codes to improve detection of surgical site infections following hip arthroplasty, knee arthroplasty, and vascular surgery. *Infect Control Hosp Epidemiol* 2012;**33**: 40–49.
37. Olsen MA, Fraser VJ. Use of diagnosis codes and/or wound culture results for surveillance of surgical site infection after mastectomy and breast reconstruction. *Infect Control Hosp Epidemiol* 2010;**31**: 544–547.
38. Bolon MK, Hooper D, Stevenson KB, et al. Improved surveillance for surgical site infections after orthopedic implantation procedures: extending applications for automated data. *Clin Infect Dis* 2009;**48**: 1223–1229.
39. Yokoe DS, Noskin GA, Cunnigham SM, et al. Enhanced identification of postoperative infections among inpatients. *Emerg Infect Dis* 2004;**10**: 1924–1930.
40. Network NHS. The NHSN Standardized Infection Ratio (SIR). Updated January 2017. 2017.
41. Mu Y, Edwards JR, Horan TC, Berrios-Torres SI, Fridkin SK. Improving risk-adjusted measures of surgical site infection for the national healthcare safety network. *Infect Control Hosp Epidemiol* 2011;**32**: 970–986.
42. Broderick A, Mori M, Nettleman MD, Streed SA, Wenzel RP. Nosocomial infections: validation of surveillance and computer modeling to identify patients at risk. *Am J Epidemiol* 1990;**131**: 734–742.
43. Stratton CW, Ratner H, Johnston PE, Schaffner W. Focused microbiologic surveillance by specific hospital unit as a sensitive means of defining antimicrobial resistance problems. *Diagn Microbiol Infect Dis* 1992;**15**: 11s–18s.
44. Stratton CW, Ratner H, Johnston PE, Schaffner W. Focused microbiologic surveillance by specific hospital unit: practical application and clinical utility. *Clin Ther* 1993;**15** Suppl A: 12–20.
45. Srinivasan A, Wolfenden LL, Song X, et al. An outbreak of Pseudomonas aeruginosa infections associated with flexible bronchoscopes. *N Engl J Med* 2003;**348**: 221–227.
46. Classen DC, Evans RS, Pestotnik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *N Engl J Med* 1992;**326**: 281–286.
47. Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med* 2006;**355**: 2725–2732.
48. Warren DK, Cosgrove SE, Diekema DJ, et al. A multicenter intervention to prevent catheter-associated bloodstream infections. *Infect Control Hosp Epidemiol* 2006;**27**: 662–669.
49. Berenholtz SM, Pronovost PJ, Lipsett PA, et al. Eliminating catheter-related bloodstream infections in the intensive care unit. *Crit Care Med* 2004;**32**: 2014–2020.
50. Edwards JR, Peterson KD, Andrus ML, Dudeck MA, Pollock DA, Horan TC.

National Healthcare Safety Network (NHSN) Report, data summary for 2006 through 2007, issued November 2008. *Am J Infect Control* 2008;**36**: 609–626.

51. Rosenthal VD, Maki DG, Graves N. The International Nosocomial Infection Control Consortium (INICC): goals and objectives, description of surveillance methods, and operational activities. *Am J Infect Control* 2008;**36**:e1–e12.
52. Rosenthal VD, Maki DG, Mehta A, et al. International Nosocomial Infection Control Consortium report, data summary for 2002–2007, issued January 2008. *Am J Infect Control* 2008;**36**: 627–637.
53. Rosenthal VD, Maki DG, Salomao R, et al. Device-associated nosocomial infections in 55 intensive care units of 8 developing countries. *Ann Intern Med* 2006;**145**: 582–5891.
54. Rosenthal VD, Maki DG. Prospective study of the impact of open and closed infusion systems on rates of central venous catheter–associated bacteremia. *Am J Infect Control* 2004;**32**: 135–141.
55. Wenzel RP, Osterman CA, Hunting KJ, Gwaltney JM, Jr. Hospital-acquired infections. *I. Surveillance in a university hospital. Am J Epidemiol* 1976;**103**: 251–260.
56. Haley RW, Culver DH, White JW, et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. *Am J Epidemiol* 1985;**121**: 182–205.
57. Pittet D, Harbarth S, Ruef C, et al. Prevalence and risk factors for nosocomial infections in four university hospitals in Switzerland. *Infect Control Hosp Epidemiol* 1999;**20**: 37–42.
58. Climo M, Diekema D, Warren DK, et al. Prevalence of the use of central venous access devices within and outside of the intensive care unit: results of a survey among hospitals in the prevention epicenter program of the Centers for Disease Control and Prevention. *Infect Control Hosp Epidemiol* 2003;**24**: 942–945.
59. Schifman RB, Palmer RA. Surveillance of nosocomial infections by computer analysis of positive culture rates. *J Clin Microbiol* 1985;**21**: 493–495.
60. McGuckin MB, Abrutyn E. A surveillance method for early detection of nosocomial outbreaks. *Apic* 1979;**7**: 18–21.
61. Wright MO, Perencevich EN, Novak C, Hebden JN, Standiford HC, Harris AD. Preliminary assessment of an automated surveillance system for infection control. *Infect Control Hosp Epidemiol* 2004;**25**: 325–332.
62. Reich NG, Cummings DA, Lauer SA, et al. Triggering interventions for influenza: the ALERT algorithm. *Clin Infect Dis* 2015;**60**: 499–504.
63. Trick WE, Zagorski BM, Tokars JI, et al. Computer algorithms to detect bloodstream infections. *Emerg Infect Dis* 2004;**10**: 1612–1620.
64. Gross PA, Beaugard A, Van Antwerpen C. Surveillance for nosocomial infections: can the sources of data be reduced? *Infect Control* 1980;**1**: 233–236.
65. Glenister HM. How do we collect data for surveillance of wound infection? *J Hosp Infect* 1993;**24**: 283–289.
66. Maragakis LL, Winkler A, Tucker MG, et al. Outbreak of multidrug-resistant Serratia marcescens infection in a neonatal intensive care unit. *Infect Control Hosp Epidemiol* 2008;**29**: 418–423.
67. Maragakis LL, Chaiwarith R, Srinivasan A, et al. Sphingomonas paucimobilis bloodstream infections associated with contaminated intravenous fentanyl. *Emerg Infect Dis* 2009;**15**: 12–18.
68. Maragakis LL, Cosgrove SE, Song X, et al. An outbreak of multidrug-resistant Acinetobacter baumannii associated with pulsatile lavage wound treatment. *JAMA* 2004;**292**: 3006–3011.
69. Manian FA, Meyer L. Comprehensive surveillance of surgical wound infections in outpatient and inpatient surgery. *Infect Control Hosp Epidemiol* 1990;**11**: 515–520.
70. Glenister H, Taylor L, Bartlett C, Cooke M, Sedgwick J, Leigh D. An assessment of selective surveillance methods for detecting hospital-acquired infection. *Am J Med* 1991;**91**: 121s–124s.
71. Ford-Jones EL, Mindorff CM, Pollock E, et al. Evaluation of a new method of detection of nosocomial infection in the pediatric intensive care unit: the Infection Control Sentinel Sheet System. *Infect Control Hosp Epidemiol* 1989;**10**: 515–520.
72. Sands K, Vineyard G, Platt R. Surgical site infections occurring after hospital discharge. *J Infect Dis* 1996;**173**: 963–970.
73. Holtz TH, Wenzel RP. Postdischarge surveillance for nosocomial wound infection: a brief review and commentary. *Am J Infect Control* 1992;**20**: 206–213.
74. Yokoe DS, Christiansen CL, Johnson R, et al. Epidemiology of and surveillance for postpartum infections. *Emerg Infect Dis* 2001;**7**: 837–841.
75. Nettleman MD, Nelson AP. Adverse occurrences during hospitalization on a general medicine service. *Clinical Perform Qual Health Care* 1994;**2**: 67–72.
76. Emori TG, Culver DH, Horan TC, et al. National nosocomial infections surveillance system (NNIS): description of surveillance methods. *Am J Infect Control* 1991;**19**: 19–35.
77. Gastmeier P, Geffers C, Sohr D, Dettenkofer M, Daschner F, Ruden H. Five years working with the German nosocomial infection surveillance system (Krankenhaus Infektions Surveillance System). *Am J Infect Control* 2003;**31**: 316–321.
78. Gastmeier P, Weigt O, Sohr D, Ruden H. Comparison of hospital-acquired infection rates in paediatric burn patients. *J Hosp Infect* 2002;**52**: 161–165.
79. Jodra VM, Rodela AR, Martinez EM, Fresnena NL. Standardized infection ratios for three general surgery procedures: a comparison between Spanish hospitals and U.S. centers participating in the National Nosocomial Infections Surveillance System. *Infect Control Hosp Epidemiol* 2003;**24**: 744–748.
80. Nosocomial infection rates for interhospital comparison: limitations and possible solutions. A Report from the National Nosocomial Infections Surveillance (NNIS) System. *Infect Control Hosp Epidemiol* 1991;**12:** 609–621.
81. Tokars JI, Richards C, Andrus M, et al. The changing face of surveillance for health care-associated infections. *Clin Infect Dis* 2004;**39**: 1347–1352.
82. Pronovost P. Interventions to decrease catheter-related bloodstream infections in the ICU: the Keystone Intensive Care Unit Project. *Am J Infect Control* 2008;**36**:S171.e1–e5.
83. Marschall J, Mermel LA, Classen D, et al. Strategies to prevent central line–associated bloodstream infections in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;**29** Suppl 1:S22–S30.
84. Lee TB, Montgomery OG, Marx J, Olmsted RN, Scheckler WE. Recommended practices for surveillance: Association for

Professionals in Infection Control and Epidemiology (APIC), Inc. *Am J Infect Control* 2007;**35**: 427–440.

85. Outline for Healthcare-Associated Infections Surveilland. 2006. Available at: www.cdc.gov/ncidod/dhqp/nhsn.html. Accessed March 15, 2009,
86. Williams JD SK, Atukorala SD. *Guidelines on Prevention and Control of Hospital-Associated Infections*. New Dehli: World Health Organization; 2002.
87. Wong ES, Rupp ME, Mermel L, et al. Public disclosure of healthcare-associated infections: the role of the Society for Healthcare Epidemiology of America. *Infect Control Hosp Epidemiol* 2005;**26**: 210–212.
88. Haley RW, Shachtman RH. The emergence of infection surveillance and control programs in US hospitals: an assessment, 1976. *Am J Epidemiol* 1980;**111**: 574–591.
89. Nguyen GT, Proctor SE, Sinkowitz-Cochran RL, Garrett DO, Jarvis WR. Status of infection surveillance and control programs in the United States, 1992–1996. Association for Professionals in Infection Control and Epidemiology, Inc. *Am J Infect Control* 2000;**28**: 392–400.
90. Evans RS, Larsen RA, Burke JP, et al. Computer surveillance of hospital-acquired infections and antibiotic use. *JAMA* 1986;**256**: 1007–1011.
91. Chalfine A, Cauet D, Lin WC, et al. Highly sensitive and efficient computer-assisted system for routine surveillance for surgical site infection. *Infect Control Hosp Epidemiol* 2006;**27**: 794–801.
92. Landers T, Davis J, Crist K, Malik C. APIC MegaSurvey: Methodology and overview. *Am J Infect Control* 2017; **45**: 584–588.
93. Dellit TH, Owens RC, McGowan JE Jr., et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007;**44**: 159–177.
94. Wisniewski MF, Kieszkowski P, Zagorski BM, Trick WE, Sommers M, Weinstein RA. Development of a clinical data warehouse for hospital infection control. *J Am Med Inform Assoc* 2003;**10**: 454–462.

Chapter 11

Outbreak Investigations

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Introduction

Outbreaks have generally been defined as localized increase in the incidence of disease.[1] In healthcare settings, reported outbreaks often involve the presence of clusters of patients infected or colonized with an organism of interest (e.g., carbapenem-resistant Enterobacteriaceae [CRE]), with similar types of healthcare-associated infections (HAIs, e.g., surgical site infections following coronary artery bypass grafting), or with similar signs or symptoms (e.g., anaphylactic reactions). Healthcare outbreaks can have infectious or noninfectious causes. Although outbreaks receive substantial attention, only the minority of HAIs occur as part of a cluster. One study from seven community hospitals estimated that about 11 percent of HAIs occurred as part of a cluster affecting about 0.09 percent of all discharges.[2]

Investigating healthcare-associated outbreaks can be a challenging and stressful experience, but these efforts are critical in identifying and correcting issues that impact patient safety. Not all outbreaks require an extensive investigation to resolve; some healthcare-associated outbreaks have well-described causes with interventions that have been shown to be effective. In these instances, interventions might be applied following only a brief investigation. Many outbreaks resolve without formal interventions. In one study of statistically significant clusters identified by applying an automated cluster detection method to microbiology data, the majority of detected clusters appeared to resolve without active intervention.[3]

Outbreak investigations can have a number of valuable outcomes beyond resolving the problem at the institution. For example, investigations at single healthcare facilities have identified issues with national and international implications. In 2008, the Centers for Disease Control and Prevention (CDC) assisted in an investigation of a cluster of anaphylactic reactions at a small dialysis center in Missouri. The investigation identified contaminated heparin from a single manufacturer that had been distributed around the world as the likely cause, leading to an international recall of the product.[4] Investigations can also identify important patient safety issues that require a reconsideration of current practice. In 2013, an investigation of a cluster of CRE identified properly reprocessed duodenoscopes as the likely cause of transmission leading to a re-evaluation of the design and methods for reprocessing these devices.[5] Outbreak investigations also provide a valuable training opportunity to teach basic principles of epidemiology and study design.

Outbreaks in healthcare settings have evolved over time. Historically, CDC has been primarily asked to assist in investigating clusters in short-stay acute care hospitals. These investigations have most often focused on clusters of common HAIs (e.g., surgical site infections) or unusual or emerging bacteria. As healthcare delivery has changed, and hospital and health department capacity has increased, CDC has increasingly been asked to assist in investigations in outpatient settings, including oncology clinics and dialysis centers. Although HAIs and multidrug-resistant organisms are a common reason for investigations in these settings, CDC assistance is often requested in investigations of injection safety lapses resulting in transmission of hepatitis B or hepatitis C or in assisting in evaluating lapses in device reprocessing. Between 2012 and early 2013, only 47 percent of healthcare investigations CDC participated in were in acute care hospitals; ambulatory facilities, dialysis centers, and long-term care facilities each were the setting for about 10 percent of investigations. During that time, clusters of multidrug-resistant organisms or of inpatient HAIs were the most common reasons for an investigation, accounting for about 30 percent of all investigations. HAIs in outpatient settings were the third most common reason and were the underlying problem in 22 percent of investigations.

When a formal investigation is required, the key is to take a systematic approach to the process. This provides a framework for investigators to fall back on that ensures all the critical steps are covered. In this chapter, we will review the steps involved in identifying, evaluating, and terminating an outbreak. Throughout the chapter we will also discuss common associations that should be considered when faced with familiar outbreak scenarios and review strategies for communication with patients and other stakeholders during outbreaks.

Detecting Outbreaks

Surveillance for healthcare outbreaks can be a challenging, labor-intensive task. Historically, outbreak detection often relied on reports from clinicians or laboratorians regarding an increase in infections or deaths or identification of an unusual pathogen. These clusters frequently involve an uncommon anatomic site of infection, an unusual organism, or infections occurring within a special subpopulation or specific location in a facility. For example, a national outbreak caused by a contaminated compounded steroid product was recognized when a case of an unusual clinical syndrome (i.e., fungal meningitis) was reported by an astute clinician to public health officials.[6] Outbreaks may also be detected through the

analysis of surveillance data from healthcare-associated infection reporting systems. These systems are capable of identifying significant increases in specific types of HAIs that might be indicative of acute or chronic problems. Laboratory data can also be used to detect outbreaks. This frequently involves the identification of a particular organism in a number of clinical isolates that exceeds the expected baseline from a specific setting or within a specific period of time.

The major drawbacks to these methods for outbreak detection are the reliance on human judgment to detect abnormal clusters, the need for clinicians or the laboratory to notify the appropriate staff, and the potential lack of sensitivity and specificity of rules used for detection (e.g., more than 2 cases of a pathogen of interest within a prespecified time). These approaches may miss true clusters that do not meet the prespecified rules and may also identify situations that reflect random variation rather than true outbreaks.

Automated detection methods have the potential to identify outbreaks more quickly and consistently.[3,7] One study of an automated system identified clusters that had not been detected using the previous facility methods and reclassified some of the clusters that had been detected by facility staff as random events.[3] In addition, the increasing availability of novel advanced laboratory technologies (i.e., whole-genome sequencing) have the potential to improve outbreak detection through more precise identification of genetic relatedness within a potential cluster.[8] Integrating these new technologies into outbreak surveillance may improve the specificity and timeliness of outbreak detection.

Investigation Steps

The following sections describe a stepwise approach to these investigations that can help ensure all aspects of the investigation are covered. Incomplete investigations can fail to identify the underlying source of the problem or lead to erroneous conclusions. The steps are summarized in Table 11.1. While not all steps will be relevant to all investigations, consideration should be given to each step. In addition, although this information is presented in a stepwise manner, several steps may take place simultaneously or in a different order.

Table 11.1 Steps of an outbreak investigation

Immediate first steps
Request that the laboratory save isolates from affected patients and any suspected sources or vehicles
Establish the existence of an outbreak (e.g., verify the diagnosis, review historical surveillance for expected baseline infection rate)
Engage appropriate authorities (e.g., state health department)
Institute any necessary immediate control interventions
Definitive investigation
Review published literature
Review existing information
Create a case definition
Find cases
Collect information (e.g., review records of existing case-patients)
Graph an epidemic curve
Summarize case-patient data in a line list, revise or refine case definition if needed, propose hypotheses
Infection control observations
Confirming hypotheses
Consider analytic studies (e.g., case-control or cohort)
Consider laboratory testing of isolates or other microbiologic evaluation
Consider environmental sampling and/or culturing of personnel
Implementing interventions and follow-up
Develop plan and timeline for implementing control measures
Ensure personnel adherence to control measures
Continue surveillance to determine if outbreak is controlled and reassess need for ongoing control measures
Communications
Continue updating appropriate authorities of the investigation
Consider need for patient notification
Prepare for media and public inquiries

Immediate First Steps

Once a possible outbreak is identified, the microbiology laboratory should be asked to save all isolates that might be part of the outbreak in case these are needed later for further evaluation. In the absence of detailed information, the initial request about which isolates to save may be broad and can be refined as more is known.

The investigation team should take steps to confirm whether an outbreak is actually occurring and whether or not it is clinically meaningful. This process often involves initially confirming the diagnosis. Determining if antimicrobial susceptibilities or organism identification are correct might be one approach for outbreaks of specific bacteria; clusters of specific syndromes might require review of pathology records or of records of some or all putative "case-patients." When available, historical surveillance data (6–12 months before first case) is useful for establishing an expected baseline rate to determine if the reported increase is new. Cursory review of microbiology records to assess approximate numbers of cases over time also can be helpful in determining if a reported increase in HAIs might represent an outbreak. Thought should also be given to the meaningfulness of the cluster before deciding to investigate further. Some clusters might represent an increase in incidence above baseline but not be clinically

meaningful (e.g., an increase in *Staphylococcus epidermidis* from nonsterile cultures) and therefore might not warrant the utilization of additional resources.

Thought should also be given to the possibility that the cluster represents a pseudo-outbreak, or an increase in incidence that is unrelated to a true increase in disease. Pseudo-outbreaks can be due to changes in the laboratory method of detection; for example, switching from enzyme immunoassay (EIA) to polymerase chain reaction (PCR) for the detection of *C. difficile* or changes in case definitions.[9] Pseudo-outbreaks can also be due to contamination of samples from contaminated medical equipment[10,11] or contamination in the laboratory.[12] Indications of a pseudo-outbreak can be the presence of multiple case-patients without clear epidemiologic links or multiple cases lacking symptoms of disease. The line between pseudo-outbreaks and outbreaks can become blurred when investigating clusters of multidrug-resistant organisms that might represent patient colonization rather than true infection. Finally, pseudo-outbreaks may still be clinically meaningful, warranting investigation and institution of control efforts.

Attention should also be given to the need for any immediate control interventions, for example, cohorting or isolating patients with multidrug-resistant organisms, including *C. difficile*. In addition, facilities should consider a temporary discontinuation of new admissions or in performing a procedure if there are exposures or procedures with high index of suspicion based on initial presentation

The initial steps of an outbreak investigation should include a review of published literature. There are thousands of published articles on healthcare-associated outbreaks available through PubMed (www.ncbi.nlm.nih.gov/sites/entrez?db=pmc), and the information they provide can help inform investigation efforts. Another useful resource is the "Worldwide Database for Nosocomial Outbreaks" (www.outbreak-database.com/About.aspx), a free database that contains summary information on >3000 healthcare-associated outbreaks, including information on potential sources of healthcare outbreaks and control measures that were implemented. Certain procedures, vehicles, and technical errors are repeatedly associated with healthcare outbreaks. Infection control personnel will be able to investigate outbreaks more efficiently if they are aware of these associations. For example, contamination of environmental surfaces along with lapses in infection control precautions, like hand hygiene and contact precautions, have been implicated repeatedly in outbreaks of vancomycin-resistant enterococci (VRE), *C. difficile*, and *Acinetobacter* species. Some common outbreak associations are shown in Table 11.2.

When an outbreak is identified, it is important to keep lines of communication open with managers, frontline healthcare providers, and other staff who need to be aware of the ongoing outbreak and any immediate remediation steps or precautions determined appropriate by the investigators. All states require that outbreaks be reported to public health officials; infection control staff should check and know their local and state laws for reporting requirements. In addition, infection control personnel should report adverse events that are suspected to be related to human medical products including medications, biologics, or medical devices to the U. S. Food and Drug Administration's MedWatch Program (www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home).

Case Definition

As part of the investigation, differentiating between what constitutes the outbreak and what does not is important. This requires development of a case definition. Case definitions should be narrow enough to focus the effort but broad enough to capture as many of the affected population as possible; however, remember the goal of the investigation is to halt the outbreak, which may not require identifying every case. Using the information from the initial review, a preliminary case definition can be generated; this definition might be refined as more information becomes available. The key components of a case definition generally include "what" or the required symptoms or findings (e.g., a positive culture for *S. aureus*), "who" or the patient population, "where" or the location associated with symptoms or findings (e.g., hospital, ward or unit), and "when" or the time frame during which the symptoms or findings occurred. A case definition can be based on clinical, laboratory, radiologic, pathologic, or other data, if available. For example, during an outbreak of hepatitis C linked to an outpatient clinic the investigators defined a case as "acute hepatitis C or laboratory-confirmed HCV infection occurring in a susceptible person who had undergone an endoscopy procedure at the clinic on 25 July 2007 or 21 September 2007."[43] Of note, generally the term "case" refers to the infection, illness, or laboratory finding, whereas the case-patient refers to the person experiencing the problem. When including a specific exposure in a case definition, as in the previous example (i.e., "undergone an endoscopy procedure at the clinic") it is critical that such exposures only be included if all suspect cases share that common exposure. In this way the further development and refinement of a case definition may arise out of a line listing (as discussed below) using a preliminary, broader case definition.

Case Finding

Once the preliminary case definition is established, efforts can begin to identify additional cases. If the case definition includes a laboratory result or finding, laboratory records are a logical place to start and can facilitate rapid identification of possible cases. If the outbreak involves a healthcare-associated infection, adverse event, or a multidrug-resistant pathogen for which the facility is performing surveillance, then infection control and surveillance records can be useful for case finding. Radiology, pathology, and pharmacy records might also be useful, if the infection has typical radiologic or pathologic findings or antimicrobial treatments.

Case finding can become problematic when patients harbor a pathogen and therefore might meet the case definition but they are not manifesting symptoms and therefore might not be recognized as a case. In these instances, examining only clinical

Table 11.2 Commonly identified causes of various types of healthcare-associated outbreaks, 2000–2015

Outbreak	Common cause	Reference(s)
Group A streptococcal surgical site infection	Dissemination by colonized healthcare personnel or patient	Thigpen et al.,[13] Dooling et al.[14]
Bacterial meningitis (e.g., *Streptococcus salivarius*) in patients following spinal injection procedures	Transmission from colonized healthcare personnel via medication preparation lapse and/or failure to adhere to recommended facemask use	CDC,[15] Chitnis et al.,[16] CDC website[17]
Norovirus gastroenteritis	Contact with infectious patients or staff or with contaminated food, water, or aerosolized particles in healthcare settings	Gaspard et al.,[18] Kambhampati et al.,[19] Repp et al.[20]
Carbapenem-resistant Enterobacteriaceae sterile-site infections and urinary tract infections	Contact with colonized or infected patients or with the contaminated hands of healthcare personnel; contaminated medical equipment	Epstein et al.,[5] Chitnis et al.,[21] Munoz-Price et al.[22]
Acinetobacter baumannii sterile-site infections	Contact with contaminated environmental surfaces or medical equipment or with the contaminated hands of healthcare personnel; contact with colonized or infected patients	Maragakis et al.,[23] Simor et al.[24]
Nontuberculous mycobacterium skin and soft tissue infections, surgical site infections, or other sterile site infections	Exposure to environmental surfaces, medications, or medical equipment contaminated by tap water	Astagneau et al.,[25] Chroneou et al.,[26] Williams et al.,[27] Edens et al.[72]
Burkholderia cepacia complex sterile site infections among noncystic fibrosis patients	Exposure to intrinsically and extrinsically contaminated medical products; contact with contaminated environmental surfaces or water	Peterson et al.,[28] Kutty et al.,[29] Nasser et al.[30]
Endophthalmitis outbreak among patients with retinal disorders	Exposure to bevacizumab that was extrinsically contaminated during repackaging for off-label use to treat retinal disorders	Edison et al.,[31] Frost et al.[32]
Healthcare-associated bloodborne pathogen infections	Exposure to contaminated parenteral medications due to failure of healthcare personnel to follow safe injection or medication preparation practices, including reuse of syringes to access shared medications and reuse of single-dose vials on multiple patients; improper handling of devices for assisted blood glucose monitoring, including reuse of fingerstick devices between patients	Dobbs et al.,[33] Guh et al.,[34] Zheteyeva et al.,[35] CDC[36]
Tightly clustered healthcare-associated bloodstream infections	Exposure to intrinsically (particularly if compounded product) or extrinsically contaminated medical product	Blossom et al.,[37] See et al.,[38]
Healthcare-associated bloodborne pathogen infections and other bloodstream infections in patients prescribed parenteral narcotics	Exposure to contaminated parenteral narcotics due to drug diversion by an infected healthcare personnel (e.g., hepatitis C virus infection)	Hellinger et al.,[39] Schaefer[40]
Postoperative infections after allograft and organ transplantation	Receipt of contaminated allografts and organs from donors with unrecognized infections	Article I. Kainer et al.,[41] Iwamoto et al.,[42] Basavaraju et al.[71]

culture results will underestimate the number of cases and could compromise control efforts if the colonized patients continue to serve as a reservoir for transmission. Surveillance cultures can be used to identify this unrecognized reservoir. For example, in one outbreak of CRE in a long-term acute care facility, investigators used serial point prevalence surveys (rectal cultures) to identify cases, the first of which identified 16 additional cases.[21]

If a medical product or device is suspected as the source of the outbreak, in addition to contacting the appropriate public health agencies, facilities might also consider a call for cases locally or more broadly as part of their case finding efforts. This can often be accomplished through relevant professional societies or state-based infection control listservs. In general, calls for additional cases should be detailed to avoid inclusion of unrelated reports and are often most useful when the problem is not common. In an investigation of anaphylactoid reactions related to use of contaminated heparin, although the initial cases were reported from one facility, a wider call for cases identified a large number of reactions at additional facilities and was critical for identifying heparin as the likely causative exposure.[4]

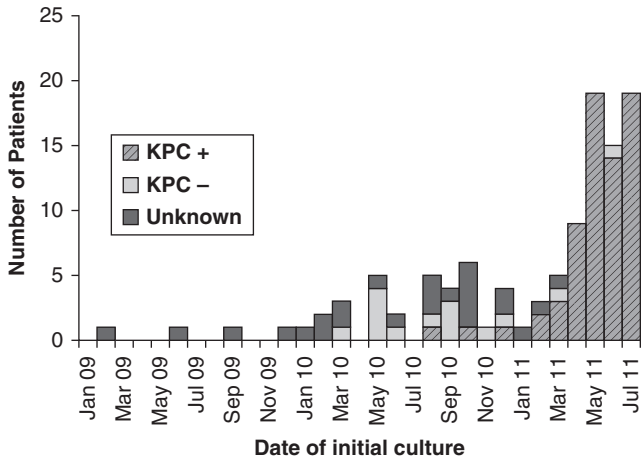

Figure 11.1 Example of an epidemic curve of a carbapenem-resistant *Klebsiella pneumoniae* outbreak, showing the number of case-patients identified during January 2009–July 2011, by month of their initial culture positive for carbapenem-resistant *K. pneumoniae* and by their *K. pneumoniae* carbapenemase (KPC) status (CDC unpublished data). While this epidemic curve depicts the distribution of case-patients by monthly intervals, note that the unit of time of epidemic curves can be smaller, e.g., weekly intervals, depending on the incubation period of the illness and the time interval of the outbreak.

Collecting and Organizing Data

Once cases are identified, data should be collected and organized to begin the evaluation for common exposures. Data collected during an outbreak investigation can be organized several ways, including in a line list, an epidemic curve or "epi curve," and, at times, a spot map.

Information on each case-patient should be systematically assembled into a line list, where each row represents a single case or case-patient and each column represents a variable of interest. The line list enumerates and characterizes all affected patients, allowing investigators to characterize the outbreak and generate hypotheses. Investigators should also make note of case-patients that represent outliers, as they can provide insight toward hypothesis generation. Variables of interest collected from the medical record might include demographics, date of onset, symptoms, outcomes, laboratory findings, co-morbidities, patient location information, healthcare staff contact, host risk factors, and other relevant exposures. As part of data collection, it is important to collect details including dates, frequency, duration, and amount. Instruments are available to help guide data collection (www.cdc.gov/hai/pdfs/outbreaks/Response_Toolkit_Abstraction_Form-508.pdf; www.cdc.gov/hai/pdfs/outbreaks/Response_Toolkit_Users_Guide-508.pdf).

The epidemic curve is a graphical depiction, or timeline, of the onset or detection of illness among case-patients. The horizontal x-axis is the date/time of onset or detection, and the vertical y-axis is the number of cases. The epidemic curve can provide information on outliers, the magnitude of the outbreak, trends over time, and possible exposure period(s). The shape of the epidemic curve can provide information on the possible mode(s) of transmission although transmission in healthcare can often be multifactorial (e.g., from a contaminated device or product and person-to-person transmission). An example of an epidemic curve is shown in Figure 11.1.

Spot maps depict the locations where patients resided and/or received care before becoming cases and can also help infer mode of transmission; if clustering is observed within a facility, this might suggest person-to-person transmission or a common source. If cases are scattered throughout the facility, this is more consistent with a widespread source (e.g., mobile x-ray machine) or a common source unlinked to where the patients reside in the facility, for example a dining hall, compounding pharmacy, or radiology suite. An example of one from a CRE outbreak in a long-term care facility is shown in Figure 11.2.

Infection Control Observations

In many outbreak investigations, observations of practices ultimately identify the potential cause. The line list is critical in identifying common procedures or exposures among patients to guide both the type and location of observations needed. For example, exposure to a reusable instrument should prompt a review of the facility's reprocessing procedures for that instrument. Infections associated with indwelling devices, such as central-line–associated bloodstream infections, will require a review of procedures pertaining to the access and maintenance of these devices. For infectious disease outbreaks, the type of pathogen and infection being investigated are important factors in determining the types of observations and reviews performed. For example, investigations of outbreaks of multidrug-resistant organisms should include an assessment of staff adherence to hand hygiene and contact precautions, as well as cleaning and disinfection of high-touch surfaces and shared medical equipment.[44] Outbreaks of certain environmental organisms like *Aspergillus* should include review and observations of construction activities in or near patient areas. Investigations of outbreaks associated with waterborne pathogens, such as nontuberculous mycobacteria and

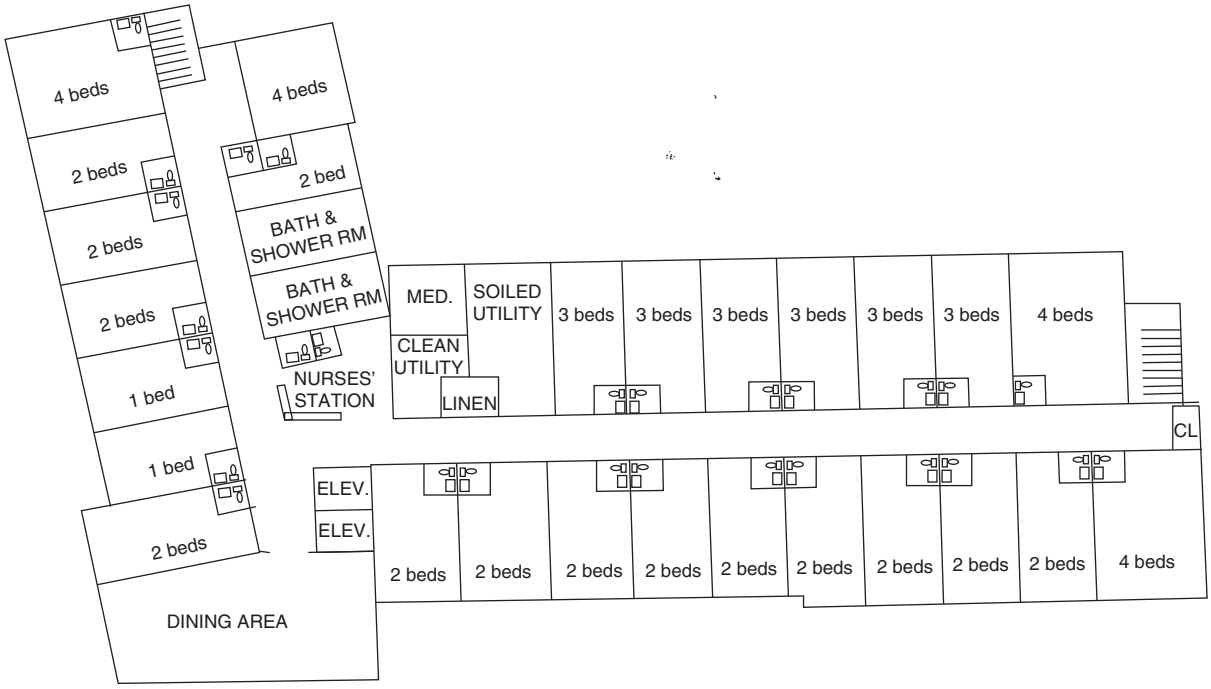

Figure 11.2 Example of a spot map depicting the locations of case-patients with carbapenem-resistant *Enterobacteriaceae* (CRE) and control-patients (without CRE) in a facility ward. In this example, case-patients were distributed throughout the ward, with no clear pattern of clustering to indicate a common source in the ward (CDC unpublished data).

Pseudomonas aeruginosa, should prompt an assessment for potential routes of exposure to tap water; depending on the site of infection, this might include a review of local wound care practices, preparation and handling of injectable or aerosolized medications, and procedures performed in the vicinity of sinks where patients might be exposed to splash-back of droplets or aerosols.[27] Receipt of similar types of injectable medications among case-patients should prompt a review of medication preparation and handling in the affected unit, central pharmacy, particularly if the medication was prepared or compounded onsite. Common exposure to injectable narcotics in an outbreak of viral hepatitis or bacterial bloodstream infections should prompt a careful review of the facility's security measures for accessing injectable controlled substances to exclude narcotics diversion by healthcare personnel as the cause of the outbreak.[40]

Because impressions and recollections might change during the course of the investigation, infection control personnel should interview staff and review procedures soon after they recognize a potential outbreak. Interviews should be conducted separately with all relevant staff, including supervisory staff, and include questions about procedural changes implemented before, during, or after the outbreak. Semistructured interviews that pose similar questions to all staff members might be effective in identifying procedures that are being undertaken in different ways by specific staff members. Written protocols should also be reviewed to guide infection control observations and identify areas for improvement. Ideally, investigators should directly observe the implicated procedures and have an opportunity to question personnel about their techniques. If the actual procedure cannot be observed, investigators should ask personnel to carry out a mock procedure or to walk the investigators through each step of the procedure. Observing different personnel on the same and different shifts as they perform the procedures of interest might also provide valuable information about potential deviations from recommended practices.

Initial observations of procedures might be unstructured (i.e., performed without using a detailed observation form) and focus on practice patterns and workflow that deviate from recommended infection control practices and facility or unit policies. However, more detailed and focused observation tools can be developed, as needed, and can be informed by the free-form observations. CDC has an infection control checklist that investigators can use for observing certain procedures, such as hand hygiene, personal protective equipment use, and the preparation and handling of injectable medications (www.cdc.gov/HAI/pdfs/guidelines/ambulatory-care-checklist-07–2011.pdf). Similar tools for acute care hospitals are available from the Centers for Medicare and Medicaid Services (www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertificationGenInfo/Downloads/Survey-and-Cert-Letter-15–12-Attachment-1.pdf).

Tools also exist for specifically assessing environmental cleaning and disinfection, although the exact role each of these methods plays in assessing the cleanliness of surfaces remains controversial, and evidence is lacking for any associations between their use and reduction in transmission. These include fluorescent markers that can be applied to environmental surfaces prior to cleaning and disinfection and, through assessing their removal, are intended to provide an indication of how frequently and thoroughly surfaces are wiped.[45–47]

Adenosine triphosphate (ATP) bioluminescence assay can also be used to detect residual organic material after cleaning.[48]

Confirming Hypotheses

Once hypotheses about the cause of an outbreak have been generated, targeted interventions should be employed to address these issues. In addition, consideration should be given to methods to confirm these hypotheses as possible causes; the two most common methods for this include analytic studies and laboratory testing.

Analytic Studies

The objective of a formal comparative study is to assess the presence of associations between potential causal exposures and illness; these associations present through differences in frequency between two comparison groups. Because of the resources required, the investigators should consider whether a formal study is appropriate and necessary, particularly if the problem is an acute, self-limited, one-time incident, (e.g., a recognized contamination event) or if the problem has well-known causes and corrective interventions. In healthcare outbreaks, some exposures that might be of interest, like exposure to specific healthcare workers, might not be readily available from retrospective review of medical records and therefore a study evaluating these factors might be difficult to perform. However, if the initial investigation did not provide a clear source of the outbreak, new hypotheses are needed, or confirmation of hypotheses generated by the initial investigation are needed, a formal study can be useful. Finally, analytic studies are powerful teaching tools and might be undertaken as an educational opportunity for trainees in healthcare epidemiology, infection control, or public health.

In healthcare outbreaks, case-control and cohort studies are generally the most frequently employed. Case-control studies are more common than cohort because they are well-suited for uncommon events (e.g., when prevalence is less than 10 percent) and are typically faster to conduct than cohort studies.[49,50] However, control selection is challenging, especially as investigators are often limited by a small population from which to select controls. It is essential to select controls from a population that shares key characteristics with the cases that would make it possible for them also to have become a case. Selecting inappropriate controls can render the results of a case-control study invalid. The relative advantages and disadvantages of these study designs are described in detail in the "Epidemiologic Methods in Infection Control" chapter (Chapter 6).

The first step in any analytic study is the gathering of relevant data. Investigators should design a standardized form for data collection, which includes demographic data, co-morbidities and information about exposures. Each variable evaluated as a possible risk factor will increase the time and effort required for the analysis. Furthermore, each additional variable increases the likelihood that a characteristic entirely unrelated to the outbreak will appear to be a risk factor (i.e., statistically significant by chance alone). To avoid these pitfalls, investigators should include few, if any, characteristics that are not plausible risk factors. Obviously, a narrow interpretation of biologic plausibility might inappropriately restrict investigations to only previously suspected or confirmed risk factors. Such inappropriate restriction can be avoided by ensuring during the early phase of the studies (particularly the design of the line list) that a careful review of cases casts a very wide net for hypothesis generation, but that the data collected for the comparative study be more limited. Finally, if multiple individuals are abstracting data, providing training and initially co-abstracting some charts to ensure data interpretation and abstraction are as uniform as possible is important.

In addition to deciding which risk factors to analyze, investigators should consider whether or not to perform a matched study. The match can never be undone, meaning, the data must be evaluated as a matched study design and the variables on which case-patients and controls were matched cannot be evaluated as potential risk factors. Furthermore, matching can make controls and case-patients so similar that the investigators would miss all but the most obvious risk factors (i.e., overmatching). However, matching increases the efficiency of the study by ensuring the cases and controls are more similar with regard to characteristics associated with the epidemic condition, but are not the real cause(s) ("confounders"). Matching avoids the loss of precision that occurs when confounders are adjusted for during the analysis of the data. Frequency matching can be performed when there are a small number of levels in the confounders of interest (e.g., sex), while pair matching is more useful if confounders have many levels. Selecting the number of controls to match with each patient is often based on the available pool from which controls can be selected and available resources to perform chart review; multiple controls will increase precision of estimates of association. A ratio beyond three to four controls per case will generally increase precision only marginally.

Many investigators choose not to match, but to control for confounding variables by either stratifying the analysis by possible confounders or by using multivariable analysis. Unfortunately, the limited power available in most healthcare outbreaks, due to the typically small number of cases, often limits the ability to control for multiple confounders. Another alternative to matching is restriction. In this situation, cases and controls are restricted to a specific high-risk subpopulation. For example one might restrict an analytic study during outbreak of mucormycosis to transplant patients or restrict an outbreak of certain multidrug-resistant organisms to patients on specific wards.

Because healthcare outbreaks generally involve a small number of cases, the causative factor may not achieve statistical significance. Any factor with an odds ratio or relative risk that suggests an association should be further investigated, even if the difference between cases and controls only approaches, but does not achieve, statistical significance.

Laboratory Evaluation of Isolates

During outbreak investigations that involve common bacteria, typing is often useful to identify which isolates are part of the

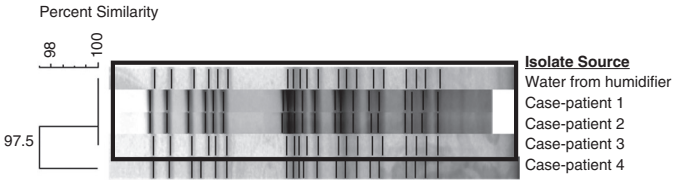

Figure 11.3 Example of a pulsed-field gel electrophoresis (PFGE) gel of isolates collected during an investigation of *Mycobacterium chelonae* at an ambulatory surgical center. Four isolates, including three case-patient isolates and an isolate recovered from water in a humidifier at the facility were indistinguishable by PFGE. The isolate from the fourth case-patient was highly related (>95% similar). These results, along with the epidemiologic links identified during the investigation, suggest the humidifier was the source of the outbreak (CDC Unpublished data).

outbreak and which are not, and to better understand modes of transmission. Typing can be costly, time consuming, and is not always readily available at healthcare facilities; for these reasons it should be used judiciously. Typing might not be necessary for investigations of rare pathogens with strong epidemiologic links, as these isolates are more likely to be related. In addition, the information gained from typing might not influence the type of interventions that are implemented.

A number of techniques can be used for typing isolates during outbreaks; each method has inherent advantages and disadvantages. Although readily available, using antibiograms to identify related isolates is not very sensitive or specific, and is therefore not generally recommended.[51] Pulsed-field gel electrophoresis (PFGE) has historically been considered the gold standard for healthcare outbreak investigations based on its discriminatory power.[52,53] In addition, the Tenover criteria allow for standard interpretation of isolate relatedness using PFGE results. These criteria were the result of a large analysis of epidemiologic and PFGE data to establish a set of interpretation guidelines across a variety of pathogens.[54] An example of a PFGE gel is shown in Figure 11.3. More recently, whole genome sequencing (WGS) using next-generation sequencing platforms has become more readily available, providing another alternative. WGS has been used in a number of investigations to assist with identifying related isolates and understanding transmission during outbreaks.[55,56] Currently, the use of WGS is limited by a lack of standardized criteria for identifying single-nucleotide polymorphism differences between sequences and the need for access to experienced bioinformaticians to analyze and interpret the data provided by this technique. Additional information on typing techniques can be found in Chapter 23.

For interpretation of any typing method, evaluating the laboratory data in the context of the available epidemiologic data is crucial. Outbreaks of pathogens from environmental sources such as water or biofilms, can be composed of a diverse microbial population including not only different bacterial and fungal species, but also different strains within a single species. Indistinguishable isolates can point to a single source of infection;[28] however, nonclonal (genetically diverse) isolates do not rule out the possibility of an outbreak. In addition, some common multidrug-resistant organisms can appear very similar with some typing techniques and if interpreted without epidemiologic information can lead to erroneous conclusions about relatedness. For example, clones of USA300 community MRSA from diverse unrelated sources can appear related by PFGE.[57]

Performance of Environmental and Personnel Cultures

Environmental sampling and/or culturing of personnel can be powerful investigative tools for confirming the source of healthcare outbreaks. Although this is often one of the first steps employed in investigations, this approach can often lead to more questions than answers. Before performing environmental cultures, facilities should consider a number of factors. First, organisms that cause healthcare outbreaks (e.g., Gram-negative "water" organisms; fungi) can be isolated frequently from nonsterile environmental sources. Without sufficient epidemiologic data to guide environmental and personnel culturing, isolation of organisms from cultures can be difficult to interpret and sometimes can even lead to erroneous conclusions. Therefore, sampling should only be conducted after a hypothesis has been generated and be directed at sources for which there are epidemiologic data from the line-list, observations, or analytic studies that link them to the outbreak. Second, culturing of personnel or environmental sampling might be more relevant for organisms that have been previously documented to be transmitted by colonized or infected HCP (e.g., MRSA)[58,59] or for organisms known to colonize the environment (e.g., *Acinetobacter*) and result in transmission to patients.[60,61] Third, a number of factors can impact the ability to recover the outbreak organism from the environment or healthcare personnel, including the sensitivity of the sampling technique and whether or not the contamination or colonization is occurring intermittently. Thus, negative cultures for the organism alone should not be used to rule out an environmental source or personnel as the cause of the outbreak, especially when strong epidemiologic links suggest otherwise.

To maximize the yield and utility of environmental cultures, surface sampling should focus on high-touch areas and should not include walls, floors, or other nonsterile areas that do not have plausible connections to the outbreak. Materials used for sampling depend on the surface type and area. For example, culture swabs used in many facilities to sample surfaces can only be used on small surface areas (approximately 4 in^2). Larger spongesticks should be selected when sampling larger areas. The yield of surface cultures might also be limited by residual disinfectants that must be neutralized before the sample is processed. Sampling of tap water for waterborne pathogens usually requires large volumes of water (e.g., at least 1 liter), which should ideally be collected from sink faucets after several hours of inactivity. However, because the yield from water samples is often low, direct sampling of sink aerators and drains often provides useful information about the organisms that may contaminate the environment from sinks. Samples of adjacent countertops could also be collected to evaluate for contamination due to splash from the sink. In addition, some environmental pathogens, particularly

waterborne agents, have adapted to survive in very low-nutrient settings and require special low-nutrient media (e.g., Reasoner's 2 agar)[62] to grow in the microbiology laboratory. Given the methodologic challenges in both obtaining and processing environmental samples, consultation with an experienced microbiologist before sampling and arrangement for testing by a specialty laboratory should be considered.

Environmental sampling can also be useful in situations involving suspected intrinsic contamination of compounded medications.[37] In these investigations, pooling of unopened vials or containers of medications for sampling and sterility testing can often increase the yield as all units might not be contaminated and sampling a small number might miss potential contamination.

Culturing of healthcare personnel can be useful during outbreaks of *S. aureus* infections, in which swabs of nares from implicated healthcare personnel can be collected to look for carriage of *S. aureus* strain that matches the outbreak strain.[63] Cultures of healthcare personnel have also been useful during investigations outbreaks of bacterial meningitis associated with spinal injection procedures and have implicated the failure of colonized healthcare personnel to wear a mask during the procedure.[16]

Implementing Interventions

Although this section is included at the end of the outbreaks steps, interventions should be instituted to correct deficiencies as soon as they are identified. In some situations, interventions that correct common problems associated with specific outbreaks may be employed as an initial step. Interventions should focus on the immediate cause of an outbreak and use the simplest measures to correct the problem. The more focused the control measures, the more feasible their implementation and the more likely healthcare staff will be to adhere to the measures. Investigators should develop a plan and timeline for implementing the control measures. After implementation, they should continue to work closely with the staff in the affected area to ensure that they understand and efficiently implement the recommendations, and that they continue to comply with the recommendations over time. Continued follow-up through ongoing surveillance should be instituted to determine whether the measures are effective. Once outbreaks are controlled, reviewing the control measures that were implemented is important to determine which measures, if any, might no longer be necessary.

Additional Considerations during Outbreak Investigations

Outbreaks are a considerable source of stress for healthcare providers, administrators, and patients. It is natural for staff to be defensive and wary of investigations that may be seen as an attempt to blame them for an outbreak. Healthcare personnel must understand that the investigation is a collaboration and not an attempt to affix culpability. Techniques that are seen as clearly fact-finding and encourage confidentiality are far more effective than interviews that appear to target specific tasks or staff members. Particularly effective strategies include questionnaire surveys of all staff in which open-ended questions are administered face-to-face by a neutral party. All activities related to the investigation must be conducted in a neutral and supportive manner, respecting the right to privacy of staff members and patients. A culture that focuses on systemic changes to protect patients and healthcare facility staff is clearly preferable to a culture that appears to focus primarily on blame (see Chapter 30 on administering an infection prevention program). Infection control staff must strive to create this culture of safety in the context of the outbreak investigation and emphasize that the investigation is designed to improve the systems that might be the cause. The infection prevention and control department should be the strongest advocate for patient safety and work with the facility administration in creating an environment that promotes a culture of safety.

Medico-Legal Concerns

Healthcare facility staff often are concerned about the protection of the privacy of living case-patients, their families, and healthcare staff, particularly since the passage of the Health Insurance Portability and Accountability Act (HIPAA). However, HIPAA does allow covered entities to share protected health information with public health officials for public health purposes. Likewise, facility personnel often are concerned about the legal implications of sharing information on outbreaks with health departments, providers, and the public. There is no doubt that healthcare outbreaks have and will continue to result in litigation. However, facilities that are proactive in reporting and investigating outbreaks and that openly share information in a timely manner with public health often find that they benefit from the assistance that they receive and that they are in a better position with respect to lawsuits that might arise. Infection control staff should be aware of the possibility of litigation and take steps to be prepared for legal action, should it arise. Investigators should ensure that all appropriate facility staff, including risk managers and facility leadership, are notified and engaged. Record keeping should be thorough and clearly document the investigation steps and findings. Lawsuits are often filed long after outbreaks have occurred, and having detailed information available can be critical in reconstructing past events.

Communications and Patient Notifications

Communication with various stakeholders, including public health officials, patients, and healthcare personnel is a critical component of any outbreak investigation. Even in the absence of specific reporting requirements for healthcare-associated outbreaks, healthcare facilities should engage health department officials when an outbreak is first suspected or detected. Expertise in investigating healthcare outbreaks has grown dramatically in state and local health departments over the last decade; these skills complement expertise in epidemiology and infectious diseases that have always been available from health departments. State and local public health officials can often

advise on case-finding, assist with infection control observations, provide epidemiologic and laboratory support, and engage relevant subject matter experts from CDC, as needed. Alerting health department officials to an outbreak is also critical in identifying problems that might extend to multiple facilities, such as the distribution of a contaminated product or device.[4] Health departments have a central role in promoting implementation of recommended practices across facilities within a region, particularly in situations involving emerging multidrug-resistant organisms. Furthermore, given the sensitivity of healthcare outbreaks, public health officials can often provide an objective assessment of the situation and advise healthcare facilities on some of the ethical and logistical considerations for notifying patients.

Previously, most patient notifications related to an infection control breach were conducted in the context of a viral hepatitis outbreak resulting from an unsafe injection practice (e.g., reuse of syringes to access shared injectable medications).[43,64,65] Because of the high risk of bloodborne pathogen transmission associated with unsafe injection practices, the discovery of such lapses even in the absence of a recognized outbreak has prompted notifications of patients for bloodborne pathogen testing (hepatitis B virus, hepatitis C virus, human immunodeficiency virus).[34,66] For example, from 2001 through 2011, at least 35 patient notification events related to unsafe injection practices occurred in the United States, of which 22 stemmed from outbreak investigations, whereas 11 were prompted by the recognition of unsafe injection practices in the absence of documented disease transmission.[34] In addition, widespread patient notifications have occurred when the risk of bloodborne pathogen transmission posed by the infection control breach is uncertain, such as with instrument reprocessing errors.[67–70] More recently, patient notifications have also resulted from potential exposure to other infectious pathogens, such as bacterial and fungal organisms, due to an unsafe healthcare practice or procedure, including exposure to a piece of potentially contaminated reusable equipment or an intrinsically contaminated compounded medication.[5,6] While the primary purpose of a notification is to inform potentially exposed patients of actionable steps that they can take (e.g., bloodborne pathogen testing, screening for a multidrug-resistant organism), increasingly, to be transparent, healthcare facilities are also notifying affected patients even when no actions are recommended. Given the tremendous stress and emotional anxiety that patients might experience, the decision for patient notification should take into consideration its potential benefits and harms and be made in consultation with public health officials and relevant facility staff, including involved healthcare providers, infection control staff, and risk management.

Once a decision to notify patients has been made, several important steps need to be taken as part of the notification process, including identifying the potentially exposed patients, determining the most appropriate method of notification (e.g., phone call, letter), developing communication materials, and arranging logistics for any patient testing and follow up of results. Ideally, patient notifications should occur in a timely manner and include a description of the nature and source of the outbreak (if known), infection control measures implemented to date, and any recommended course of action for patients. In situations where the number of potentially exposed patients is exceedingly high, ranging from hundreds to thousands, there is often a greater breach of public trust in the affected facility, and a more comprehensive communication strategy might be required. This might consist of having a dedicated website with regular updates on the outbreak investigation and/or a call center to address questions from patients and healthcare personnel. To assist healthcare facilities and health departments with the notification process, CDC developed a Patient Notification Toolkit containing resources and sample patient letters as well as some essential communication tips and strategies (www.cdc.gov/injectionsafety/pntoolkit/index.html). While the template materials in the toolkit are largely based on incidents involving bloodborne pathogen exposure, they can be tailored for incidents involving other types of exposures or outbreaks.

Outbreaks and the Media

Healthcare outbreaks can sometimes generate significant media attention, particularly those that involve a large number of patients or are associated with severe infections or adverse events. Healthcare facilities should be prepared to address media inquiries about the outbreak and investigation efforts. This might include developing talking points and press releases in advance as well as designating a spokesperson for communicating with the media to ensure consistency in messaging. Media can also be helpful in rapidly disseminating critical information to patients who cannot be readily contacted. Facilities should also consider involving the health department in developing its communication strategy. The CDC's Patient Notification Toolkit (www.cdc.gov/injectionsafety/pntoolkit/index.html) also contains tips and resources for communicating with the media, including sample press releases and fact sheets facilities can tailor for their use.

Conclusion

Although the settings and circumstances have changed over the years, outbreaks in healthcare settings continue to occur. Infection preventionists and healthcare epidemiologists must continue to recognize and rapidly respond to these crises as they arise. Outbreak investigations play an important role in identifying problems that compromise patient safety at individual institutions, but they also have the potential to detect issues that have impact beyond the involved healthcare facility. Employing a systematic approach to these investigations helps to ensure that they are complete and thorough, that the indicated approaches and resources are brought to bear, and provides the best opportunity that the ultimate cause will be identified.

References

1. Porta M. *A Dictionary of Epidemiology*. 5th ed. New York, NY: Oxford University Press, 2008.
2. Haley RW, Tenney JH, Lindsey JO II, Garner JS, Bennet JV. How frequent are outbreaks of nosocomial infection in community hospitals? *Infect Control*. 1985;**6**(6): 233–236.
3. Huang SS, Yokoe DS, Stelling J, et al. Automated detection of infectious disease outbreaks in hospitals: a retrospective cohort study. *PLoS Med*. 2010;23;**7**(2): e1000238.
4. Blossom DB, Kallen AJ, Patel PR, et al. Outbreak of adverse reactions associated with contaminated heparin. *N Engl J Med*. 2008;**359**(25): 2674–2684.
5. Epstein L, Hunter JC, Arwady MA, et al. New Delhi metallo-β-lactamase-producing carbapenem-resistant *Escherichia coli* associated with exposure to duodenoscopes. *JAMA*. 2014;**312** (14): 1447–1455.
6. Smith RM, Schaefer MK, Kainer MA, et al. Fungal infections associated with contaminated methylprednisolone injections. *N Engl J Med*. 2013;**369**(17): 1598–1609.
7. Rhoads DD, Sintchenko V, Rauch CA, Pantanowitz L. Clinical microbiology informatics. *Clin Microbiol Rev*. 2014;**27**(4): 1025–1047.
8. Eyre DW1, Golubchik T, Gordon NC, et al. A pilot study of rapid benchtop sequencing of *Staphylococcus aureus* and *Clostridium difficile* for outbreak detection and surveillance. *BMJ Open*. 2012;**2**(3): e001124.
9. Gould CV, Edwards JR, Cohen J, et al. Effect of nucleic acid amplification testing on population-based incidence rates of *Clostridium difficile* infection. *Clin Infect Dis*. 2013;**57**(9): 1304–1307.
10. Koo HS, Kim JS, Eom JS, et al. Pseudooutbreak of *Pantoea* species bacteremia associated with contaminated cotton pledgets. *Am J Infect Control*. 2006;**34**(7): 443–446.
11. Herrmann M, Jungmann S, Halfmann A, et al. A pseudo-outbreak due to *Acinetobacter* species (GIM-1) contamination of the pneumatic transport system of a Large University Hospital. *Infect Control Hosp Epidemiol*. 2014;**35**(11): 1364–1372.
12. Blossom DB, Alelis KA, Chang DC, et al. Pseudo-outbreak of *Mycobacterium abscessus* infection caused by laboratory contamination. *Infect Control Hosp Epidemiol*. 2008;**29**(1): 57–62.
13. Thigpen, MC, Thomas DM, Gloss D, et al. Nursing home outbreak of invasive group a streptococcal infections caused by 2 distinct strains. *Infect Control Hosp Epidemiol*. 2007:**28**(1); 68–74.
14. Dooling KL, Crist MB, Nguyen DB, et al. Investigation of a prolonged Group A Streptococcal outbreak among residents of a skilled nursing facility, Georgia, 2009–2012. *Clin Infect Dis*. 2013;**57**(11): 1562–1567.
15. Centers for Disease Control and Prevention. Bacterial meningitis after intrapartum spinal anesthesia – New York and Ohio, 2008–2009. *MMWR Morb Mortal Wkly Rep*. 2010;**59**(3): 65–69.
16. Chitnis AS, Guh AY, Benowitz I et al. Outbreak of bacterial meningitis among patients undergoing myelography at an outpatient radiology clinic. *J Am Coll Radiol*. 2012;**9**(3): 185–190.
17. Centers for Disease Control and Prevention. Injection Safety. CDC Clinical Reminder: Spinal Injection Procedures Performed without a Facemask Pose Risk for Bacterial Meningitis. Available at: www.cdc.gov/injectionsafety/SpinalInjection-Meningitis.html. Accessed on September 14, 2015.
18. Gaspard P, Ambert-Balay K, Mosnier A, et al. Burden of gastroenteritis outbreaks: specific epidemiology in a cohort of institutions caring for dependent people. *J Hosp Infect*. 2015;**91**(1): 19–27.
19. Kambhampati A, Koopmans M, Lopman BA. Burden of norovirus in healthcare facilities and strategies for outbreak control. *J Hosp Infect*. 2015;**89** (4): 296–301.
20. Repp KK, Keene WE. A point-source norovirus outbreak caused by exposure to fomites. *J Infect Dis*. 2012;**205**(11): 1639–1641.
21. Chitnis AS, Caruthers PS, Rao AK, et al. Outbreak of carbapenem-resistant Enterobacteriaceae at a long-term acute care hospital: sustained reductions in transmission through active surveillance and targeted interventions. *Infect Control Hosp Epidemiol*. 2012;**33** (10): 984–992.
22. Munoz-Price LS, Quinn JP. Deconstructing the infection control bundles for the containment of carbapenem-resistant Enterobacteriaceae. *Curr Opin Infect Dis*. 2013;**26**(4): 378–387.
23. Maragakis LL, Cosgrove SE, Song X, et al. An outbreak of multidrug-resistant *Acinetobacter baumannii* associated with pulsatile lavage wound treatment. *JAMA*. 2004;**292**(24): 3006–3011.
24. Simor AE, Lee M, Vearncombe M, et al. An outbreak due to multiresistant *Acinetobacter baumannii* in a burn unit: risk factors for acquisition and management. *Infect Control Hosp Epidemiol*. 2002;**23**(5): 261–267.
25. Astagneau P, Desplaces N, Vincent V, et al. *Mycobacterium xenopi* spinal infections after discovertebral surgery: investigation and screening of a large outbreak. *Lancet*. 2001;**358**(9283): 747–751.
26. Chroneou A, Zimmerman SK, Cook S, et al. Molecular typing of *Mycobacterium chelonae* isolates from a pseudo-outbreak involving an automated bronchoscope washer. *Infect Control Hosp Epidemiol*. 2008;**29**(11): 1088–1090.
27. Williams MM, Armbruster CR, Arduino MJ. Plumbing of hospital premises is a reservoir for opportunistically pathogenic microorganisms: a review. *Biofouling*. 2013;**29**(2): 147–162.
28. Peterson AE, Chitnis AS, Xiang N, et al. Clonally related *Burkholderia contaminans* among ventilated patients without cystic fibrosis. *Am J Infect Control*. 2013;**41**(12): 1298–1300.
29. Kutty PK, Moody B, Gullion JS, et al. Multistate outbreak of *Burkholderia cenocepacia* colonization and infection associated with the use of intrinsically contaminated alcohol-free mouthwash. *Chest*. 2007;**132**(6): 1825–1831.
30. Nasser RM, Rahi AC, Haddad MF, Daoud Z, Irani-Hakime N, Almawi WY. Outbreak of *Burkholderia cepacia* bacteremia traced to contaminated hospital water used for dilution of an alcohol skin antiseptic. *Infect Control Hosp Epidemiol*. 2004;**25**(3): 231–239.
31. Edison LS, Dishman HO, Tobin-D'Angelo MJ, Allen CR, Guh AY, Drenzek CL. Endophthalmitis outbreak associated with repackaged bevacizumab. *Emerg Infect Dis*. 2015;**21**(1): 171–173.

32. Frost BA, Kainer MA. Safe preparation and administration of intravitreal bevacizumab injections. *N Engl J Med*. 2011;**365**(23): 2238.
33. Dobbs TE, Guh AY, Oakes P, et al. Outbreak of *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* bloodstream infections at an outpatient chemotherapy center. *Am J Infect Control*. 2014;**42**(7): 731–734.
34. Guh AY, Thompson ND, Schaefer MK, Patel PR, Perz JF. Patient notification for bloodborne pathogen testing due to unsafe injection practices in the US health care settings, 2001–2011. *Med Care*. 2012;**50**(9): 785–791.
35. Zheteyeva YA, Tosh P, Patel PR et al. Hepatitis B outbreak associated with a home health care agency serving multiple assisted living facilities in Texas, 2008–2010. *Am J Infect Control*. 2014;**42**(1): 77–81.
36. Centers for Disease Control and Prevention. Transmission of hepatitis B virus among persons undergoing blood glucose monitoring in long-term-care facilities – Mississippi, North Carolina, and Los Angeles County, California, 2003–2004. *MMWR Morb Mortal Wkly Rep*. 2005;**54**(9): 220–223.
37. Blossom D, Noble-Wang J, Su J, et al. Multistate outbreak of *Serratia marcescens* bloodstream infections caused by contamination of prefilled heparin and isotonic sodium chloride solution syringes. *Arch Intern Med*. 2009;**169**(18): 1705–1711.
38. See I, Nguyen DB, Chatterjee S, et al. Outbreak of *Tsukamurella* species bloodstream infection among patients at an oncology clinic, West Virginia, 2011–2012. *Infect Control Hosp Epidemiol*. 2014;**35**(3): 300–306.
39. Hellinger WC, Bacalis LP, Kay RS, et al. Health care–associated hepatitis C virus infections attributed to narcotic diversion. *Ann Intern Med*. 2012;**156**(7): 477–482.
40. Schaefer MK, Perz JF. Outbreaks of infections associated with drug diversion by US health care personnel. *Mayo Clin Proc*. 2014;**89**(7): 878–887.
41. Kainer MA, Linden JV, Whaley DN. Clostridium infections associated with musculoskeletal-tissue allografts. *N Eng J Med*. 2004;**350**(25): 2564–2571.
42. Iwamoto M, Jernigan DB, Guasch A. Transmission of West Nile virus from an organ donor to four transplant recipients. *N Eng J Med*. 2003;**348**(22): 2196–2203.
43. Fischer GE, Schaefer MK, Labus BJ, et al. Hepatitis C virus infections from unsafe injection practices at an endoscopy clinic in Las Vegas, Nevada, 2007–2008. *Clin Infect Dis*. 2010;**51**(3): 267–273.
44. Centers for Disease Control and Prevention. 2012 CRE Toolkit – Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE). Available at: www.cdc.gov/hai/pdfs/cre/CRE-guidance-508.pdf. Accessed on September 14, 2015.
45. Boyce JM, Havill NL, Havill HL, Mangione E, Dumigan DG, Moore BA. Comparison of fluorescent marker systems with 2 quantitative methods of assessing terminal cleaning practices. *Infect Control Hosp Epidemiol*. 2011;**32**(12): 1187–1193.
46. Carling PC, Briggs JL, Perkins J, Highlander D. Improved cleaning of patient rooms using a new targeting method. *Clin Infect Dis*. 2006;**42**(3): 385–388.
47. Luick L, Thompson PA, Loock MH, Vetter SL, Cook J, Guerrero DM. Diagnostic assessment of different environmental cleaning monitoring methods. *Am J Infect Control*. 2013;**41**(8): 751–752.
48. Boyce JM, Havill NL, Dumigan DG, Golebiewski M, Balogun O, Rizvani R. Monitoring the effectiveness of hospital cleaning practices by use of an adenosine triphosphate bioluminescence assay. *Infect Control Hosp Epidemiol*. 2009;**30**(7): 678–684.
49. Rotham KJ. Types of epidemiologic study. In: Rotham KJ, ed. *Modern Epidemiology*. Boston, MA: Little, Brown and Co, 1986.
50. Schlesselman JJ. *Case Control Studies*. New York, NY: Oxford University Press, 1982.
51. Azarian T, Cook RL, Johnson JA, et al. Whole-genome sequencing for outbreak investigations of methicillin-resistant *Staphylococcus aureus* in the neonatal intensive care unit: time for routine practice? *Infect Control Hosp Epidemiol*. 2015; **36**(7): 777–785.
52. Sails AD, Swaminathan B, Fields PI. Utility of multilocus sequence typing as an epidemiological tool for investigation of outbreaks of gastroenteritis caused by *Campylobacter jejuni*. *J Clin Microbiol*. 2003;**41**(10): 4733–4739.
53. Machado GE, Matsumoto CK, Chimara E, et al. Multilocus sequence typing scheme versus pulsed-field gel electrophoresis for typing *Mycobacterium abscessus* isolates. *J Clin Microbiol*. 2014;**52**(8): 2881–2891.
54. Tenover FC, Arbeit RD, Goerin RV, et al. Interpreting chromosomal DNA restriction patterns produced by pulsed-field gel electrophoresis: criteria for bacterial strain typing. *J Clin Microbiol*. 1995;**33**(9): 2233–2239.
55. Epson EE, Pisney Lm, Wendt JM, et al. Carbapenem-resistant *Klebsiella pneumoniae* producing New Delhi metallo-beta-lactamase at an acute care hospital, Colorado, 2012. *Infect Control Hosp Epidemiol*. 2014;**35**(4): 390–397.
56. Palmore TN, Henderson DK. Managing transmission of carbapenem-resistant Enterobacteriaceae in healthcare settings: a view from the trenches. *Clin Infect Dis*. 2013;**57**(11): 1593–1599.
57. Tenover FC, Goering RV. Methicillin-resistant *Staphylococcus aureus* strain USA300: origin and epidemiology. *J Antimicrob Chemoth*. 2009; **64**(3): 441–446.
58. Haill C, Fletcher S, Archer R, et al. Prolonged outbreak of methicillin-resistant *Staphylococcus aureus* in a cardiac surgery unit linked to a single colonized healthcare worker. *J Hosp Infect*. 2013;**83**(3): 219–225.
59. Bertin ML, Vinski J, Schmitt S, et al. Outbreak of methicillin-resistant *Staphylococcus aureus* colonization and infection in a neonatal intensive care unit epidemiologically linked to a healthcare worker with chronic otitis. *Infect Control Hosp Epidemiol*. 2006;**27**(6): 581–585.
60. Markogiannakis A, Fildisis G, Tsiplakou S, et al. Cross-transmission of multidrug-resistant *Acinetobacter baumannii* clonal strain causing episodes of sepsis in a trauma intensive care unit. *Infect Control Hosp Epidemiol*. 2008;**29**(5): 410–417.
61. Senok A, Garaween G, Raji A, Khubnani Harish, Sing GK, Shibl A. Genetic relatedness of clinical and environmental *Acinetobacter baumanii* isolates from an intensive care unit outbreak. *J Infect Ctries*. 2015;**9**(6): 665–669.
62. American Public Health Association. APHA Method 9215: standard methods for the examination of water and wastewater. *Code of Federal Regulations*. 1992;**40** CFR 141.121: 9000–9126. https://archive.org/details/gov.law.apha.method.9215.1992.
63. Calfee DP, Salgado CD, Milstone AM, et al. Strategies to prevent methicillin-resistant *Staphylococcus aureus* transmission and infection in acute care

hospitals: 2014 update. *Infect Control Hosp Epidemiol*. 2014;**35**(7): 772–796.

64. Warner AE, Schaefer MK, Patel PR, et al. Outbreak of hepatitis C virus infection associated with narcotics diversion by an hepatitis C virus–infected surgical technician. *Am J Infect Cont*. 2015; **43** (1): 53–58.
65. Macedo de Oliveira A, White KL, Leschinsky DP, et al. An outbreak of hepatitis C virus infections among outpatients at a hematology/oncology clinic. *Ann Intern Med*. 2005;**142**(11): 898–902.
66. Patel PR, Srinivasan A, Perz JF. Developing a broader approach to management of infection control breaches in health care settings. *Am J Infect Control*. 2008;**36**(10): 685–690.
67. Holodniy M, Oda G, Schirmer PL, et al. Results from a large-scale epidemiologic look-back investigation of improperly reprocessed endoscopy equipment. *Infect Control Hosp Epidemiol*. 2012 ;**33**(7): 649–656.
68. Associated Press. 456 colonoscopy patients at an Atlanta surgery center warned of infection risk. 1 May 2013. www.timesfreepress.com/news/local/story/2013/may/01/456-colonoscopy-patients-atlanta-surgery-center-wa/106828/.
69. Clark C. Hospital Sends Letters to 3,400 Patients About Possible Endoscopic Equipment Contamination. HealthLeaders Media. 16 June 2010. http://healthleadersmedia.com/content/QUA-252543/Hospital-Sends-Letters-to-3400-Patients-About-Possible-Endoscopic-Equipment-Contamination.
70. Harper J, DeVries A, Danila R, Lesher L. Reported Endoscope Reprocessing Breaches, Minnesota, 2010–2011 [Abstract]. In: APIC 39th Annual Educational Conference & International Meeting; 2012, June 4–6; San Antonio, TX. *Am J Infect Cont;* **40**(5): e112.
71. Basavaraju SV, Kuehnert MJ, Zaki SR, Sejvar JJ. Encephalitis caused by pathogens transmitted through organ transplants, United States, 2000–2013. *Emerg Infect Dis*. 2014;**20**(9): 1443–1451.
72. Edens C, Liebich L, Halpin AL, et al. Notes from the field: *Mycobacterium chelonae* eye infections associated with humidifier use in an outpatient LASIK clinic – Ohio, 2015. *Morbidity and Mortality Weekly Report*. 23 October 2015. **41**(41);1177.

Chapter 12

Urinary Tract Infection

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Urinary tract infection (UTI) is one of the most common types of healthcare-associated infection (HAI) reported to the National Healthcare Safety Network (NHSN).[1] Approximately 75 percent of these infections develop in patients with indwelling urinary catheters. Urinary catheters disrupt normal host defense mechanisms and allow for the formation of biofilm, thereby affecting the frequency of microbial colonization and the etiologic organisms found in catheter-associated UTI (CAUTI).[2] These factors have important implications for prevention and treatment of UTI in the catheterized patient.

Pathogenesis

The human urinary tract has multiple natural defense mechanisms that prevent attachment of potential pathogens to the uroepithelium, including the length of the urethra, micturition, and urine flow.[2] The urinary tract mucosa has antibacterial properties and secretes inhibitors of bacterial adhesion (e.g., Tamm-Horsfall proteins and bladder mucopolysaccharides) that prevent attachment of bacteria. Urine osmolality and pH inhibit growth of most organisms. The use of a urinary catheter interferes with these normal defenses and allows colonization and attachment of organisms.

The vast majority of organisms associated with CAUTI enter the bladder by ascending the urethra from the perineum.[3] Rarely, organisms such as *Staphylococcus aureus* cause upper tract infection through hematogenous spread. In the presence of a urinary catheter, organisms ascend into the bladder in one of two ways. First, organisms may enter through extraluminal migration in the mucous film surrounding the external aspect of the catheter. Organisms entering by this route are primarily endogenous organisms, originating from the rectum and colonizing the patient's perineum. Approximately 70 percent of episodes of bacteriuria among catheterized women are believed to involve an extraluminal route.[2] The second route of entry into the bladder is through intraluminal reflux or migration, which occurs when organisms gain access to the internal lumen of the catheter through failure of a closed drainage system.[2,3] Most of these organisms are exogenous and result from cross-transmission via the hands of healthcare personnel.

Tambyah and colleagues[3] performed a prospective study to determine the probable route by which organisms gained access to the catheterized bladder. Serial paired quantitative cultures of the specimen port and the collection bag were performed. Of 173 CAUTIs, 115 (66 percent) were thought to be acquired through extraluminal migration of organisms ascending from the perineum along the external surface of the catheter. A smaller proportion of infections (34 percent) was acquired from intraluminal contamination of the collection system.

While most UTIs due to Enterobacteriaceae are thought to originate from an endogenous source, organisms causing healthcare-associated UTI may be transmitted from one patient to another in an institution. An estimated 15 percent of episodes of healthcare-associated bacteriuria occur in clusters, often involving highly antibiotic-resistant organisms.[2,4] Most hospital-based outbreaks have been associated with lack of proper hand hygiene by healthcare personnel. Despite these occasional clusters, most cases of healthcare-associated UTI are associated with a patient's own endogenous organisms.

The formation of biofilm on the inner and outer surfaces of urinary catheters has important implications for prevention and treatment of CAUTI.[2] Adhesion of organisms to catheter materials is dependent on the hydrophobic nature of organisms and the catheter surface. Once organisms attach to the catheter and multiply, they secrete an extracellular matrix of glycocalyces. Organisms in the biofilm multiply more slowly than planktonic bacteria growing within the urine itself but can ascend the inner surface of the catheter in 1–3 days. Some organisms in the biofilm, such as *Proteus* species, *Pseudomonas aeruginosa, Klebsiella pneumoniae*, and *Providencia* species, have the ability to hydrolyze urea in the urine to free ammonia. The resulting increase in pH allows precipitation of minerals, such as hydroxyapatite or struvite, which then deposit in the catheter biofilm, causing mineral encrustations along the catheter. Encrustations are a feature of biofilms uniquely associated with urinary catheters.

Epidemiology

Descriptive Epidemiology

CAUTI accounts for approximately 12 percent of all healthcare-associated infections in acute care hospitals, but UTIs make up a smaller proportion of healthcare-associated infections in intensive care unit (ICU) patients.[5,6] The incidence of UTI varies by ICU type; rates of CAUTI reported to the NHSN in 2012 ranged from 1.2 infections per 1,000 catheter-days in small (<15 beds) medical-surgical ICUs to 5.0 infections per 1,000 catheter-days in neurosurgical ICUs.[6] CAUTI was reported at an incidence of 2.7 infections per 1,000 catheter-days in medical-surgical pediatric ICUs; rates for neonatal ICUs were not reported, but CAUTI has been identified

Table 12.1 Organisms associated with catheter-associated urinary tract infections (CAUTIs)

Organism	Percentage of CAUTIs
Escherichia coli	27.7
Klebsiella species	23.1
Enterococcus species	16.9
Pseudomonas aeruginosa	10.8
Candida species and unspecified yeast	10.8
Other Enterobacteriaceae (*Enterobacter* species, *Citrobacter* species, *Serratia* species)	7.7
Staphylococcus aureus	3.1
Stenotrophomonas maltophilia	3.1
Streptococcus species	3.1

Data are from Magill et al.[5]

infrequently in these units previously.[7] Rates of CAUTI in general care and chronic care units were equivalent to or higher than those in the ICU, ranging from 1.4 infections per 1,000 catheter-days in adult medical-surgical units to 4.8 infections per 1,000 catheter-days in chronic ventilator units.[6]

Microbial Etiology

Enterobacteriaceae are the pathogens most commonly associated with CAUTI hospital-wide (Table 12.1).[5] Other significant pathogens include enterococci, *P. aeruginosa*, and *Candida* species, although yeasts are excluded from the most recent NHSN definition for CAUTI as they rarely cause symptomatic infection.[5,8,9] Most infections (80 percent) associated with short-term indwelling urinary catheters are due to a single species of organism. Conversely, infections associated with long-term indwelling catheters are polymicrobial in 77 percent to 95 percent of cases. This pathogen distribution has not changed significantly from previous reports between 1986 and 2011.[5] However, organisms that cause CAUTI are increasingly resistant to antibiotics. Among *Escherichia coli* urinary isolates reported to NHSN between 2009 and 2010, 31 percent were resistant to fluoroquinolones, and 12 percent were resistant to extended-spectrum cephalosporins.[10] Among *Klebsiella* isolates, 27 percent were resistant to extended-spectrum cephalosporins, and 12.5 percent were resistant to carbapenems.

Risk Factors

Most studies on CAUTI have focused on bacteriuria, a precursor of symptomatic infection. The most important, consistently described risk factor for healthcare-associated bacteriuria is the duration of catheterization. Bacteriuria develops rapidly and frequently in catheterized patients, with an average risk of 3 percent to 10 percent per day.[2] Among patients with a urinary catheter in place for 2–10 days, 26 percent will develop bacteriuria. Nearly all patients catheterized for a month will have bacteriuria, making this duration the dividing line between short-term and long-term catheterization.

Females have a higher risk of catheter-associated bacteriuria than males (odds ratio [OR], 1.8–3.8).[11] Systemic antibiotic therapy at the time of urinary catheter insertion has a protective effect against the development of bacteriuria (OR, 1.8–3.9). Other risk factors identified in one or more studies include the following: older age, diabetes, serum creatinine level greater than 2 mg/dL, and nonsurgical disease. Nonadherence to catheter care recommendations has also been associated with increased risk of bacteriuria.

CAUTI is the leading cause of secondary healthcare-associated bloodstream infection (BSI). Although BSI occurs in only 1–4 percent of cases, approximately 20 percent of healthcare-associated BSIs arise from the urinary tract, and mortality rates among patients with urinary tract-related BSI may be as high as 33 percent.[12] In one study, risk factors for healthcare-associated urinary tract-related BSI included neutropenia (OR, 10.99), renal disease (OR, 2.96), and male sex (OR, 2.18). Receipt of insulin (OR, 4.82) or immunosuppressive medications (OR, 1.53) was associated with increased risk for BSI, and receipt of antibacterials (OR, 0.66) was protective.

Diagnosis and Surveillance

The terms "bacteriuria" and "urinary tract infection" are often used interchangeably in the published literature pertaining to healthcare-associated UTI and CAUTI. The distinction between them is important clinically because asymptomatic catheter-associated bacteriuria is rarely associated with adverse outcomes and generally does not require treatment with antibiotics.[9] Most studies of CAUTI use bacteriuria as the primary outcome. In general, bacteriuria in a catheterized patient is defined as growth in culture of 10^2 colony-forming units (cfu) or more of a predominant pathogen per milliliter of urine collected aseptically from a sampling port.[4]

The NHSN has developed surveillance definitions for healthcare-associated UTI that allow for standardization and interfacility comparison of infection rates.[8] The definitions distinguish between symptomatic UTI and asymptomatic bacteriuria. In order to meet criteria for a symptomatic UTI, an adult patient must have at least one sign or symptom (temperature >38°C, urinary urgency, urinary frequency, dysuria, suprapubic tenderness, or costovertebral angle pain or tenderness) and a positive urine culture ($\geq 10^5$ cfu/mL with no more than 2 species of organisms detected). Symptomatic UTI is considered to be catheter-associated if a urinary catheter has been in place for more than 2 days and at least one of the above signs or symptoms is present (with the exception of urgency, frequency, or dysuria if the catheter is still in place). Asymptomatic bacteriuria is defined as a positive urine culture ($\geq 10^5$ cfu/mL with no more than 2 species of organisms detected) in the absence of signs or symptoms. One change that was made with the most recent NHSN surveillance definitions is that yeasts are no longer considered urinary pathogens, and patients with urine cultures growing yeast only are not considered to have symptomatic UTI.

Clinical diagnosis of CAUTI is quite difficult. Pyuria is not a reliable indicator of UTI in a patient with a catheter in place. Musher and colleagues[13] found that most catheterized patients with bacteriuria had pyuria, but 30 percent of patients with pyuria did not have bacteriuria. Diagnosis of UTI in patients with long-term urinary catheters is particularly difficult, as bacteriuria is invariably present. Systemic symptoms of infection may be the only indications of UTI, especially in patients who have spinal cord injuries.[14]

Surveillance for CAUTI had not been a priority for most hospitals in the past, mostly because of lack of resources required to perform full hospital surveillance. However, in January 2012, most acute care facilities began reporting CAUTIs from adult and pediatric ICUs to the NHSN in order to meet the requirements of the Centers for Medicare and Medicaid Services (CMS) Inpatient Prospective Payment System final rule.[15] Beginning in January 2015, acute care hospitals were also required to report CAUTIs from adult and pediatric medical and surgical wards. CAUTI rates are publicly reported on the CMS Hospital Compare website.[16] Some states also have requirements for CAUTI reporting.

Surveillance for CAUTI should be performed using NHSN definitions, and data collection forms utilizing these standardized criteria are available from the NHSN. The incidence of CAUTI is typically expressed as the number of infections per 1,000 urinary catheter-days.[17] However, the use of device-days as a denominator may mask successful CAUTI prevention efforts, as an overall reduction in catheter use may paradoxically lead to higher CAUTI rates. Thus, the standardized infection ratio (SIR) may be a preferred performance measure. The SIR is a summary measure that is calculated by dividing the observed number of infections by the predicted number of infections. The predicted number of infections is based on infections reported to NHSN during a baseline period and is risk-adjusted based on patient care location and hospital characteristics. In addition to performing surveillance for CAUTI, hospitals may monitor compliance with process measures such as documentation of catheter insertion and removal dates and documentation of indication for catheter placement.

Prevention of CAUTI

General Strategies for Prevention

Compliance with hand hygiene before and after patient care is recommended for prevention of all healthcare-associated infections, including UTI.[18] The urinary tracts of hospitalized patients and patients in long-term care facilities represent a significant reservoir for multidrug-resistant organisms; hospital transmission of these organisms has been reported. Use of contact precautions with gowns and gloves is currently recommended as part of a multifaceted strategy to prevent transmission of multidrug-resistant organisms.[19] In addition, UTI has been found to be an important cause of antibiotic use in hospitalized patients.[20] Repeated antibiotic treatment for infections related to long-term urinary catheterization is an important risk factor for colonization with multidrug-resistant organisms, yet much of this use of antibiotics may be inappropriate. Reduction in use of broad-spectrum antibiotics is an important strategy to prevent development of antibiotic resistance associated with urinary catheters. Antibiotic stewardship programs should develop facility-specific clinical practice guidelines for treatment of UTIs.[21]

Table 12.2 Key strategies for prevention of catheter-associated urinary tract infection

Avoid use of indwelling urinary catheters
• Place only for appropriate indications
• Follow institutional protocols for placement, including perioperatively
• Use alternatives to indwelling catheterization (intermittent catheterization, condom catheter, or portable bladder ultrasound scanner)
Remove indwelling catheters early
• Use nurse-based interventions
• Use electronic reminders
Use proper techniques for insertion and maintenance of catheters
• Adhere to sterile insertion practices
• Use a closed drainage system
• Avoid routine bladder irrigation

Specific Strategies for Prevention

Multiple guidelines have been developed to outline strategies for the prevention of CAUTI.[17,22] Key strategies for prevention of CAUTI are summarized in Table 12.2.

Limitation of Use and Early Removal of Urinary Catheters

The most effective strategy for prevention of CAUTI is avoidance of urinary catheterization.[23] The incidence of urinary catheter placement for an inappropriate indication has been documented to be 21 percent to 50 percent.[24–26] Physician documentation of the indication for a urinary catheter has been reported to be present in less than 50 percent of cases.[27] Physicians are frequently unaware of the presence of urinary catheters in their patients, and this lack of awareness has been correlated with inappropriate catheter use.[28]

Indwelling urinary catheterization should be limited to certain indications (Table 12.3).[17,22] Catheters should not be inserted for convenience or for incontinence in the absence of another compelling indication. Each institution should develop written guidelines and explicit criteria for indwelling urinary catheterization based on these widely accepted indications, although modifications based on local needs may be appropriate. Regular education of medical and nursing staff regarding proper indications and supporting rationale should

Table 12.3 Appropriate indications for placement of a urinary catheter

Accurate monitoring of urine output in a critically ill patient
Acute anatomical or functional urinary retention or obstruction
Perioperative use for selected surgical procedures
• For surgical procedures of anticipated long duration
• For urologic procedures
• For procedures in patients with urinary incontinence
• For procedures requiring intraoperative urinary monitoring or expected large volume of intravenous infusions
Urinary incontinence in patients with open perineal or sacral wounds
Improved comfort for end-of-life care, if desired

be undertaken. If appropriate criteria for catheter placement are not met, nursing staff should be encouraged to discuss alternatives with the ordering physician. Physician orders should be required prior to any catheter insertion, and institutions should implement a system for documenting placement of catheters. Interventions for limiting urinary catheter use should be targeted at hospital locations where initial placement often occurs, such as emergency departments and operating rooms.

A number of nurse-driven interventions have demonstrated promising effectiveness in reducing the duration of catheterization. A nurse-based reminder to physicians to remove unnecessary urinary catheters in an adult ICU in a Taiwanese hospital resulted in a reduction in the incidence of CAUTI from 11.5 to 8.3 cases per 1,000 catheter-days.[29] Nurse-initiated reminders to physicians of the presence of urinary catheters also decrease the number of catheter-days.[30,31] Such interventions are relatively easy to implement and may consist of either a written or electronic notice or verbal contact with the physician regarding the presence of a urinary catheter and alternative options.

The advent of electronic medical records and computerized physician order entry systems allow targeted interventions both to reduce the number of catheters placed and to reduce the duration of catheterization. Cornia and colleagues[32] found that use of a computerized reminder reduced the duration of catheterization by 3 days. In some settings, an infection prevention specialist may have the capability of working with the information technology department to integrate catheter protocols into electronic physician order entry sets.

Perioperative Management of Urinary Retention

Specific protocols for the management of perioperative urinary retention may be beneficial. Although only a limited number of prospective studies have addressed optimal postoperative bladder management strategies, indwelling urinary catheterization following surgery has become ubiquitous in some centers. In one large cohort study, the authors demonstrated that 85 percent of patients admitted for major surgical procedures had perioperative indwelling catheters, and the half of these patients with duration of catheterization greater than 2 days were significantly more likely to develop UTI and less likely to be discharged to home.[33] Older surgical patients in particular are at risk for prolonged catheterization. In another study, 23 percent of surgical patients older than 65 years of age were discharged to skilled nursing facilities with an indwelling catheter in place, and these patients were substantially more likely to be rehospitalized or die within 30 days.[34]

In a large prospective clinical trial involving orthopedic patients, incorporation of a multifaceted protocol for perioperative catheter management resulted in a two-thirds reduction in the incidence of UTI.[35] The intervention consisted of limiting catheterization to patients who underwent surgery with a duration of more than 5 hours or who underwent total hip or knee replacement if the patient met one of several conditions. Urinary catheters were removed on postoperative day 1 after total knee arthroplasty and on postoperative day 2 after total hip arthroplasty. Although this protocol was effective at this particular hospital, each institution should develop protocols written by a local, multidisciplinary group.

Alternatives to Indwelling Urinary Catheters

Intermittent urinary catheterization may reduce the risk of UTI compared with indwelling urinary catheterization. In particular, patients with neurogenic bladder and long-term urinary catheters may benefit from intermittent catheterization. One meta-analysis demonstrated reduced risk of asymptomatic bacteriuria and symptomatic UTI in postoperative patients following hip or knee surgery with intermittent catheterization compared with indwelling catheterization (relative risk, 2.90) but included only 2 studies with a total of 194 patients.[36] Several studies of intermittent catheterization in postoperative patients have demonstrated increased risk of urinary retention and bladder distention.[37,38] Incorporating use of a portable bladder ultrasound scanner with intermittent catheterization may attenuate this risk.[39,40]

External catheters, or condom catheters, should be considered as an alternative to indwelling catheters in appropriately selected male patients without urinary retention or bladder outlet obstruction. A randomized trial demonstrated a decrease in the composite outcome of bacteriuria, symptomatic UTI, and death in patients with condom catheters compared with patients with indwelling catheters, although the benefit was limited to those men without dementia.[41] Condom catheters may also be more comfortable than indwelling catheters.[42]

Proper Techniques for Insertion and Maintenance of Urinary Catheters

Once a decision has been made to proceed with urinary catheterization, proper catheter insertion and maintenance are essential for prevention of CAUTI. Urinary catheters should be inserted using sterile equipment and aseptic technique by

a trained healthcare practitioner.[17,22] Cleaning of the meatal area should be undertaken prior to catheter insertion, but there is currently no consensus regarding the use of sterile water, compared with use of an antiseptic preparation. A randomized study comparing sterile water with 0.1 percent chlorhexidine for cleaning of the meatal area prior to insertion demonstrated no difference in the development of bacteriuria.[44] Ongoing catheter maintenance with daily meatal cleaning using an antiseptic has also not shown clear benefit, and it may actually increase rates of bacteriuria compared with routine care with soap and water.[45,46] A single-use packet of sterile lubricant jelly should be used for insertion to reduce urethral trauma, but it does not need to possess antiseptic properties.[22] Urinary catheters should not be routinely exchanged, except for mechanical reasons, because any reduction in the rate of bacteriuria with routine changing is generally only transient.[47]

Use of closed urinary catheter systems with sealed catheter-tubing junctions reduces the risk of CAUTI.[17,22] Breaches of the closed system should be avoided, and urine should be sampled only from a port after cleaning with an antiseptic solution or from the drainage bag using sterile technique if a large sample is required. Breach of the closed system to instill antibiotics is associated with increased rates of infection, and irrigation of the bladder with antibiotics can cause the organisms colonizing the catheter biofilm to flow into the bladder.[48]

Anti-Infective Catheters

Use of antiseptic and antibiotic-impregnated urinary catheters may have an impact on the rates of catheter-associated bacteriuria.[49] Antiseptic catheters currently available are coated with silver alloy. Earlier catheters coated with silver oxide lacked efficacy compared with silver alloy–coated catheters and are no longer available. Other antibiotic-impregnated catheters have utilized various types of antibiotics, including nitrofurazone, minocycline, and rifampin.

In a large meta-analysis, use of silver alloy–coated catheters significantly reduced the incidence of asymptomatic bacteriuria (RR, 0.54) among adult patients catheterized for less than 7 days compared with use of latex catheters.[49] Among patients catheterized for more than 7 days, a reduction in asymptomatic bacteriuria was less pronounced (RR, 0.64). In the same meta-analysis, antibiotic-impregnated catheters were compared with standard catheters and were found to decrease the rate of asymptomatic bacteriuria (RR, 0.52) for duration of catheterization less than 7 days but demonstrated no benefit for duration of catheterization of more than 7 days. Another meta-analysis demonstrated similar reductions in asymptomatic bacteriuria in patients with short-term catheterization.[50] There are few trials assessing antiseptic- and antibiotic-coated catheters in patients with long-term urinary catheterization, and no conclusions can be drawn regarding such patients.[51]

Use of anti-infective urinary catheters appears to be one option to reduce the incidence of bacteriuria in patients with short-term urinary catheterization (for less than 7 days), but the effect on the more important outcomes of symptomatic CAUTI and urinary catheter-associated bloodstream infection are not clear from the current literature. The current consensus is that anti-infective urinary catheters should not be used routinely to prevent CAUTI.[17]

Summary

UTI remains one of the most common types of healthcare-associated infection, and attention to these infections has increased in recent years due to public reporting and financial consequences for healthcare facilities. Because urinary catheters account for the majority of healthcare-associated UTIs, the most important interventions are directed at avoiding placement of urinary catheters and promoting early removal when appropriate. Alternatives to use of indwelling catheters, such as intermittent catheterization and use of condom catheters, should be considered. If indwelling catheterization is appropriate, use of proper aseptic practices for catheter insertion and maintenance and use of closed urinary-catheter collection systems are essential for prevention of CAUTI.

References

1. Centers for Disease Control and Prevention. Catheter-associated Urinary Tract Infections (CAUTI). www.cdc.gov/HAI/ca_uti/uti.html. Accessed October 1, 2015.
2. Saint S, Chenoweth CE. Biofilms and catheter-associated urinary tract infections. *Infect Dis Clin North Am* 2003;**17**: 411–432.
3. Tambyah PA, Halvorson KT, Maki DG. A prospective study of pathogenesis of catheter-associated urinary tract infections. *Mayo Clin Proc* 1999;**74**: 131–136.
4. Maki DG, Tambyah PA. Engineering out the risk of infection with urinary catheters. *Emerging Infect Dis* 2001;7(2): 1–6.
5. Magill SS, Edwards JR, Bamberg W, et al. Multistate point-prevalence survey of healthcare-associated infections, 2011. *N Engl J Med* 2014;**370**: 1198–1208.
6. Dudeck MA, Weiner LM, Allen-Bridson K, et al. National Healthcare Safety Network (NHSN) report, data summary for 2012, device-associated module. *Am J Infect Control* 2013;**41**: 1148–1166.
7. Langley JM, Hanakowski M, LeBlanc JC. Unique epidemiology of nosocomial urinary tract infection in children. *Am J Infect Control* 2001;**29**: 94–98.
8. Centers for Disease Control and Prevention. Urinary tract infection (catheter-associated urinary tract infection [CAUTI] and non-catheter-associated urinary tract infection [UTI]) and other urinary tract system (USI) events. Available at: www.cdc.gov/nhsn/PDFs/pscManual/7pscCAUTIcurrent.pdf. Accessed February 1, 2016.
9. Tambyah PA, Maki DG. Catheter-associated urinary tract infection is rarely symptomatic: a prospective study of 1,497 catheterized patients. *Arch Intern Med* 2000;**160**(5): 678–682.
10. Sievert DM, Ricks P, Edwards JR, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009–2010. *Infect Control Hosp Epidemiol* 2013;**34**(1): 1–14.

11. Platt R, Polk BF, Murdock B, Rosner B. Risk factors for nosocomial urinary tract infection. *Am J Epidemiol* 1986;**124**(6): 977.
12. Greene MT, Chang R, Kuhn L, et al. Predictors of hospital-acquired urinary tract-related bloodstream infection. *Infect Control Hosp Epidemiol* 2012;**33** (10): 1001–1007.
13. Musher DM, Thorsteinsson SB, Airola VW II. Quantitative urinalysis: diagnosing urinary tract infection in men. *JAMA* 1976;**236**: 2069–2072.
14. Biering-Sorenson F, Bagi P, Hoiby N. Urinary tract infections in patients with spinal cord lesions: treatment and prevention. *Drugs* 2001;**61**(9): 1275–1287.
15. Centers for Disease Control and Prevention. Healthcare facility HAI reporting requirements to CMS via NHSN – current or proposed requirements. Available at: www.cdc .gov/nhsn/pdfs/cms/cms-reporting -requirements.pdf. Accessed October 1, 2015.
16. Centers for Medicare and Medicaid Services. Hospital compare. Available at: www.medicare.gov/hospitalcompare/search.html. Accessed October 1, 2015.
17. Lo E, Nicolle LE, Coffin SE, et al. Strategies to prevent catheter-associated urinary tract infection in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014;**35**(S2): S32–S47.
18. Boyce JM, Pittet D. Guideline for hand hygiene in health-care settings: recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/ APIC/IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. *MMWR Recomm Rep* 2002;**51**(RR-16): 1–45.
19. Siegel JD, Rhinehart E, Jackson M, Chiarello L. 2007 Guideline for isolation precautions: preventing transmission of infectious agents in health care settings. *Am J Infect Control* 2007;**35**(10 Suppl 2):S65–S164.
20. Gandhi T, Flanders SA, Markovitz E, Saint S, Kaul DR. Importance of urinary tract infection to antibiotic use among hospitalized patients. *Infect Control Hosp Epidemiol* 2009;**30**(2): 193–195.
21. Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* 2016;**62**(10): e51–e77.
22. Gould CV, Umscheid CA, Agarwal RK, Kuntz G, Pegues DA, HICPAC. Centers for Disease Control and Prevention. Guideline for prevention of catheter-associated urinary tract infections (draft). 2008. Available at: wwwn.cdc .gov/PUBLICCOMMENTS/com ments/guidelines-for-prevention-of -catheter-associated-urinary-tract -infections-2008.aspx. Accessed August 30, 2009.
23. Nicolle LE. The prevention of hospital-acquired urinary tract infection. *Clin Infect Dis* 2008;**46**(2): 251–253.
24. Gardam MA, Amihod B, Orenstein P, Consolacion N, Miller MA. Overutilization of indwelling urinary catheters and **t**he development of nosocomial urinary tract infections. *Clin Perform Qual Health Care* 1998;**6** (3): 99–102.
25. Jain P, Parada JP, David A, Smith LG. Overuse of the indwelling urinary tract catheter in hospitalized medical patients. *Arch Intern Med* 1995;**155**(13): 1425–1429.
26. Munasinghe RL, Yazdani H, Siddique M, Hafeez W. Appropriateness of use of indwelling urinary catheters in patients admitted to the medical service. *Infect Control Hosp Epidemiol* 2001;**22**(10): 647–649.
27. Conybeare A, Pathak S, Imam I. The quality of hospital records of urethral catheterisation. *Ann R Coll Surg Engl* 2002;**84**(2): 109–110.
28. Saint S, Wiese J, Amory JK, et al. Are physicians aware of which of their patients have indwelling catheters? *Am J Med* 2000;**109**: 476–480.
29. Huang WC, Wann SR, Lin SL, et al. Catheter-associated urinary tract infections in intensive care units can be reduced by prompting physicians to remove unnecessary catheters. *Infect Control Hosp Epidemiol* 2004;**25**(11): 974–978.
30. Fakih MG, Dueweke C, Meisner S, et al. Effect of nurse-led multidisciplinary rounds on reducing the unnecessary use of urinary catheterization in hospitalized patients. *Infect Control Hosp Epidemiol* 2008;**29**(9): 815–819.
31. Saint S, Kaufman SR, Thompson M, Rogers MA, Chenoweth CE. A reminder reduces urinary catheterization in hospitalized patients. *Jt Comm J Qual Patient Saf* 2005;**31**(8): 455–462.
32. Cornia PB, Amory JK, Fraser S, Saint S, Lipsky BA. Computer-based order entry decreases duration of indwelling urinary catheterization in hospitalized patients. *Am J Med* 2003;**114**(5): 404–407.
33. Wald HL, Ma A, Bratzler DW, Kramer AM. Indwelling urinary catheter use in the postoperative period: analysis of the national surgical infection prevention project data. *Arch Surg* 2008;**143**(6): 551–557.
34. Wald HL, Epstein AM, Radcliff TA, Kramer AM. Extended use of urinary catheters in older surgical patients: a patient safety problem? *Infect Control Hosp Epidemiol* 2008;**29**(2): 116–124.
35. Stephan F, Sax H, Wachsmuth M, Hoffmeyer P, Clergue F, Pittet D. Reduction of urinary tract infection and antibiotic use after surgery: a controlled, prospective, before-after intervention study. *Clin Infect Dis* 2006;**42**(11): 1544–1551.
36. Niel-Weise BS, van den Broek PJ. Urinary catheter policies for short-term bladder drainage in adults. *Cochrane Database Syst Rev* 2005(3): CD004203.
37. Michelson JD, Lotke PA, Steinberg ME. Urinary-bladder management after total joint-replacement surgery. *N Engl J Med* 1988;**319**(6): 321–326.
38. Oishi CS, Williams VJ, Hanson PB, Schneider JE, Colwell CW Jr, Walker RH. Perioperative bladder management after primary total hip arthroplasty. *J Arthroplasty* 1995;**10**(6): 732–736.
39. Moore DA, Edwards K. Using a portable bladder scan to reduce the incidence of nosocomial urinary tract infections. *Medsurg Nurs* 1997;**6**(1): 39–43.
40. Stevens E. Bladder ultrasound: avoiding unnecessary catheterizations. *Medsurg Nurs* 2005;**14**(4): 249–253.
41. Saint S, Kaufman SR, Rogers MA, Baker PD, Ossenkop K, Lipsky BA. Condom versus indwelling urinary catheters: a randomized trial. *J Am Geriatr Soc* 2006;**54**(7): 1055–1061.
42. Saint S, Lipsky BA, Baker PD, McDonald LL, Ossenkop K. Urinary catheters: what type do men and their nurses prefer? *J Am Geriatr Soc* 1999;**47** (12): 1453–1457.
43. Guidelines for preventing infections associated with the insertion and management of short term indwelling urethral catheters in acute care. *J Hosp Infect* 2001;**47**(Suppl): S39–S46.

44. Webster J, Hood RH, Burridge CA, Doidge ML, Phillips KM, George N. Water or antiseptic for periurethral cleaning before urinary catheterization: a randomized controlled trial. *Am J Infect Control* 2001;**29**(6): 389–394.

45. Burke JP, Garibaldi RA, Britt MR, Jacobson JA, Conti M, Alling DW. Prevention of catheter-associated urinary tract infections: efficacy of daily meatal care regimens. *Am J Med* 1981;**70**(3): 655–658.

46. Saint S, Lipsky BA. Preventing catheter-related bacteriuria: should we? Can we? How? *Arch Intern Med* 1999;**159**(8): 800–808.

47. Tenney JH, Warren JW. Bacteriuria in women with long-term catheters: paired comparison of indwelling and replacement catheters. *J Infect Dis* 1988;**157**(1): 199–202.

48. Warren JW, Platt R, Thomas RJ, Rosner B, Kass EH. Antibiotic irrigation and catheter-associated urinary-tract infections. *N Engl J Med* 1978;**299**(11): 570–573.

49. Saint S, Elmore J, Sullivan S, Emerson S, Koepsell T. The efficacy of silver alloy-coated urinary catheters in preventing urinary tract infection: a meta-analysis. *Am J Med* 1998;**105**: 236–241.

50. Johnson JR, Kuskowski MA, Wilt TJ. Systematic review: antimicrobial urinary catheters to prevent catheter-associated urinary tract infection in hospitalized patients. *Ann Intern Med* 2006;**144**(2): 116–126.

51. Jahn P, Preuss M, Kernig A, Langer G, Seifert-Huehmer A. Types of indwelling urinary catheters for long-term bladder drainage in adults. *Cochrane Database Syst Rev* 2007(3): CD004997.

Chapter 13

Ventilator-Associated Events

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Introduction

The U.S. Centers for Disease Control and Prevention (CDC) introduced a new paradigm for safety surveillance in ventilated patients in early 2013. The new paradigm, called "ventilator-associated events" (VAE), was designed to overcome many of the limitations associated with traditional ventilator-associated pneumonia (VAP) surveillance.[1] VAE definitions shift the focus of surveillance from pneumonia alone to complications of mechanical ventilation in general. The proposed advantages of this shift include broadening the focus of prevention to encompass multiple potential causes of deterioration in ventilated patients and facilitating objective surveillance definitions amenable to automation.[2]

The shift from VAP to VAE introduced new challenges for infection prevention and control programs. The concept is still new to both infection preventionists and critical care physicians. Many practitioners do not have an intuitive feel for VAEs as a clinical entity and hence find it difficult to interpret VAE rates or to suggest interventions to prevent VAEs. In addition, VAE surveillance and prevention compels hospital epidemiologists and infection preventionists to contend with new data sources (e.g., ventilator settings) and new care processes (e.g., ventilator and sedation management) that have not been part of the traditional purview of infection prevention and control programs. As such, the shift from VAP to VAE surveillance asks practitioners to do more than simply learn a new set of definitions. VAE surveillance invites practitioners to consider new partnerships with critical care colleagues to collectively find new ways to improve the total care of ventilated patients, not just prevent pneumonia.

In this chapter we will review CDC's rationale for switching from VAP to VAE surveillance, key points of VAE epidemiology, and emerging approaches to surveillance and prevention.

Limitations of Traditional VAP Surveillance Definitions

Limitations of traditional VAP definitions include their complexity, subjectivity, lack of specificity, limited capacity for automation, and inconsistent associations with adverse outcomes.[3–7] These limitations were particularly concerning to hospitals and quality improvement advocates when some payors and regulators started to propose using VAP rates for public reporting, hospital benchmarking, and pay-for-performance initiatives.[8,9] Investigators documented very high rates of interobserver variability in VAP classifications amongt infection preventionists both within and between hospitals, calling into question whether VAP rates in one hospital were at all comparable to VAP rates in another hospital.[3–5] Furthermore, the subjectivity of traditional VAP criteria (e.g., "increase in secretions," "worsening oxygenation," "new or progressive infiltrate," etc.) allowed for the possibility that VAP rates could decrease over time simply by interpreting subjective criteria more strictly.[10]

Many institutions noted a growing discrepancy between surveillance and clinical VAP rates. Observers speculated that this might have been because of the rising levels of attention being paid to VAP by regulators, payors, and quality improvement advocates, leading infection preventionists to consciously or subconsciously apply VAP criteria more and more strictly, which in turn led to fewer and fewer perceived cases.[10,11] Indeed, multiple institutions reported surveillance VAP rates as much as an order of magnitude lower than their concurrent clinical rates of VAP diagnosis and treatment.[12–14] The median VAP rate in nonteaching medical ICUs participating in the National Healthcare Safety Network (NHSN) in 2012 was zero. These numbers stirred disbelief and distrust in clinicians since they were at odds with clinical diagnosis and treatment rates for VAP, which remained high.[15–17]

Finally, the infection prevention community noted the paucity of VAP prevention initiatives associated with improvements in patient-centered outcomes such as length-of-stay or mortality.[18–20] These observations raised the question whether focusing on VAP prevention per se was the best strategy to catalyze better outcomes for all mechanically ventilated patients. Interventions designed to decrease duration of mechanical ventilation, prevent delirium, minimize fluid overload, and prevent ARDS might ultimately be more impactful ways to improve outcomes for ventilated populations.[21]

VAE Definitions

VAE definitions were designed to overcome many of the perceived limitations of traditional VAP definitions. VAE surveillance is predicated upon identifying patients who have a trajectory change in their respiratory status as marked by new and sustained increases in their levels of ventilator support. The advantages of this approach are twofold: 1) it expands the focus of surveillance and hence prevention to encompass a broad array of potential sources of harm in ventilated patients, not just pneumonia; and 2) it allows for an objective, quantitative surveillance definition based solely on identifying patients with sustained increases in their

ventilator settings above specified thresholds. The disadvantage of this approach is that VAEs are not associated with a single, consistent clinical diagnosis and hence the interpretation of VAE rates can be opaque to both clinicians and infection preventionists.

Two ventilator settings in particular are used to measure the level of ventilator support for the purposes of VAE surveillance: the daily minimum positive end expiratory pressure (PEEP) and the daily minimum fraction of inspired oxygen (FiO_2). Daily minimum values are used for both these parameters in order to capture patients' "best" values of the day and to prevent VAEs from being triggered by transient disturbances in respiratory function due to mucous plugging, position changes, or procedures.

The technical definition of a VAE is as follows:

- ≥2 days of stable or decreasing daily minimum PEEP values followed by ≥2 days of daily minimum PEEP ≥3 cm H_2O higher than each of the two baseline days *or*
- ≥2 days of stable or decreasing daily minimum FiO_2 values followed by ≥2 days of daily minimum FiO_2 ≥20 percent points higher than each of the two baseline days

Once a VAE has been detected, there are additional criteria that one can use to classify a VAE as an infection-related ventilator-associated complication (IVAC) and/or a possible ventilator-associated pneumonia (PVAP). IVAC is defined as a patient with VAE who has concurrent signs of possible infection, namely an abnormal temperature or white blood cell count and at least four days of new antibiotics. These signs need to be present within 2 days before or after the first day of increased ventilator settings that triggered a VAE, excluding the first two days on the ventilator. PVAP is defined as a patient with IVAC who has concurrent evidence of a possible respiratory infection, namely a bronchoalveolar lavage or endotracheal aspirate with quantitative or semiquantitative growth of a potentially pathogenic organism above specified thresholds, or ≥25 neutrophils per low power field along with any amount of growth of a potentially pathogenic organism. PVAP can also be triggered by positive tests for respiratory viruses, *Legionella* spp., positive pleural fluid cultures, or histological evidence of pneumonia.

Epidemiology

Incidence

The incidence of VAE varies by hospital and by intensive care unit (ICU) type. As of this writing, CDC has not published national benchmarks for VAE rates, but a number of institutions from around the world have published their local rates. VAE incidence rates range from 5–10 events per 100 episodes of mechanical ventilation or 5–15 events per 1000 ventilator-days.[22–25] Rates tend to be higher in medical, surgical, and thoracic ICUs (8–10 events per 100 episodes of mechanical ventilation or 12–16 events per 1000 ventilator-days) and lower in cardiac surgery units (1 event per 100 episodes or 6 events per 1000 ventilator-days).[26] VAE rates have tended to be higher than traditionally-defined VAP rates among units that have conducted concurrent surveillance using both definitions.[22–25] Most VAEs occur within the first two weeks of mechanical ventilation; the risk thereafter diminishes but never disappears.[26] About 30 percent to 45 percent of VAEs qualify as IVACs; the proportion appears to vary by ICU type.[26]

Table 13.1 Attributable mortality of ventilator-associated events (VAE) versus ventilator-associated pneumonia (VAP)

Study	Measure of Effect	VAE	VAP
Klompas et al. 2011	Odds ratio (95% CI)	2.0 (1.3–3.2)	1.1 (0.5–2.4)
Klompas et al. 2012	Odds ratio (95% CI)	1.9 (1.5–2.3)	–
Hayashi et al. 2013	Hazard ratio (95% CI)	0.9 (0.6–1.4)	–
Muscedere et al. 2013	Hazard ratio (95% CI)	2.1 (1.6–2.8)	1.5 (1.1–2.1)
Klein Klouwenberg et al. 2014	Subdistribution hazard ratio (95% CI)	3.9 (2.9–5.3)	7.2 (5.1–10.3)
Klompas et al. 2014	Odds ratio (95% CI)	2.0 (1.6–2.4)	–
Lilly et al. 2014	Odds ratio (95% CI)	1.8 (1.0–3.6)	1.0 (0.6–1.7)
Stevens et al. 2014	Odds ratio (95% CI)	1.9 (1.5–2.4)	–

Adapted from reference number.[53]

Attributable Morbidity and Mortality

Most studies have found that patients with VAEs are approximately twice as likely to die compared to similar patients without VAEs (Table 13.1).[22–24,26–30] VAEs also appear to extend duration of mechanical ventilation, ICU length-of-stay, and hospital lengths-of-stay.[26,28,31] Four studies have directly compared the attributable mortality of VAE and traditionally-defined VAP within common populations. Three of the four studies reported higher attributable mortality rates for VAEs compared to VAP.[23,27,29] The fourth study found the reverse.[22] VAEs in general and IVACs in particular have also been found to correlate closely with antimicrobial utilization.[30,31]

Surveillance Strategies

VAE definitions were intentionally designed to allow for the possibility of automated surveillance using electronic clinical data. A number of facilities have now reported successful implementation of automated VAE surveillance systems.[22,24,32,33] These implementations have been associated with substantial

time-savings and superior case detection compared to manual surveillance by infection preventionists.[32,33] Indeed, manual surveillance may be error prone and insensitive compared to automated surveillance. Mann and colleagues, for example, compared manual VAE detection by three different individuals to automated detection using an algorithm.[33] The three manual surveyors all identified different numbers of VAE cases, and all missed cases accurately identified by the automated algorithm.

Automated VAE detection need not be an all-or-nothing operation. Daily minimum PEEP and FiO_2 settings alone are all that are needed to detect ventilator-associated conditions (VACs), the first tier of the VAE definition set. If a hospital infection prevention program can access these data electronically and automate VAC detection, this can be a great boon to efficiency since IVAC and PVAP are subsets of VAC (i.e., only patients with VACs can possibly meet IVAC and PVAP criteria). Only 5–10 percent of ventilated patients tend to trigger VAC criteria, hence automated screening for VAC can effectively eliminate the vast majority of ventilated patients from further consideration for IVAC and PVAP. This can make the additional work required to gather data for IVAC and PVAP evaluations considerably more tolerable, even if it has to be done manually, since it need only be done for a very small number of patients.

Likewise, hospitals that are unable to obtain ventilator settings electronically can consider partnering with nursing and/or respiratory therapy colleagues to collect these data manually on their behalf. Partnering with these departments makes sense both in terms of surveillance efficiency and in terms of team building when it comes to implementing strategies to prevent VAEs. Colleagues from these departments might view requests to participate in data collection more favorably if they can believe it will ultimately contribute to their ongoing efforts to improve the care that they provide and outcomes for their patients. Moreover, the request is small – literally two pieces of data per patient per day (daily minimum PEEP and daily minimum FiO_2). Once these data are in hand, they should be arrayed into a line list organized by patient with one row per patient per day. Organizing the data in this fashion can simplify VAE detection since one need only run one's eye down the list of daily minimum PEEPs and daily minimum FiO_2s to identify patients with ≥2 days of stable or decreasing settings followed by ≥2 days of higher settings.

Of note, CDC has developed electronic tools to assist facilities with VAE detection.[34] The first tool is an online VAE calculator. Infection preventionists can use the calculator to enter data about a case and then receive an annotated explanation of whether and why the patient does or does not meet VAE criteria. This is useful both as a reference and teaching tool for infection preventionists working to familiarize themselves with VAE surveillance. The limitation of the online calculator, however, is that it can only be used for one patient at a time. CDC is therefore developing two additional tools. One is a synthetic data set for a hypothetical population of ventilated patients. Software developers can use this dataset as a foil for creating electronic algorithms and as a validation tool once they have developed candidate code for VAE detection. The second is a web-service that hospitals or EHR vendors can use to automate VAE detection. Participants upload a de-identified data set with daily ventilator settings, temperatures, white blood cell counts, and antibiotic exposures from an entire population of patients. The web service then analyzes these data, identifies patients with VAEs, and returns details about these VAEs to the submitter.

VAE in Children and Neonates

As of this writing, VAE definitions are only intended for use with adults. CDC has convened a working group of stakeholders, however, to explore whether and how to adapt VAE definitions for children and neonates. In the interim, researchers at Texas Children's Hospital went ahead and applied adult VAE definitions to patients in their pediatric intensive care unit.[35] They found that 14.5 percent of ventilated children in their unit met criteria for VAC and 8.1 percent for IVAC. As in adults, VACs were associated with longer ventilator time, ICU, and hospital stays as well as significantly higher mortality rates. Risk factors for VACs included immunocompromised state, tracheostomy dependence, and chronic respiratory disease. Most VACs were attributable to pneumonias, atelectasis, pulmonary edema, and shock.

Other pediatric specialists have proposed modifications to adult VAE criteria to make them more suitable for younger populations, particularly neonates. A multicenter collaborative proposed substituting surveillance for increases in daily minimum PEEP with surveillance for increases in daily minimum mean airway pressure (MAP) of ≥4 cm H_2O.[36] They also proposed increasing the threshold for significant changes in FiO_2 from 20 points to 25 points. They reasoned that MAP is a better reflection of pulmonary function than PEEP and that some modes of mechanical ventilation frequently used in neonates (such as high frequency oscillatory ventilation) only include MAPs, not PEEPs. In an exploratory regression analysis using retrospective data from five US hospitals, they affirmed that this variant definition remained significantly associated with increased mortality compared to matched controls.

VAE Prevention

VAE definitions were purposefully created to broaden the scope of surveillance beyond pneumonia to encompass additional morbid complications of mechanical ventilation. VAE prevention is therefore necessarily broader than VAP prevention alone. In addition, a number of investigations over the past few years have raised questions about what constitutes best practices to prevent VAP. The switch from VAP to VAE definitions invites quality improvement advocates to re-evaluate and redesign traditional ventilator bundles to better reflect current understanding of best practices for ventilated patients.

Indeed, some components of traditional ventilator bundles may be harmful for ventilated patients. For example, stress ulcer prophylaxis may increase pneumonia risk.[37] Oral care with chlorhexidine may increase mortality risk.[38,39] Other

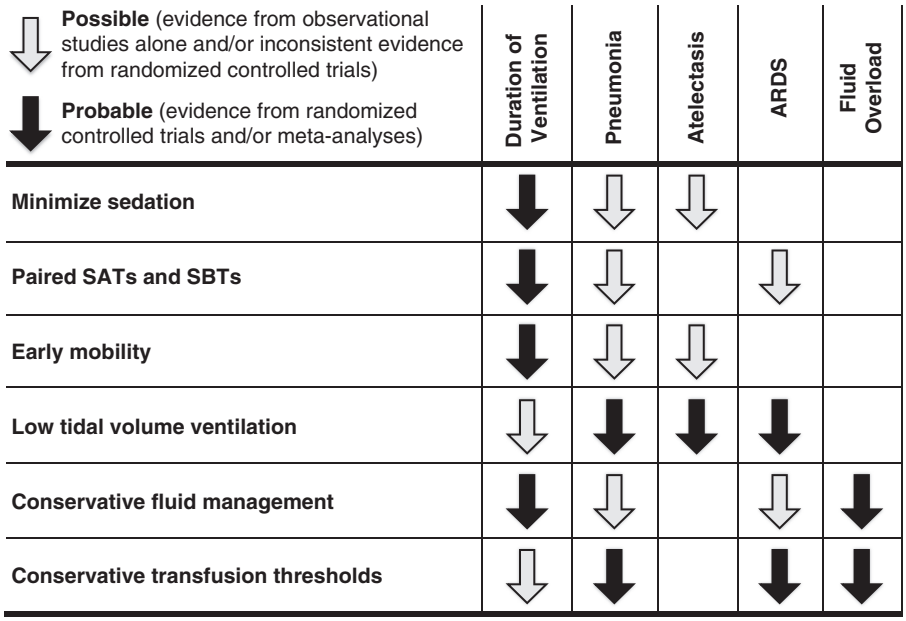

Figure 13.1 Potential strategies to prevent ventilator-associated events. These strategies are all associated with shortening the duration of mechanical ventilation and reducing one or more of the clinical conditions most frequently associated with VAEs. Reprinted with permission of the American Thoracic Society. Copyright © 2017 American Thoracic Society. Klompas M. (2015) Potential Strategies to Prevent Ventilator-associated Events. *Am J Respir Crit Care Med*. 192:1420–1430. The American Journal of Respiratory and Critical Care Medicine is an official journal of the American Thoracic Society.

interventions have been associated with lower VAP rates but not with improvements in concrete patient outcomes such as length of stay or mortality. This may be because of circularity between VAP definitions and VAP prevention strategies.[20] Interventions that decrease microbial colonization of the oropharynx (e.g., oral antiseptics) or decrease the volume of secretions (e.g., subglottic secretion drainage) may lead to fewer observed VAPs because endotracheal cultures and secretion characteristics are common diagnostic criteria for VAP.[38,40] It is unclear, however, if these decreases are attributable to true decreases in invasive pneumonias or cosmetic decreases in nonspecific clinical signs alone. It is therefore critical to assess the impact of prevention strategies on concrete outcomes such as VAEs, duration of mechanical ventilation, ICU length of stay, mortality, and antimicrobial dispensing.[18,19,41]

A logical approach to VAE prevention is to try to decrease exposure and duration of mechanical ventilation, and to adopt practices that target the most common conditions that trigger VAEs.[42] Potential strategies include avoiding intubation, minimizing sedation and avoiding benzodiazepines, performing paired daily spontaneous awakening and breathing trials, early mobility, elevating the head of the bed, using fluids conservatively, setting low tidal volumes for ventilation, and setting restrictive blood transfusion thresholds.[42–47] Root cause analyses may reveal additional institution-specific opportunities to prevent VAEs.

Clinical Correlates

Four studies have characterized the clinical events that most frequently trigger VAEs: 25–40 percent are caused by VAP, 20–40 percent are caused by fluid overload including pulmonary edema, 10–15 percent are caused by atelectasis, and 10–20 percent are caused by the acute respiratory distress syndrome (ARDS). Prevention efforts for VAE should therefore include best practices to prevent these conditions. Figure 13.1 depicts the interplay between potential VAE prevention strategies and the conditions most commonly associated with VAEs.[42]

Risk Factors

There has been relatively little work on modifiable risk factors for VAEs. A case-control study of 110 patients with VAEs matched to 110 patients without VAEs found that possible risk factors included mandatory modes of mechanical ventilation, positive fluid balances, use of benzodiazepines prior to intubation, opioid exposures, and use of neuromuscular blockers.[48] Other studies have identified spontaneous awakening trials and spontaneous breathing trials as protective against VAEs.[29,49]

A substantial fraction of VAEs may be attributable to iatrogenic events. A large series from France, for example, attributed 14 percent of VAEs to iatrogenic complications such as pneumothorax, thromboembolism, and failed extubations.[30] These observations suggest the wisdom of conducting root cause analyses of VAEs to try to discern if there are specific patterns of practice in a given institution that may predispose to VAEs. Likewise, the same study reported that 17 percent of VAEs occurred during or soon after patient transport.[30] Root cause analyses may shed light on possible reasons for these cases. Were these VAEs attributable to laying patients supine during transfers, loss of tracheal cuff pressure during movement, failure to remove subglottic secretions prior to movement, changes in ventilator mode and settings during surgery, or something else altogether? Root cause analyses may be able to help providers hone in on specific opportunities for improvements.

Intervention Trials

The Canadian Critical Care Trials Group retrospectively analyzed the impact of a 2-year quality improvement program in

11 ICUs on VAE rates.[29] The investigators organized a series of educational sessions and intermittent reminders to improve adherence with evidence-based recommendations for the care of ventilated patients.[50] The recommendations included semi-recumbent positioning, oral care with chlorhexidine, use of endotracheal tubes with subglottic secretion drainage, oral rather than nasal intubation, use of closed endotracheal suctioning systems, changing ventilator circuits only when soiled or damaged, and changing heat and moisture exchangers every 5–7 days.

Increases in adherence rates were modest. The only interventions that significantly improved were use of endotracheal tubes with subglottic secretion drainage (36 percent adherence at baseline vs. 58 percent adherence at 24 months), semirecumbent positioning (29 percent at baseline vs. 41 percent at 24 months), and oral care with chlorhexidine (16 percent at baseline vs. 60 percent at 24 months). Despite these modest improvements, the investigators did note a decrease in VAE rates from 13.6 to 9.7 cases per 100 patients (p = .05).

The significance of the observed decrease in VAE rates is unclear given the marginal level of statistical significance and the modest improvements in process measure adherence. Furthermore, the intervention bundle did not include some key interventions such as spontaneous awakening and breathing trials, early physical therapy and mobilization, and conservative fluid management. Indeed, the investigators conducted a post hoc multivariable analysis to identify which processes might be protective against VAE.[29] The only two measures potentially protective against VAEs were percentage of ventilator days with spontaneous awakening trials (OR 0.93, 95 percent CI 0.87–1.00, p = .05) and percentage of days with spontaneous breathing trials (OR 0.97, 95 percent CI 0.94–1.01, P = .10). One is left wondering what effect the investigators might have seen if their intervention package had encouraged these processes in addition to or instead of some of the measures they did include. Nonetheless, this study was the first to demonstrate that changes in care processes can potentially lower VAE rates.

The CDC Prevention Epicenters subsequently organized a multicenter quality improvement collaborative to prevent VAEs by minimizing sedation and encouraging early extubation.[49] The collaborative pursued these goals by encouraging paired daily spontaneous awakening and breathing trials in all eligible patients. The study included 3,425 episodes of mechanical ventilation and 22,991 ventilator-days. Over the 19-month period of the collaborative, the 12 participating ICUs were able to increase the frequency of spontaneous awakening trials from 14 percent to 77 percent of days where indicated, the frequency of spontaneous breathing trials from 49 percent to 75 percent of days where indicated, and the frequency of spontaneous breathing trials performed off sedation from 6.1 percent to 87 percent. These improvements were accompanied by significant and sustained decreases in VAEs. The total VAE rate decreased from 9.7 to 5.2 events per 100 episodes of mechanical ventilation (OR 0.63, 95 percent CI 0.42–0.97). The IVAC rate decreased from 3.5 to 0.52 events per 100 patients (OR 0.35, 95 percent CI 0.17–0.71). There was also nonsignificant decrease in pneumonia rates from 0.88 to 0.52 events per 100 patients (OR 0.51, 95 percent CI 0.19–1.3). Decreases in VAEs were paralleled by significant decreases in mean duration of mechanical ventilation (–2.4 days, 95 percent CI –1.7 to –3.1 days), ICU length-of-stay (–3.0 days, 95 percent CI 1.6–4.3 days), and hospital length-of-stay (–6.3 days, 95 percent CI 4.0–8.6 days). There were no significant changes in mortality rates.

Of note, when the investigators analyzed the change in VAE rates using ventilator-days as the denominator rather than episodes of mechanical ventilation, the change in VAEs was no longer significant.[49] This was felt to reflect the impact of the intervention on decreasing mean duration of mechanical ventilation. In doing so, the intervention decreased both VAEs and ventilator-days leading to a net neutral effect on VAE incidence density when expressed as events per 1000 ventilator-days. This observation, and the increasing emphasis in critical care on interventions to decrease device days, led NHSN to start allowing hospitals to report VAEs using episodes of mechanical ventilation as the denominator in addition to ventilator-days.

The third intervention trial evaluated the impact of conservative fluid management during ventilator weaning on VAE rates.[47,51] Patients were randomized to daily assessments of brain natriuretic peptide (BNP) levels versus routine care. Elevated BNP levels were a signal to clinicians that a patient might be fluid overloaded and hence to try to decrease fluid inputs and increase diuresis. Patients randomized to daily BNP levels were more likely to receive diuretics and had significantly more negative net daily fluid balances (–640 mL/day vs. –37 mL/day, P<.0001). This in turn was associated with significantly more ventilator-free days and a 50 percent decrease in VAE rates from 17.8 percent in the usual-care group to 8.6 percent in the interventional group (P = .02). This trial affirmed the importance of fluid overload as a frequent cause of VAEs and a prime target for intervention.

The fourth intervention trial published thus far considered the impact of endotracheal tubes with subglottic secretion drainage on VAE rates.[52] Investigators randomized 352 patients to subglottic secretion drainage versus routine care. There was a significant decrease in VAP rates (8.8 percent vs. 17.6 percent, P = .02) but no change in VAE rates (22 percent vs. 23 percent, P = .84). There were also no differences between groups in median ventilator days, ICU days, or hospital mortality. The mismatch between the significant decrease in VAP rates arrayed against the lack of change in VAE rates, duration of mechanical ventilation, ICU length-of-stay or mortality allowed for the possibility that the decrease in VAP rates may have been driven by fewer secretions in the subglottic secretion drainage group rather than fewer pneumonias per se. Indeed, a recent meta-analysis of subglottic secretion drainage, including over 3,300 patients drawn from 17 randomized controlled trials, also noted a significant decrease in VAPs but no impact on objective outcomes such as duration of mechanical ventilation or mortality.[40] These two studies reaffirm the concern that the clinical signs used to diagnose VAP are subjective and nonspecific. Decreases in VAP rates are not reliably paralleled

by improvements in other, more objective patient parameters.[18] Paradoxically then, this negative study helped affirm the potential merits of switching the focus of surveillance from VAP to VAE. One positive note in this study is that patients randomized to subglottic secretion drainage received 7 percent fewer days of antimicrobials compared to control patients.[52] This allows for the possibility that subglottic secretion drainage may be a tool to aid antimicrobial stewardship.

Conclusions

Clinical experience with VAE surveillance and prevention is still in its infancy. Nonetheless, several themes emerge from the growing literature on VAEs. Surveillance can be automated. VAEs are morbid events associated with high hospital mortality rates. The most common clinical events associated with VAEs are pneumonia, pulmonary edema, atelectasis, and ARDS. Positive fluid balance, sedation, and patient transportation are common risk factors for VAEs. Interventions geared to target the clinical conditions that commonly trigger VAEs and/or decrease mean duration of mechanical ventilation can prevent VAEs.

Successful interventions thus far include minimizing sedation and encouraging early extubation through paired, daily spontaneous awakening and breathing trials as well as conservative fluid management, particularly during the weaning phase of mechanical ventilation. Additional possible interventions include early physical therapy and mobility to speed extubation, low tidal volume ventilation to prevent ARDS, and conservative transfusion thresholds to prevent fluid overload and ARDS. It remains to be seen whether bundling all these interventions into a new ventilator bundle optimized for VAE prevention can have synergistic effects beyond those seen with these interventions in isolation thus far.

Finally, it is apparent that many of the interventions most likely to prevent VAEs are outside the traditional scope of most infection prevention programs. VAE prevention therefore requires an active partnership between infection prevention, critical care, respiratory therapy, pharmacy, physical therapy, and information systems in order to reach its full potential to maximize outcomes for ventilated populations.

References

1. Magill SS, Klompas M, Balk R, et al. Developing a new, national approach to surveillance for ventilator-associated events. *Crit Care Med* 2013;**41**: 2467–2475.
2. Klompas M. Complications of mechanical ventilation: the CDC's new surveillance paradigm. *N Engl J Med* 2013;**368**: 1472–1475.
3. Klein Klouwenberg PM, Ong DS, Bos LD, et al. Interobserver Agreement of Centers for Disease Control and Prevention Criteria for Classifying Infections in Critically Ill Patients. *Crit Care Med* 2013;**41**: 2373–2378.
4. Stevens JP, Kachniarz B, Wright SB, et al. When policy gets it right: variability in U.S. hospitals' diagnosis of ventilator-associated pneumonia. *Crit Care Med* 2014;**42**: 497–503.
5. Klompas M. Interobserver variability in ventilator-associated pneumonia surveillance. *Am J Infect Control* 2010;**38**: 237–239.
6. Klompas M, Kulldorff M, Platt R. Risk of misleading ventilator-associated pneumonia rates with use of standard clinical and microbiological criteria. *Clin Infect Dis* 2008;**46**: 1443–1446.
7. Muscedere JG, Day A, Heyland DK. Mortality, attributable mortality, and clinical events as end points for clinical trials of ventilator-associated pneumonia and hospital-acquired pneumonia. *Clin Infect Dis* 2010;**51** Suppl 1: S120–125.
8. van Saene HK, Silvestri L, de la Cal MA, Baines P. The emperor's new clothes: the fairy tale continues. *J Crit Care* 2009;**24**: 149–152.
9. Magill SS, Fridkin SK. Improving surveillance definitions for ventilator-associated pneumonia in an era of public reporting and performance measurement. *Clin Infect Dis* 2012;**54**: 378–380.
10. Klompas M. Eight initiatives that misleadingly lower ventilator-associated pneumonia rates. *Am J Infect Control* 2012;**40**: 408–410.
11. Klompas M. Ventilator-associated pneumonia: is zero possible? *Clin Infect Dis* 2010;**51**: 1123–1126.
12. Thomas BW, Maxwell RA, Dart BW, et al. Errors in administrative-reported ventilator-associated pneumonia rates: are never events really so? *Am Surg* 2011;**77**: 998–1002.
13. Skrupsky LP, McConnell K, Dallas J, Kollef MH. A comparison of ventilator-associated pneumonia rates as identified according to the National Healthcare Safety Network and American College of Chest Physicians criteria. *Crit Care Med* 2012;**40**: 281–284.
14. Novosel TJ, Hodge LA, Weireter LJ, et al. Ventilator-associated pneumonia: depends on your definition. *Am Surg* 2012;**78**: 851–854.
15. Wang Y, Eldridge N, Metersky ML, et al. National trends in patient safety for four common conditions, 2005–2011. *N Engl J Med* 2014;**370**: 341–351.
16. Dudeck MA, Weiner LM, Allen-Bridson K, et al. National Healthcare Safety Network (NHSN) report, data summary for 2012, Device-associated module. *Am J Infect Control* 2013;**41**: 1148–1166.
17. Kollef MH, Chastre J, Fagon JY, et al. Global prospective epidemiologic and surveillance study of ventilator-associated pneumonia due to Pseudomonas aeruginosa. *Crit Care Med* 2014;**42**: 2178–2187.
18. Bonten MJ. Healthcare epidemiology: ventilator-associated pneumonia: preventing the inevitable. *Clin Infect Dis* 2011;**52**: 115–121.
19. Bouadma L, Wolff M, Lucet JC. Ventilator-associated pneumonia and its prevention. *Curr Opin Infect Dis* 2012;**25**: 395–404.
20. Klompas M. The paradox of ventilator-associated pneumonia prevention measures. *Crit Care* 2009;**13**: 315.
21. Klompas M, Li L. Beyond pneumonia: improving care for ventilated patients. *Lancet Infect Dis* 2013;**13**: 640–641.
22. Klein Klouwenberg PM, van Mourik MS, Ong DS, et al. Electronic implementation of a novel surveillance paradigm for ventilator-associated events: feasibility and validation. *Am J Respir Crit Care Med* 2014;**189**: 947–955.

23. Lilly CM, Landry KE, Sood RN, et al. Prevalence and Test Characteristics of National Health Safety Network Ventilator-Associated Events. *Crit Care Med* 2014;**42**: 2019–2028.
24. Stevens JP, Silva G, Gillis J, et al. Automated surveillance for ventilator-associated events. *Chest* 2014;**146**: 1612–1618.
25. Magill S, Gross C, Edwards J. *Incidence rates of VAE and VAP in the NHSN 2012–2103. IDWeek 2014 Abstract 880*; October 8–12, 2014.
26. Klompas M, Kleinman K, Murphy MV. Descriptive epidemiology and attributable morbidity of ventilator-associated events. *Infect Control Hosp Epidemiol* 2014;**35**: 502–510.
27. Klompas M, Khan Y, Kleinman K, et al. Multicenter Evaluation of a Novel Surveillance Paradigm for Complications of Mechanical Ventilation. *PLoS ONE* 2011;**6**: e18062.
28. Klompas M, Magill S, Robicsek A, et al. Objective surveillance definitions for ventilator-associated pneumonia. *Crit Care Med* 2012;**40**: 3154–3161.
29. Muscedere J, Sinuff T, Heyland D, et al. The clinical impact and preventability of ventilator-associated conditions in critically ill mechanically ventilated patients. *Chest* 2013;**144**: 1453–1460.
30. Bouadma L, Sonneville R, Garrouste-Orgeas M, et al. Ventilator-associated events: prevalence, outcome, and relationship with ventilator-associated pneumonia. *Crit Care Med* 2015;**43**: 1798–1806.
31. Hayashi Y, Morisawa K, Klompas M, et al. Toward improved surveillance: the impact of ventilator-associated complications on length of stay and antibiotic use in patients in intensive care units. *Clin Infect Dis* 2013;**56**: 471–477.
32. Nuckchady D, Heckman MG, Diehl NN, et al. Assessment of an automated surveillance system for detection of initial ventilator-associated events. *Am J Infect Control* 2015;**43**: 1119–1121.
33. Mann T, Ellsworth J, Huda N, et al. Building and validating a computerized algorithm for surveillance of ventilator-associated events. *Infect Control Hosp Epidemiol* 2015: 1–5.
34. Magill SS, Rhodes B, Klompas M. Improving ventilator-associated event surveillance in the National Healthcare Safety Network and addressing knowledge gaps: update and review. *Curr Opin Infect Dis* 2014;**27**: 394–400.
35. Phongjitsiri S, Coss-Bu J, Kennedy C, et al. The Centers for Disease Control and Prevention's new definitions for complications of mechanical ventilation shift the focus of quality surveillance and predict clinical outcomes in a PICU. *Crit Care Med* 2015;**43**: 2446–2451.
36. Cocoros NM, Kleinman K, Priebe GP, et al. Ventilator-associated events in neonates and children: a new paradigm. *Crit Care Med* 2016;**44**: 14–22.
37. Herzig SJ, Howell MD, Ngo LH, Marcantonio ER. Acid-suppressive medication use and the risk for hospital-acquired pneumonia. *JAMA* 2009;**301**: 2120–2128.
38. Klompas M, Speck K, Howell MD, Greene LR, Berenholtz SM. Reappraisal of routine oral care with chlorhexidine gluconate for patients receiving mechanical ventilation: systematic review and meta-analysis. *JAMA internal medicine* 2014;**174**: 751–761.
39. Price R, MacLennan G, Glen J. Selective digestive or oropharyngeal decontamination and topical oropharyngeal chlorhexidine for prevention of death in general intensive care: systematic review and network meta-analysis. *BMJ* 2014;**348**: g2197.
40. Caroff DA, Li L, Muscedere J, Klompas M. Subglottic secretion drainage and objective outcomes: a systematic review and meta-analysis. *Crit Care Med* 2015.
41. Klompas M, Branson R, Eichenwald EC, et al. Strategies to prevent ventilator-associated pneumonia in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014;**35**: 915–936.
42. Klompas M. Potential strategies to prevent ventilator-associated events. *Am J Respir Crit Care Med* 2015;**192**: 1420–1430.
43. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. *Lancet* 2008;**371**: 126–134.
44. Schweickert WD, Pohlman MC, Pohlman AS, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet* 2009;**373**:1874–1882.
45. Determann RM, Royakkers A, Wolthuis EK, et al. Ventilation with lower tidal volumes as compared with conventional tidal volumes for patients without acute lung injury: a preventive randomized controlled trial. *Crit Care* 2010;**14**: R1.
46. Gajic O, Rana R, Mendez JL, et al. Acute lung injury after blood transfusion in mechanically ventilated patients. *Transfusion (Paris)* 2004;**44**: 1468–1474.
47. Mekontso Dessap A, Roche-Campo F, Kouatchet A, et al. Natriuretic peptide-driven fluid management during ventilator weaning: a randomized controlled trial. *Am J Respir Crit Care Med* 2012;**186**: 1256–1263.
48. Lewis SC, Li L, Murphy MV, Klompas M. Risk factors for ventilator-associated events: a case-control multivariable analysis. *Crit Care Med* 2014;**42**: 1839–1848.
49. Klompas M, Anderson D, Trick W, et al. The preventability of ventilator-associated events: The CDC Prevention Epicenters Wake Up and Breathe Collaborative. *Am J Respir Crit Care Med* 2015;**191**: 292–301.
50. Sinuff T, Muscedere J, Cook DJ, et al. Implementation of clinical practice guidelines for ventilator-associated pneumonia: a multicenter prospective study. *Crit Care Med* 2013;**41**: 15–23.
51. Mekontso Dessap A, Katsahian S, Roche-Campo F, et al. Ventilator-associated pneumonia during weaning from mechanical ventilation: role of fluid management. *Chest* 2014:ePub ahead of print.
52. Damas P, Frippiat F, Ancion A, et al. Prevention of ventilator-associated pneumonia and ventilator-associated conditions: a randomized controlled trial with subglottic secretion suctioning. *Crit Care Med* 2015;**43**: 22–30.
53. Klompas M. Ventilator-associated conditions versus ventilator-associated pneumonia: different by design. *Curr Infect Dis Rep* 2014;**16**: 430.

Chapter 14

Basics of Surgical Site Infection: Surveillance and Prevention

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Introduction

During the early years of modern surgery, many patients died from "wound sepsis." Despite scientific advances and improved practices, surgical site infections (SSIs) continue to cause substantial morbidity and increased cost of healthcare regardless of the type of healthcare system. SSIs are the most common healthcare-associated infection in the United States, accounting for approximately 20 percent to 25 percent of all infections.[1–3] Approximately 300,000 SSIs occur annually, accounting for 3.7 million excess hospital days and over 3.5 billion dollars in excess hospital costs.[4,5] Surgical patients who develop an SSI have a risk of death that is between 2- and 11-fold higher than patients without an SSI.[6–8] These numbers likely underestimate the magnitude of the problem, yet they highlight the tremendous human and financial costs of SSIs and the importance of SSI surveillance and prevention.

The Centers for Disease Control and Prevention (CDC) conducted the Study of the Efficacy of Nosocomial Infection Control (SENIC) in order to investigate and document the cost-effectiveness of infection prevention activities, including surveillance.[9] These and many subsequent investigators concluded that infection surveillance programs that report SSI rates to surgeons can decrease overall SSI rates by at least 32–50 percent.[9–11] However, several important questions about surveillance for SSIs remain.

- Which surveillance methods are best?
- Which surgical patients should we survey for SSI?
- What is the best method to identify SSI after discharge (postdischarge surveillance)?
- How can we effectively use electronic surveillance systems to enhance case-finding?
- How can surveillance activities be used to develop and inform interventions to prevent SSI?
- Does public reporting of SSI rates lead to improved outcomes?

The purpose of this chapter is to explore some of these questions and to summarize the basic steps required to implement a hospital or healthcare system–based SSI surveillance and prevention program.

I SSI Surveillance: Objectives and Definitions

A Objectives

The main objective of SSI surveillance and data feedback is to prevent SSIs, thereby reducing morbidity and improving patient outcomes. To achieve this goal, infection prevention personnel must first determine the baseline SSI rate in order to assess the magnitude of the problem for each type of surgical procedure in an institution. By monitoring SSI rates over time, infection prevention staff can identify clusters of infections, discover overall trends, and respond accordingly. SSI surveillance facilitates comparisons, both within an institution and with other similar institutions. The objective of such comparisons is timely recognition of SSI rates or computed standardized infection ratios (SIR) that are above the baseline for the institution or above national benchmarks such as those published by the CDC National Healthcare Safety Network (NHSN). Analysis of trends and internal and external comparisons allows facilities to identify potential patient safety problems and to promptly implement appropriate corrective measures. Infection prevention personnel should provide surveillance data to surgeons and other members of the surgical team as education. This intervention alone can lead to reductions in rates of SSI. However, rates or SIRs should also be provided to leaders who can help facilitate change to assure best and evidence-based practices are in place and that they are appropriately standardized across the facility or health system. Finally, the SSI surveillance program is used to assess the impact of interventions designed and implemented to prevent harm after surgery, including infections (e.g., antimicrobial prophylaxis protocols or education to reinforce aseptic technique).

B Definitions

Before implementing an SSI surveillance system, infection prevention personnel and surgeons must agree on a precise definition for SSI. Ideally, the definition should 1) be meaningful clinically and easy to apply; 2) remain unchanged so that infection prevention and surgical staff can compare

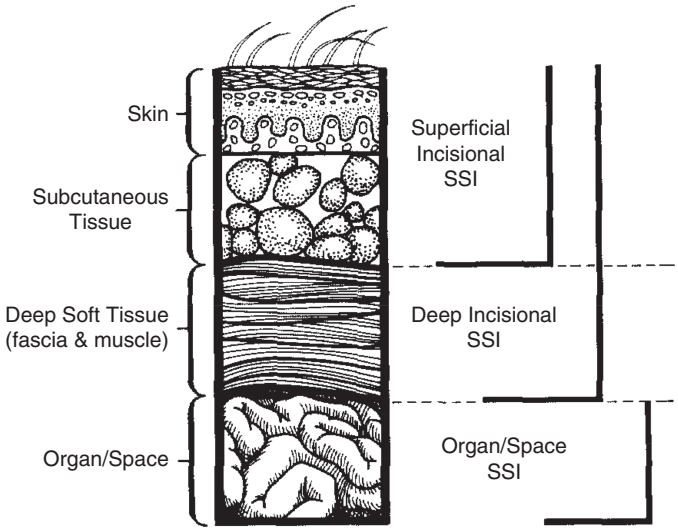

Figure 14.1 Schematic of surgical site infection (SSI) anatomy and appropriate classification. This figure depicts the cross-sectional anatomy of a surgical incision upon which is superimposed the most recent classification for SSI and the definition of an infection at each site. From Horan et al. 1992[12] © The Society for Healthcare Epidemiology of America.

data over time and evaluate interventions implemented to reduce rates; and 3) remain consistent with standard definitions to allow for valid external comparisons and benchmarking. The definition must be simple to use, accepted by nurses and surgeons, and applied consistently. Standard SSI definitions devised by the CDC and other experts are used globally and stratify infection by the depth of tissue involved (Figure 14.1). These definitions have been used successfully both in resource rich and poor settings[12] and have been adopted by other groups such as the National Surgical Quality Improvement Program (NSQIP). Finally, it is important to note that a surveillance definition may not identify a clinically defined wound infection and vice versa, as each of these definitions are used for different purposes. Importantly, the CDC-based definitions were not designed for reimbursement as they are commonly used.

We must use objective criteria to identify SSIs and apply such definitions consistently.[13] For example, an infection preventionist (IP) at a 200-bed general community hospital reported that a neurosurgeon's SSI rate was excessive. When the surgeon proposed terminating his practice, the hospital administrator asked for an independent investigation. Ultimately, external consultants determined that the IP had incorrectly categorized noninfected patients as infected. The infection control committee was charged with establishing clear standards for confirmed SSIs and applying them routinely and consistently. Over the next 2 years, none of the surgeon's patients was reported to have had SSI.[14]

According to the CDC NHSN definition, SSIs are categorized as either incisional or organ-space. Incisional SSIs are classified further as superficial (involving only the skin and subcutaneous tissue) or deep (involving deep soft tissues of the incision) (Figure 14.1). The definition of superficial-incisional SSI requires that at least one of the following occur within 30 days of the operative procedure:

- Purulent drainage from the superficial incision.
- Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
- At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat, and the surgeon deliberately opened the superficial incision, unless incision is culture negative.
- The surgeon or attending physician diagnosed a superficial-incisional SSI.

Deep-incisional and organ-space SSI are defined similarly.[12] Deep-incisional SSI can be further categorized as a deep incision primary (DIP) SSI, when the SSI occurs at the primary incision, or a deep incision secondary (DIS) SSI, when the SSI occurs in a secondary incision in a patient who had an operation with more than one incision. Surveillance is performed for 30 days following the procedure for most procedures. The NHSN has identified several situations (e.g., when an implant is placed) for which surveillance must continue for 90 days following the procedure. Still as precise as these definitions are, there are many opportunities for varied interpretation.

II Surveillance Methods

Infection prevention personnel use many different surveillance methods to identify healthcare-associated infections. Of note, the gold standard is to use trained personnel (IP) to apply strict definitions in a standard fashion. Because there is subjectivity, many programs validate the findings. We will review several common surveillance methods and discuss whether each method can be used effectively to survey for SSIs.

A 100 Percent Chart Review and Wound Examination

After conducting prospective SSI surveillance for 10 years, Olson and Lee concluded that the combination of daily hospital chart review and examination of postoperative incisions is the most sensitive and rigorous way to perform SSI surveillance.[11] This method – while precise – is tedious and time consuming. Some experts still consider this strategy to be the gold standard and recommend that SSI surveillance include daily examination of operative wounds. To facilitate this method, infection prevention personnel or surgeons can train staff nurses who see the wounds during routine care to recognize signs of infection and report all clinically suspicious signs and symptoms to the IP. The IP, then, examines all such wounds and determines which meet the criteria for infection.[15] Clearly, this comprehensive approach is not feasible in large hospitals with many surgical patients, especially if most SSIs occur after discharge from the initial hospitalization. It also would make intrahospital comparisons of SSI rates difficult due to the inherent subjectivity of the process.

B 100 Percent Chart Review

Haley et al. validated the importance of surveillance that used systematic processes to review medical records and identify

Table 14.1 Wound classification reflects extent of microbial contamination

Classification	Criteria
Clean	• Elective. not emergent procedure • No traumatic injury • Primary closure • No acute inflammation or break in surgical technique • No entry of the respiratory, gastrointestinal, biliary, or genitourinary tracts
Clean-contaminated	• Urgent or emergent procedure that is otherwise clean • Elective opening of respiratory, gastrointestinal, biliary, or genitourinary tract with minimal spillage (e.g., appendectomy) • No infected urine or bile encountered • Minor break in surgical technique during a clean procedure
Contaminated	• Nonpurulent inflammation noted at the time of surgery • Gross spillage from gastrointestinal tract • Infected urine or bile encountered • Major break in surgical technique • Penetrating trauma <4 hours old • Chronic open wounds to be grafted or covered
Dirty	• Purulent inflammation noted at the time of surgery • Preoperative perforation of respiratory, gastrointestinal, biliary, or genitourinary tract • Penetrating trauma >4 hours old.

Table 14.1 is adapted from Berard 1964.[18]

infections.[16] Many institutions utilize this strategy and review 100 percent of surgical patients' medical records for surveillance. Given the proliferation of electronic systems, the process of chart review is simplified. Cardo et al. compared surveillance performed by an IP who reviewed surgical patients' medical records and discussed each patient's progress with nurses and physicians to surveillance performed by a hospital epidemiologist who reviewed the surgical patients' medical records and examined their incisions.[17] The IP identified 84 percent of SSIs noted by the hospital epidemiologist. The authors concluded that accurate data on SSIs can be collected by persons who do not examine the operative incisions directly.[17] Importantly, the quality of the information gleaned from medical records depends on the completeness of records and on the reviewer's experience. The limitation of this strategy, however, is that it is also resource intensive. Thus, programs with limited resources must either focus on specific surgical subpopulations or use other, less time-consuming surveillance methods.

C Targeted SSI Surveillance: 100 Percent Chart Review of Selected Procedures

In most hospitals, approximately 70 percent of operative procedures are categorized as "clean" operations, which have a low microbial contamination burden and therefore a relatively low SSI risk (Table 14.1).[18] Some hospitals target SSI surveillance to only these clean operative procedures, on the assumption that SSIs are rarely preventable in the other wound classification categories with higher levels of microbial contamination. More recently, infection prevention program surveillance strategies have been influenced by Centers for Medicare and Medicaid Services (CMS), policy makers, insurers, and others who have recommended that infection rates for certain procedures be publically reported. Despite the various reasons for targeting procedures, the SENIC project demonstrated that SSI surveillance and feedback for contaminated or dirty procedures reduced SSI rates as effectively as did SSI surveillance and feedback for clean or clean-contaminated cases.[19] Therefore, we advocate for SSI surveillance that includes operative procedures from all wound classification categories. However, this approach can be resource intensive without using electronic surveillance strategies, so further prioritization may be necessary.

A potential strategy that can be used independently or combined with targeting clean operations is to target surveillance to specific operative procedures that are performed frequently at an institution, since high volume procedures pose SSI risk to a greater number of patients. For example, the vast majority of hospitals in the United States perform surveillance on colorectal procedures and abdominal hysterectomies, particularly in light of reporting requirements from the CMS. Alternatively, surveillance can be targeted to procedures for which SSIs cause substantially higher morbidity and mortality (e.g., SSI after craniotomies, spinal surgery, and coronary artery bypass procedures generally causes higher morbidity and mortality than does SSI after a hernia repair). A third strategy is to target surveillance to operative procedures that

have been identified to have high infection rates at a given institution. This approach allows a program to identify potentially modifiable contributing factors where a directed intervention can be applied. Depending on the resources available for surveillance, combinations of these targeting strategies may be employed. Regardless of the strategies used, the list of surveillance activities should be periodically reassessed to determine appropriate priorities. Such risk assessments and targeted surveillance assure that infection prevention personnel optimize available resources to focus SSI surveillance on high-volume or high-risk procedures so that they can intervene immediately if the SSI rates are found to be high or increase substantially.

SSI surveillance should not be targeted to specific hospital units because this approach will likely underestimate the SSI rates for specific procedures and may miss problems or clusters that occur in units not under surveillance. For example, hospitals that limit SSI surveillance to the surgical intensive care unit (SICU) will miss many infections, because the average SSI occurs 21 days postoperatively,[20,21] while most patients leave the SICU within a few days of surgery.

D Targeted SSI Surveillance: 100 Percent Chart Review of High-Risk Patients

Another option for targeted surveillance is to stratify patients according to their risk of developing an SSI and then perform surveillance on patients at high risk for an SSI. One strategy to identify patients at risk for SSI is to develop a risk index. The ideal risk index is a simple additive scale that can be calculated at the end of surgery to predict those patients who are at high risk of developing an SSI. Ideally, the risk index should be validated prospectively on specific services in individual hospitals to document that it predicts a patient's risk accurately. Risk indices are also used to risk-adjust SSI surveillance data so that infections are stratified and reported according to the relative risk of different patient populations. This is particularly important when evaluating rates of SSI for specific surgeons, services, or institutions that care for high-risk groups of patients.

Used alone, variables such as wound classification[18] have limited ability to stratify patients because infection rates vary substantially within each group.[22] Therefore, investigators have developed risk indices that include multiple variables to better predict which patients are at highest risk of developing SSI. In 1985, Haley et al. published the SENIC risk index[23] which includes four factors; abdominal operation, duration of surgery more than two hours, wound classification, and number of discharge diagnoses. The SENIC risk index predicts the risk of SSI twice as well as the traditional wound classification, but one of the index components, discharge diagnoses, must be obtained retrospectively. Therefore, Culver et al. adapted the SENIC risk index and assessed underlying severity of illness with the American Society of Anesthesiologists (ASA) score rather than with discharge diagnoses. This risk index (Table 14.2) also includes a component that accounts for the expected variability in the duration of the operative procedure.[24] Instead of using a constant two-hour cut point for length of surgery as used by the SENIC index, the CDC index defines "T time" as the 75th percentile of the duration for each operative procedure. This risk index is a simple additive scale with scores that range from 0 to 3, and the three index variables are usually available in the anesthesia record at the end of a surgical procedure.

Table 14.2 The CDC risk index

Risk Factors	Score[a]
ASA[b] preoperative assessment score of 3, 4, or 5	1
Operative procedure lasting longer than "T" hours[c]	1
Operative procedure classified as either contaminated or dirty by the traditional wound classification system	1

[a] To calculate total score, sum factors present. Total score ranges from 0 to 3.
[b] ASA = American Society of Anesthesiologists.
[c] "T" depends on the procedure being performed. (www.cdc.gov/nhsn/PDFs/pscManual/9pscSSIcurrent.pdf).

No method for risk adjustment is perfect. For example, the newer index has rarely been validated in populations other than those participating in the Centers for Disease Control and Prevention's (CDC) National Health Safety Network. Very few studies have compared the various SSI risk indices. Some investigators report that the CDC risk index does not stratify patients accurately by their SSI risk, particularly for cardiac procedures and Cesarean section. For example, the risk index had low sensitivity (24 percent) and positive predictive value (43 percent) for identifying SSI after cardiothoracic operative procedures in one study.[25]

Alternative strategies for risk adjustment have been proposed. For example, Nichols et al. published a risk index that accurately predicted postoperative septic complications in a subset of patients who underwent operations after penetrating abdominal trauma.[26] Additionally, they showed that the risk factors included in the index could identify high-risk patients who benefited from prolonged (5 days) antibiotic therapy and delayed wound closure, and low-risk patients who did well with short-term (2 days) antibiotic therapy and primary wound closure.[26] Thus, this risk index not only stratifies patients by their risk of infection but also helps predict which patients will benefit from specific preventive strategies. Other surgical databases, such as the American College of Surgeons' National Surgical Quality Improvement Program (NSQIP) and the Society for Thoracic Surgeons' (STS) national database, use similar methods for risk adjustment and incorporate large numbers of patient-specific preoperative risk factors in their predictor pools (around 70 and 40 variables, respectively).[18,19] In 2012, NHSN updated their risk adjustment approach by publishing specific models for individual surgical procedures. Although these models represent an improvement over the CDC risk index, the improvement was

small or modest at best. A "c-index" of 0.5 indicates that a multivariate prediction model has the predictive ability of a coin-flip. Using a cutoff c-index of 0.7 as indication of "adequate" predictive ability, only 16 (41 percent) procedure-specific models would be considered adequate. Models could not be created for nine procedures, while five models included only one risk factor to differentiate risk. Users of these specific models need to be aware of their limitations and realize that results are either raw or minimally risk-adjusted when comparing outcomes of SSI.

E Selective Chart Review

Wenzel et al. studied the sensitivity of reviewing selected medical records compared with reviewing all medical records to detect healthcare-associated infections.[27] The infection preventionist scanned the medical record for signs of possible healthcare-associated infection such as fever or antibiotic use. If one or more concerning signs were noted, the infection preventionist evaluated the patient's medical record more thoroughly. The infection preventionist correctly identified 82 percent to 94 percent of healthcare-associated infections using this type of selective review. Selective review saved many hours of the infection preventionist's time.[27] The success of the selective method depends upon the completeness and accuracy of the data that is screened to detect fever and antibiotic utilization. Although the selective method may be a good source of information about certain healthcare-associated infections, screening for fever and antibiotic utilization is probably not sufficiently sensitive to detect patients with SSI. Unfortunately, more useful indicators such as the frequency with which wound dressings are changed and descriptions of discharge from the wound are not readily available without a full review of each medical record. These limitations may be overcome with the increasing use of electronic medical records where algorithms and or techniques such as natural language processing could be used to identify patients at risk of developing an SSI.

Antimicrobial utilization can be a useful indicator of healthcare-associated infection. For example, antibiotics beyond the "expected" number of days postoperatively is a strong predictor for SSI.[27–30] Still, infection prevention programs should not rely solely upon pharmacy data when conducting SSI surveillance. Some patients may continue to receive prophylactic antibiotics postoperatively for infections not related to the surgery, and some patients receive antimicrobial agents for infections that were present preoperatively (e.g., peritonitis caused by a ruptured appendix). Administrative data may also be used or included in these strategies to increase the efficiency of surveillance, reporting, and validation.[31,32]

Similarly, microbiology data can be a useful component of SSI surveillance, but these data should not be used as the sole source of case-finding. Surveillance for healthcare-associated infections that relies only on microbiology data has a sensitivity of only 33 percent to 65 percent.[27,30] Two-thirds of inpatient surgical wounds, and even fewer outpatient wounds, are cultured, despite clinical evidence of SSI.[33] Frequently, surgeons do not obtain cultures because they treat SSI with operative drainage and empiric antibiotics. Some clinicians feel that it is not necessary to know the etiologic agent or its antibiotic susceptibility. In contrast, it is also important to note that a wound culture that grows an organism does not necessarily mean that the patient has an SSI. Instead, the organism(s) may be colonizing the wound. This scenario is particularly relevant in burns or skin that is left to heal by secondary intention. The opposite is also true; a culture that does not grow organisms does not eliminate the possibility of SSI. For example, wound cellulitis, deep wound abscess, or SSI from organisms that are not detected by routine culture methods could lead to superficial wound cultures that do not grow. In addition, atypical pathogens such as *Mycobacterium* other than *M. tuberculosis* and *Legionella* that have been reported to cause infection require specialized media and techniques to be identified. Novel diagnostic procedures and polymerase chain reaction (PCR)-based technologies with improved efficiency, accuracy, and speed will enhance surveillance.

Finally, some surveillance approaches utilize random chart sampling. For example, trained personnel in hospitals that participate in the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) randomly sample charts of patients who have undergone specific surgical procedures (e.g., colectomy). These personnel extract detailed information on preoperative risk factors, intraoperative variables, and outcomes. SSI is currently defined using the same definitions from the CDC. These data are then electronically submitted to the central program and a detailed, risk-adjusted report is generated. Of note, while many institutions are adopting this strategy for performance improvement, it may not identify clusters of infections.

F Postdischarge Surveillance

The proportion of surgeries performed in the outpatient setting continues to increase, and postoperative length of stay following inpatient surgery is decreasing. In addition, the severity of illness among surgical patients is increasing, and operative procedures are becoming more complex. While these dramatic shifts in patient populations, operative techniques, and healthcare delivery increase the need for outpatient surveillance, they also increase the complexity of performing accurate surveillance.

The majority of SSIs occur following discharge, either in the outpatient setting or in a subsequent readmission. In three studies, 45 percent to 81 percent of the SSIs were detected after discharge from the index hospitalization.[34–36] Sands found that 84 percent of 132 SSIs among 5,572 nonobstetric operative procedures in adult patients became apparent after the patients were discharged.[20] According to one study, postdischarge SSI leads to more outpatient visits, readmissions, emergency room visits, home health services, and increased costs ($5,155 vs. $1,773 for the 8 weeks after discharge).[37]

The cost and time required to perform postdischarge surveillance may discourage many infection prevention and control programs from instituting such systems. As a result, programs use inconsistent approaches to perform

postdischarge surveillance. However, these programs must acknowledge that inpatient surveillance alone will vastly underestimate the actual rates of SSI.[34,35,38,39] Therefore, strategies that identify SSIs after discharge are necessary and will likely become increasingly available as the use of integrated electronic medical records increase.

The census approach, surveying each patient or physician for a defined time period, was used in several studies to measure healthcare-associated infection rates during the postdischarge period.[35,40] Telephone surveys and questionnaires sent to patients or physicians also have been used.[20,41,42] Seaman and Lammers found that patients, despite using verbal or printed instructions, were unable to recognize infections.[41] The authors concluded that "reliance on printed instructions, telephone interviews, or any other means of patient self-evaluation may not allow early recognition of infection" and therefore should not be used for clinical investigations of wound healing. Similarly, Sands et al. found that questionnaires sent to patients and to surgeons had sensitivities of 28 percent and 15 percent, respectively.[20]

Sands et al. subsequently identified a method that appears more reliable. They used automated pharmacy dispensing information, administrative data, and electronic records to identify postdischarge SSI.[43] In this method, specific codes for diagnoses, tests, and treatments were evaluated for their ability to predict postdischarge SSI. They found that an automated system of surveillance of hospital discharge diagnosis codes plus pharmacy dispensing data had a sensitivity of 77 percent and specificity of 94 percent, far better than questionnaires to patients and surgeons.[43]

Delgado et al. reported that the majority of postdischarge SSIs occurred following clean surgery (e.g., hernia, breast, or vascular surgery) and clean contaminated surgery of the biliary tract.[35] These results may give some guidance to infection prevention personnel when choosing procedures to target for postdischarge surveillance. Delgado et al. also found that risk factors for in-hospital SSI were not determinants of postdischarge SSI, with the exception of body mass index.[35]

The trend is to develop networks of infection prevention groups or health system programs that link programs between hospitals, nursing homes, same-day surgery centers, and home healthcare. If these are not developed, we suggest that infection prevention programs link with home healthcare agencies or other agencies that provide care for outpatients to develop mechanisms by which SSIs can be identified.

G Electronic Surveillance

Computerization of medical records and technological advances promise to improve the quality of data and make surveillance more automated. Infection prevention programs and private companies are developing new automated methods by which they can identify patients with all healthcare-associated infections including SSIs, particularly those whose signs and symptoms occur after discharge. Electronic data are available from a variety of sources that can enhance SSI surveillance including data on antimicrobial prescribing, hospital readmissions, additional or repeat surgery, and microbiology culture results.[28,42,44] Sands et al. found that individual components of an automated screening system could identify SSIs.[43] They determined that:

- Use of coded diagnoses, tests, and treatments in the medical record had a sensitivity of 74 percent.
- Specific codes and combinations of codes identified a subset of 2 percent of all procedures among which 74 percent of SSIs occurred.
- Use of hospital discharge diagnosis codes plus pharmacy dispensing data had a sensitivity of 77 percent and specificity of 94 percent.

Several studies confirm that automated claims and pharmacy data from several health insurance plans can be combined to allow routine monitoring for indicators of postoperative infection.[32,45,46] Bouam et al. demonstrated how cooperation between infection prevention and medical informatics can lead to an automated system of surveillance.[47] They compared computerized prospective surveillance of the electronic medical record with standard prospective review of lab data and charts by an infection preventionist. The automated method required much less time and performed well with sensitivity and specificity of 91 percent.[47] Chalfine et al. found that a combination of microbiology culture results and surgeon questionnaires was much less time consuming and had a sensitivity of 84.3 percent and specificity of 99.9 percent compared with conventional chart review surveillance of patients who underwent gastrointestinal surgery.[44] Yokoe et al. found that electronic data on antimicrobial drug exposure and diagnosis codes enhanced conventional SSI surveillance and substantially decreased the number of medical charts that infection preventionists had to review to determine patients' SSI status following coronary artery bypass surgery, Cesarean section procedures, and breast surgery.[28]

In a 2003 editorial, Burke suggested that computers can do more than simply automate traditional surveillance methods.[48] Computerized event monitoring can be used to trigger epidemiologic investigations and data mining can uncover small outbreaks and trends that might otherwise be missed. Time saved by automating surveillance liberates infection prevention staff to interpret the new data, answer new questions, and design new interventions to prevent SSIs.[48] Several academic groups and entrepreneurial companies have developed novel systems that access administrative and clinical data to facilitate SSI surveillance. This need is becoming more acute as more states require institutions to report their SSI rates publically. This strategy to improve quality of care has also lead to "gaming" of the system. As a result, many experts are calling for surveillance strategies that are comparable and valid.

H Summary of Surveillance Methods

Surveillance activities are the cornerstones of prevention activities, as they identify the important events that need tracking. In the current era of public reporting of infection including SSI and the trend to decrease reimbursement for what is seen as a preventable adverse event, the importance of surveillance, its

accuracy, and its use as a tool to enhance best practice cannot be highlighted more. That being said, we feel that surveillance is most effective when coupled with interventions to prevent SSI. These two competing activities must be balanced, but more effective and efficient surveillance strategies are needed to achieve this goal.

When selecting surveillance methods, infection preventionists, hospital epidemiologists, and hospital leaders must consider their objectives and the various sources from which the necessary data may be obtained. Although wound examination and chart review of all surgical patients is considered the gold standard, most institutions will need to set priorities and perform some type of targeted SSI surveillance. Surveillance can be targeted to focus on high-volume procedures, high-risk procedures, high-risk patients, or procedures of particular interest at a given institution. Data sources available at one institution may not be available at others, although ongoing changes in electronic medical records are helping to standardize available information. Diagnostic procedures, such as computerized tomography or magnetic resonance imaging, may help to identify deep or organ-space infections; the operating room schedules and readmission lists allow epidemiology staff to identify patients who return to the hospital or the operating room for drainage and debridement. Review of the pharmacy records or microbiology reports can enhance case-finding, but in themselves should not be used as the sole method of identifying patients who have SSIs. Electronic data from computerized databases can help infection preventionists perform surveillance efficiently, particularly postdischarge surveillance. The availability of resources will determine, in part, which surveillance methods are most useful in individual healthcare facilities. No surveillance method is perfect, and any chosen strategy must be validated and periodically reassessed.

III Collection, Tabulation, Analysis, and Reporting of Data

A Data Sources

Data collected during SSI surveillance can be classified into three categories: host factors, surgical and environmental factors, and microbial factors (Figure 14.2). Host factors are conditions that reflect the patient's intrinsic susceptibility to infection. These conditions usually are present when the patient is admitted to the hospital. Some of these factors increase the risk of SSI after many different operative procedures (e.g., remote infection, age, preoperative length of stay),[49,50] while others may increase the risk only after specific operative procedures.[51] Surgical and environmental factors can increase the probability of bacterial contamination at the time of the procedure and lead to SSI. For example, a contaminated wound, a long procedure, and poor surgical technique are risk factors for SSI.[49] Microbial factors, such as the virulence of the organism or the ability of the organism to adhere to sutures may alter the risk of SSI. To conduct routine surveillance for SSI, infection preventionists rarely need to know whether the patient carries specific organisms. However, during an outbreak, or when trying to answer specific research questions, they may need to obtain preoperative surveillance cultures from specific body sites.

The amount of data that infection preventionists should collect depends on the purpose of the surveillance program and on the specific issues identified at a given institution. In general, the basic data that should be collected include the following: the patient's identification, date of admission, date of surgery, type of procedure, wound classification[18] (i.e., clean, clean-contaminated, contaminated, and dirty),

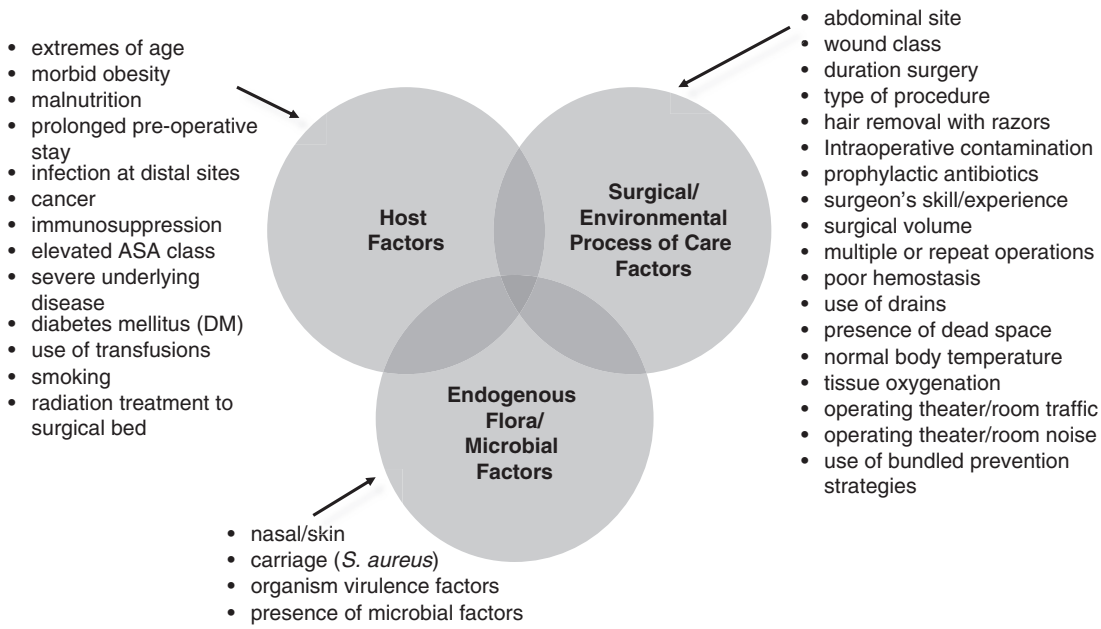

Figure 14.2 Risk factors for surgical site infection. This figure indicates that the patient's risk of developing a surgical site infection (SSI) varies with numerous host factors, surgical and environmental factors, and microbial factors. A complex interaction of these factors determines whether the patient will acquire an SSI. ASA = American Society of Anesthesiologists.

surgeon's identification code, the date that the SSI was diagnosed, and the type of infection (i.e., superficial-incisional, deep-incisional, or organ space). Other useful data are the American Society of Anesthesiologists (ASA) score, the procedure's duration and urgency, the organism identified, and type and timing of perioperative antibiotics. Data on specific risk factors and infection prevention process measures may also be collected, especially to determine the cause of elevated rates and to monitor the progress of prevention efforts.

Because surgical patients are readily identifiable, the denominator (patients who undergo a surgical procedure) is easier to obtain than other healthcare-associated infections such as pneumonia, urinary tract infection, or bacteremia, for which the number of ventilator days, urinary catheter days, or intravenous-catheter days must be determined retrospectively. All surgical patients can be included in a registry at the end of the operative procedure. Indeed, most hospitals maintain computer databases for financial management (i.e., procedure or diagnosis codes) that allow infection prevention staff to identify the appropriate patients who have undergone operations to be included in the denominator. Hospitals that have a separate database for surgical services may collect demographic data and patient, operative, and environmental data that are useful to the infection prevention program. In hospitals that do not collect these data, infection prevention personnel must consider what information they need before they spend time and resources collecting data. Several investigators have found that they collected data on variables that ultimately did not help them determine which patients were at highest risk of developing an infection or facilitate prevention efforts.[25]

B Equations

Once data are collected and entered into a computerized database, one can tabulate SSI rates. The following formulas are used to calculate basic SSI rates. To calculate the rate of the outcome (e.g., SSI) in a clearly delineated population, for a given time (e.g., 1 month, 1 quarter, or 1 year), divide the numerator (the number of patients with SSI following the procedure of interest during the specified time period) by the denominator (the total number of patients who had the surgical procedure of interest during the specified time period), and then multiply the result by 100 to obtain a percentage. In general, 50 procedures should be performed before rates are calculated. Some examples follow.

1. **Service-specific rates:**
   Number of patients with SSI following a neurosurgical procedure × 100
   Number patients who had a neurosurgical procedure
2. **Surgeon-specific rates:**
   Number patients with SSI following an operation by a particular surgeon × 100
   Number of patients operated on by that surgeon
3. **Procedure-specific rates:**
   Number of SSI occurring after a specific procedure (e.g., cholecystectomy) × 100
   Number of a specific procedure (e.g., cholecystectomies) performed
4. **Risk-specific rates:**
   Number of SSIs in patients with a risk index score of 2 × 100
   Number of patients with a risk index score of 2
5. **Standardized Infection Ration (SIR):**
   Observed number of SSIs/

   Expected number of SSIs, based on benchmarks

[Expected number of SSIs are determined by applying a benchmark rate to the total number of procedures performed. For example, if 200 procedures were performed and the benchmark of interest was 2/100 procedures, the expected number of SSIs would be 4.]

Once infection prevention staff identify the population to be surveyed, the proper denominator is determined by searching the operating room logs or the hospital's computerized database. All of the patients in the defined population are followed throughout the time frame designated by the definition of SSI (i.e., 30 days postoperatively or 90 days postoperatively if an implant was inserted). For NHSN surveillance, the denominator needs to include the procedures with the ICD-9/ICD-10 codes specified by the CDC protocol. Each patient who develops an SSI is included in the numerator. If the denominator is too broad (e.g., all surgical patients in a large hospital), the group becomes very heterogeneous, and the calculated infection rate probably will be falsely low. Consequently, infection prevention personnel might not identify clusters of SSI or other problems. Surgeon-specific or procedure-specific rates more closely reflect true SSI rates. In general, data from at least 50–100 procedures should be included before calculating overall rates. Similarly, at least 50 procedures per surgeon are ideally included to generate meaningful surgeon-specific rates.

C Reporting Recommendations

The infection prevention program should stratify SSI rates by type of procedure or by specific risk indices to allow comparisons among surgeons or among hospitals. The traditional wound classification system[14] has served this purpose for a quarter of a century, but it has some limitations, as mentioned earlier. The CDC risk index is used widely today, but it does not perform well in certain circumstances,[19] while newer models also have limitations.[1,25] Despite these limitations, it is important to stratify the patients' risk by one of the available indices, particularly if the patients have numerous comorbidities or if the operative procedures performed in the hospital are quite complex.

The infection prevention program should report SSI rates to surgeons, operating room staff, and hospital administrators. The trend toward increasing transparency has provided employees "in the trenches" with improved perspectives about the magnitude of the institutional problem. However, for surgeon-specific SSI rates, confidentiality is of utmost importance, and codes should be used instead of names if these rates are calculated and reported. Reporting SSI rates to practicing surgeons has been shown to reduce rates by the

Hawthorne effect – the effect due to having one's performance observed.[9,11,13] Infection prevention personnel should periodically present the SSI data graphically and meet with surgical personnel to discuss rates, clusters, and specific cases. These discussions improve communication and cooperation between the infection prevention and surgical teams. Infection preventionists may learn ways to make the data more useful to the surgical team and may also use these feedback sessions as a means to reinforce the importance of preventive measures to reduce the SSI risk.

Other forms of reporting infections are promoted in the era of patient safety. Some providers ask for weekly updates of infections as they are identified. This allows performance improvement teams to investigate possible omissions in care that happened with the individual patients. In essence, teams can use these cases to do individual root cause or failure mode analyses. Infection preventionists send a brief summary of each case as identified. This technique requires prospective surveillance to be effective and efficient, and while attractive in the immediacy of data, it can lead to an underestimation of the SSI rate. Finally, report cards that present data in a simple fashion have become increasingly popular as a mechanism of informing leadership about patient safety issues.

The infection prevention program should report SSI rates, costs, lengths of stay associated with SSIs, and the effects of preventive measures to the hospital's leaders. Several investigators have demonstrated that SSIs are the primary independent determinant of hospital costs and length of stay after operative procedures.[52,53] Moreover, Olson and Lee demonstrated a $3 million cost savings in a 10-year wound surveillance program.[11] If an infection prevention program can demonstrate that surveillance and interventions reduce SSI rates, length of stay, and cost, then hospital leaders will be more willing to provide the program with resources.

Finally, infection prevention and control personnel should regularly review their data to determine whether they should adjust their priorities or focus their energy on specific problems. For example, if a program analyzes its data and finds, after a few months, that the sensitivity of the case-finding method used for postdischarge surveillance is very low (e.g., only 2 percent of SSIs are identified by this method), the infection prevention and control staff may change their case-finding method instead of spending time and energy for a year or more before realizing that the method was not effective.

IV Implementation of SSI Surveillance

Below we offer a few suggestions that the healthcare epidemiologist or infection preventionist might find useful when implementing or improving an SSI surveillance and prevention program. The infection preventionist is a very important component of any surveillance program and should have personality traits that facilitate a good working relationship with surgical personnel. Infection prevention personnel need training, feedback on performance, and time to attend conferences on healthcare-associated infections. The hospital epidemiologist and infection preventionists should be active members of their institution's infection control committee. Finally, in programs that use direct wound examination to identify SSIs, a surgeon should train infection prevention staff so that they can evaluate subtle nuances of a wound's appearance. In addition, validation of this process is as important as validating other SSI surveillance methodologies.

Most important, the infection prevention and control program must communicate and work closely with the surgical personnel so that they take the responsibility for SSI prevention. To achieve this goal, infection prevention staff should:

- Review the standard definitions of SSI with the surgical personnel so they understand the accepted criteria.
- If you have multiple infection preventionists, validate the case-finding strategies and definition application among infection preventionists to assure that survey is standard within the institution.
- Ask for input from the surgical staff about the format of SSI reports and whether surgeon-specific or procedure-specific SSI rates are preferred. Risk-stratify rates, whenever possible.
- Meet with surgeons, surgical nurses, and other personnel (e.g., NSQIP staff) on a regular basis to build trust and to discuss issues such as SSI surveillance and prevention methods.
- Visit the operating room routinely to identify potential problems and to develop rapport and mutual respect.
- Encourage surgical personnel to join the infection control committee.
- Join the surgical professional societies and attend its annual meeting in order to understand the surgical perspective on SSIs.
- Discuss protocols and goals for studies of SSIs with surgical staff and encourage them to participate.
- If rates are elevated and not as low as achievable, do further analysis and examine risk factors that may be modifiable. Review prevention processes to ensure adequate compliance.
- Attempt to develop creative strategies for identifying SSIs as the medical environment changes.
- Publish results of studies in surgical journals.

In addition, the infection prevention program needs adequate resources to conduct effective surveillance. Clerical support, computerized databases, data analysts, and medical records personnel contribute significantly to the SSI surveillance program. Specifically, the databases should be relational to facilitate searches and data presentation. If possible including data that may be collected by other services such as anesthesia will be helpful to ongoing programmatic support.

V Interventions to Prevent SSI

All infection prevention programs must have specific interventions and processes in place to reduce the risk of SSI. Once data are collected, tabulated, and analyzed, the infection control program can develop, implement, or modify interventions to further prevent SSI and reduce SSI rates. Infection prevention staff examines factors in the preoperative, intraoperative, and

Table 14.3 Standard infection prevention interventions to prevent surgical site infection

1. Administer antimicrobial prophylaxis according to evidence-based standards
   a. Administer within 60 minutes prior to incision
   b. Provide an appropriate agent based on expected flora to be encountered during the procedure
   c. Stop the antibiotic after the incision is closed
   d. Adjust dose based on patient weight
   e. Re-dose agent for prolonged procedures
2. Do not use razors to remove hair
3. Control blood glucose in postoperative period for all patients
4. Maintain normothermia during and after the procedure
5. Optimize tissue oxygenation by providing supplemental O2
6. Use skin preparatory agent that contains alcohol and a second disinfectant (e.g., chlorhexidine gluconate)
7. Use a checklist to ensure compliance with best practices
8. Use impervious plastic wound protectors for gastrointestinal and biliary tract procedures
9. Educate patients and surgeons about importance of SSI prevention

* Adapted from Anderson et al, *ICHE* 2014.[64]

postoperative periods for possible factors and interventions to prevent SSI.[54]

It is important to become familiar with the guidelines, recommendations, requirements, and strategies published by major authorities and agencies regarding SSI surveillance and prevention. The Hospital Infection Control Practices Advisory Committee (HICPAC) published guidelines for SSI prevention in 1999.[54] The Surgical Care Improvement Project (SCIP) grew out of the Surgical Infection Prevention Collaborative, which was initially created in 2002 by the Centers for Medicare and Medicaid Services.[55] These surgical care improvement projects identify evidence-based process measures (e.g., antimicrobial prophylaxis and proper hair removal) that can be monitored and improved to prevent SSI.[55–57] The World Health Organization (WHO) developed a surgery safety checklist, toolkit, and implementation guide as part of their Safe Surgery Saves Lives program. Implementation of the WHO checklist resulted in significantly decreased complications and decreased death among surgical patients in eight diverse hospitals worldwide.[58–60] The Institute for Healthcare Improvement incorporates both the SCIP prevention measures and the WHO Surgical Safety Checklist into its "5 Million Lives" campaign to improve the quality of healthcare for hospitalized patients.[61] The Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America published an updated "Compendium of Strategies to Prevent Healthcare-Associated Infections" in 2014 that includes a practical, concise implementation guide regarding SSI prevention strategies.[62–64] All hospitals should implement basic prevention strategies (Table 14.3), most effectively through bundled interventions and prevention practices.[65]

A Preoperative Intervention

Preoperative preparation of the patient is one area for intervention. Some variables cannot be modified (e.g., age, gender), but others can be modified (e.g., glucose control, hair removal). Several interventions, such as minimizing the duration of preoperative hospital stay and eradicating remote infections, have been shown to reduce SSI rates.[49] Infection prevention personnel need to assure that best practices are followed for proper hair removal and antiseptic skin preparation (Table 14.2). The preoperative stay should be as short as possible. Sometimes it is prudent to send patients home and readmit them for surgery. Surveillance for such processes has helped surgical teams drive processes to improve surgical outcomes.[65]

Patients who are colonized with *S. aureus* in the anterior nares are at increased risk of the development of SSI as well as other healthcare-associated infections.[66–69] A randomized double-blind clinical trial demonstrated that treatment with preoperative mupirocin decolonized the nares of patients and decreased *S. aureus* healthcare-associated infections in patients who were colonized.[69] Treated patients also had a decrease in *S. aureus* SSI rates that was not statistically significant. Another randomized, double-blind, placebo-controlled study concluded that rapid identification and decolonization of *S. aureus* was associated with a 2-fold reduction in the risk of *S. aureus* postoperative infection and 5-fold decrease in deep-incisional SSI.[70] Authors of a recent meta-analysis of 17 studies concluded that decolonization strategies prevent *S. aureus* and MRSA SSIs, though there was significant heterogeneity among the trials evaluated.[71] Overall, the intervention seems to be most valuable in patients undergoing elective high-risk procedures, such as orthopedic or cardiovascular surgeries.[72] Currently, the recommendation to provide decolonization for *S. aureus* colonization prior to surgery is described as a "special approach" in the most recent Compendium of strategies for the prevention of SSI.[64] Further study is needed to determine if this intervention can benefit a targeted subset of surgical patients. If used, however, the approach may best be delivered in a bundle of practices, including adjustment of perioperative prophylaxis.[65]

The surgical team should perform appropriate antiseptic scrubs and avoid long or artificial nails and jewelry. Infection prevention personnel need to assure that policies are in place (and followed) to restrict patient care of surgical staff with transmissible infectious diseases.[73] If, and only if, an epidemiologic investigation suggests that the source of the outbreak might be healthcare workers who carry the organism, infection prevention personnel should obtain appropriate cultures from the implicated individuals (e.g., cultures of nares and skin lesions for *S. aureus*; cultures of the throat, skin lesions, and if necessary, the vagina and rectum for *Streptococcus pyogenes*).

Finally, antimicrobial prophylaxis is crucial to preventing SSI for some procedures and must be administered according to published guidelines for each procedure.[74] To be effective,

the appropriate prophylactic antibiotic must be given using weight-based dosing, during the appropriate time interval and for the appropriate duration. Several groups of investigators have successfully utilized automated alerts and decision support as an intervention to improve administration and redosing of antimicrobial prophylaxis.[75–77] While guidelines allow for a 60-minute window (120 minutes for specific agents such as fluoroquinolones and vancomycin), it is important to allow adequate time for the serum and tissue concentrations to increase prior to incision. Some studies show superior efficacy when the dose is administered within 30 minutes prior to incision compared with administration between 30 and 60 minutes prior to incision.[78,79] Similarly, doses should be administered prior to inflation of tourniquets in procedures using "bloodless techniques."[80,81]

B Intraoperative Intervention

Implementation of best practices during the intraoperative period can reduce SSI rates. Proper ventilation should be maintained in all operating rooms, including positive air pressure, appropriate air exchanges, and appropriate air filters. Traffic through the operating room must be kept to a minimum. Operating room door openings lead to increased microbial load.[82,83] In fact, limiting the number of door openings during vascular surgical procedures was one of several components of a bundle that helped to reduce the rate of SSIs by 36 percent.[84] Operating room personnel must regularly monitor sterilization of surgical instruments and provide the data to infection prevention personnel to assure that procedures conform to guidelines and review these data with infection prevention personnel regularly. Immediate use of steam sterilization, previously known as "flash sterilization," should be limited and never used solely for convenience. Infection prevention personnel can work with surgical staff to assure that proper surgical attire and drapes are used.

Appropriate skin preparation is important. Alcohol is the most rapidly bactericidal disinfectant available, but does not have persistent activity. As a result, most currently available skin preparation agents combine alcohol with either chlorhexidine gluconate or an iodophor. The most effective additional disinfectant is unclear. A randomized trial of 849 patients compared rates of SSI after using chlorhexidine gluconate plus alcohol, or povidone-iodine (without alcohol) for preoperative skin preparation; 40 percent fewer SSIs were observed in the chlorhexidine gluconate plus alcohol group.[85] In contrast, a single-center quasi-experimental study compared povidone-iodine plus alcohol versus chlorhexidine gluconate plus alcohol and demonstrated that the lowest rates of SSI occurred when povidone-iodine plus alcohol was used.[86]

Studies have demonstrated that intraoperative hypothermia (even mild decreases in core body temperature) approximately triples the risk of SSI and leads to many other adverse events.[87–89] Therefore, normothermia, either central or local, should be maintained during and immediately after surgery. The main methods of warming include passive insulation, fluid warming, and active warming of the patient with a forced-air system. Hyperglycemia increases mortality in critically ill patients and increases the risk of many adverse outcomes including SSI in diabetic and nondiabetic patients.[90–94] For example, Latham et al. showed that postoperative hyperglycemia and previously undiagnosed diabetes approximately doubles the risk of SSI.[92] Interventions include screening for diabetes and hyperglycemia as well as intravenous insulin therapy. The risk of SSI is also directly related to tissue oxygenation.[95] Supplemental oxygen (80 percent vs. 30 percent inspired oxygen) during surgery and the immediate postoperative period has been shown to reduce rates of SSI by approximately half, particularly when coupled with normothermia and appropriate volume replacement in patients undergoing postoperative mechanical ventilation.[88,96,97]

Hospitals have been largely successful in implementing many of the above recommendations, particularly those required for public reporting (e.g., antimicrobial prophylaxis, avoiding shaving, normothermia, and hyperglycemia). As a result, CMS and other payors are focusing on other performance measures and no longer require reporting of many SSI prevention strategies. While this change is due to hospitals' successes, it also represents an opportunity to regress to pre-SCIP and CMS processes. Infection prevention teams must remain vigilant about process compliance with these important surgical prevention strategies despite the fact that public reporting of them is no longer required.

C Postoperative Intervention

Because most contamination happens during the operation through contact, droplet, or airborne transmission, events that occur during the postoperative period (e.g., improper dressing changes or isolation techniques) are less likely to contribute to SSIs. If epidemiological data indicate that postoperative care may be associated with increased SSI rates, the infection prevention and control staff may need to investigate practices during this period. For example, red cell transfusion has been associated with an increased risk of SSI; thus, restrictive transfusion strategies lead to lower rates of postoperative infection.[98] Similarly, postoperative wound care is not standardized. Insufficient evidence exists to guide the type (i.e., sterile), duration of use, and content (e.g., antiseptic or antimicrobial components) of postoperative sterile dressings.

In summary, interventions can be designed based on problems identified during surveillance and by close observation of current practices, knowledge of published guidelines for infection control, and close collaboration with surgeons and surgical staff. Performing surveillance for both the processes important in reducing SSI and the rates themselves and providing the results back to surgeons and to leaders can lower the rates of SSI.

Conclusion

Surveillance of SSIs and processes that prevent SSI are an important component of any infection prevention program, and it is a special form of continuous quality assurance in which the ultimate benefactors of control efforts are the patients. Therefore, the infection prevention programs should

define clear objectives, utilize precise definitions, and meticulously implement a surveillance system and interventions when needed.

Although methods of case-finding are hard to choose, the infection prevention team should focus on patients or procedures at high risk of infection if their resources are limited. Collecting data and calculating rates are useless if epidemiology and surgical staff do not use the data to prevent SSIs. To succeed in such an effort, infection prevention and control personnel must collaborate closely with surgical teams and utilize available guidelines and recommendations to implement, monitor, and improve compliance with SSI prevention measures. In the age of public reporting and reduced payments related to rates of SSI, collaboration is key.

As healthcare delivery shifts to the outpatient setting, numerous aspects of SSI surveillance must change, because many factors that influence the risk of SSI also will change. Surveillance methods that worked well in the past and were supported by well-designed studies may no longer be efficacious. We need creative research to determine how to best perform surveillance for SSI, how to risk-adjust rates of SSI, to identify which methods we should use for postdischarge surveillance, and to design and test new SSI prevention strategies. Indeed, exciting opportunities are open to those willing to accept the challenges.

References

1. Lewis SS, Moehring RW, Chen LF, Sexton DJ, Anderson DJ. Assessing the relative burden of hospital-acquired infections in a network of community hospitals. *Infect Control Hosp Epidemiol* 2013;**34**: 1229–1230.
2. Burke JP. Infection control: a problem for patient safety. *N Engl J Med* 2003;**348**: 651–656.
3. Zimlichman E, Henderson D, Tamir O, et al. Health care-associated infections: a meta-analysis of costs and financial impact on the US health care system. *JAMA Intern Med* 2013;**173**: 2039–2046.
4. Martone WJ, Nichols RL. Recognition, prevention, surveillance, and management of surgical site infections: introduction to the problem and symposium overview. *Clin Infect Dis* 2001;**33** Suppl 2:S67–S68.
5. Scott, RD II. The Direct Medical Costs of Healthcare-Associated Infections in U.S. Hospitals and the Benefits of Prevention. In: Economist Division of Healthcare Quality Promotion National Center for Preparedness D, and Control of Infectious Diseases; Coordinating Center for Infectious Diseases Centers for Disease Control and Prevention, ed. 2009: 13.
6. Engemann JJ, Carmeli Y, Cosgrove SE, et al. Adverse clinical and economic outcomes attributable to methicillin resistance among patients with Staphylococcus aureus surgical site infection. *Clin Infect Dis* 2003;**36**: 592–598.
7. Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ. The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. *Infect Control Hosp Epidemiol* 1999;**20**: 725–730.
8. McGarry SA, Engemann JJ, Schmader K, Sexton DJ, Kaye KS. Surgical-site infection due to Staphylococcus aureus among elderly patients: Mortality, duration of hospitalization, and cost. *Infect Cont Hosp Ep* 2004;**25**: 461–467.
9. Haley RW, Culver DH, White JW, et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. *Am J Epidemiol* 1985;**121**: 182–205.
10. Cruse PJ, Foord R. The epidemiology of wound infection: a 10-year prospective study of 62,939 wounds. *Surg Clin North Am* 1980;**60:** 27–40.
11. Olson MM, Lee JT, Jr. Continuous, 10-year wound infection surveillance: results, advantages, and unanswered questions. *Arch Surg* 1990;**125**: 794–803.
12. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infect Control Hosp Epidemiol* 1992;**13**: 606–608.
13. Ehrenkranz NJ, Richter EI, Phillips PM, Shultz JM. An apparent excess of operative site infections: analyses to evaluate false-positive diagnoses. *Infect Control Hosp Epidemiol* 1995;**16**: 712–716.
14. Ehrenkranz NJ, Richter EI, Phillips PM, Shultz JM. An apparent excess of operative site infections: analyses to evaluate false-positive diagnoses. *Infect Control Hops Epidemiol* 1995;**16**: 712–6.
15. Lee JT. Wound infection surveillance. *Infect Dis Clin North Am* 1992;**6**: 643–656.
16. Haley RW, Schaberg DR, McClish DK, et al. The accuracy of retrospective chart review in measuring nosocomial infection rates: results of validation studies in pilot hospitals. *Am J Epidemiol* 1980;**111**: 516–533.
17. Cardo DM, Falk PS, Mayhall CG. Validation of surgical wound surveillance. *Infect Control Hosp Epidemiol* 1993;**14**: 211–215.
18. Berard F, Gandon J. Postoperative wound infections: the influence of ultraviolet irradiation of the operating room and of various other factors. *Ann Surg* 1964;**160**(Suppl 2): 192.
19. Haley RW. Surveillance by objective: a new priority-directed approach to the control of nosocomial infections: The National Foundation for Infectious Diseases lecture. *Am J Infect Control* 1985;**13**: 78–89.
20. Sands K, Vineyard G, Platt R. Surgical site infections occurring after hospital discharge. *J Infect Dis* 1996;**173**: 963–970.
21. Anderson DJ, Arduino JM, Reed SD, et al. Variation in the type and frequency of postoperative invasive Staphylococcus aureus infections according to type of surgical procedure. *Infect Control Hosp Epidemiol* 2010;**31**: 701–709.
22. Ferraz EM, Bacelar TS, Aguiar JL, Ferraz AA, Pagnossin G, Batista JE. Wound infection rates in clean surgery: a potentially misleading risk classification. *Infect Control Hosp Epidemiol* 1992;**13**: 457–462.
23. Haley RW, Culver DH, Morgan WM, White JW, Emori TG, Hooton TM. Identifying patients at high-risk of surgical wound-infection: a simple multivariate index of patient susceptibility and wound contamination. *Am J Epidemiol* 1985;**121**: 206–215.
24. Culver DH, Horan TC, Gaynes RP, et al. Surgical wound infection rates by wound class, operative procedure, and patient risk index: National

Nosocomial Infections Surveillance System. *Am J Med* 1991;**91**: 152S–157S.

25. Roy MC, Herwaldt LA, Embrey R, Kuhns K, Wenzel RP, Perl TM. Does the Centers for Disease Control's NNIS System risk index stratify patients undergoing cardiothoracic operations by their risk of surgical-site infection? *Infect Cont Hosp Ep* 2000;**21**: 186–190.
26. Nichols RL, Smith JW, Robertson GD, et al. Prospective alterations in therapy for penetrating abdominal trauma. *Arch Surg* 1993;**128**: 55–63; discussion -4.
27. Wenzel RP, Osterman CA, Hunting KJ, Gwaltney JM, Jr. Hospital-acquired infections: I. Surveillance in a university hospital. *Am J Epidemiol* 1976;**103**: 251–260.
28. Yokoe DS, Noskin GA, Cunningham SM, et al. Enhanced identification of postoperative infections among inpatients. *Emerg Infect Dis* 2004;**10**: 1924–1230.
29. Platt R, Yokoe DS, Sands KE. Automated methods for surveillance of surgical site infections. *Emerg Infect Dis* 2001;**7**: 212–216.
30. Perl TM. *Surveillance, Reporting and the Use of Computers*. 2nd ed. Williams & Wilkins; 1993.
31. Huang SS, Placzek H, Livingston J, et al. Use of Medicare claims to rank hospitals by surgical site infection risk following coronary artery bypass graft surgery. *Infect Cont Hosp Ep* 2011;**32**: 775–783.
32. Calderwood MS, Kleinman K, Bratzler DW, et al. Use of Medicare claims to identify us hospitals with a high rate of surgical site infection after hip arthroplasty. *Infect Cont Hosp Ep* 2013;**34**: 31–39.
33. Manian FA, Meyer L. Comprehensive surveillance of surgical wound infections in outpatient and inpatient surgery. *Infect Control Hosp Epidemiol* 1990;**11**: 515–520.
34. Avato JL, Lai KK. Impact of postdischarge surveillance on surgical-site infection rates for coronary artery bypass procedures. *Infect Control Hosp Epidemiol* 2002;**23**: 364–367.
35. Delgado-Rodriguez M, Gomez-Ortega A, Sillero-Arenas M, Llorca J. Epidemiology of surgical-site infections diagnosed after hospital discharge: a prospective cohort study. *Infect Control Hosp Epidemiol* 2001;**22**: 24–30.
36. Ming DY, Chen LF, Miller BA, Anderson DJ. The impact of depth of infection and postdischarge surveillance on rate of surgical-site infections in a network of community hospitals. *Infect Control Hosp Epidemiol* 2012;**33**: 276–282.
37. Perencevich EN, Sands KE, Cosgrove SE, Guadagnoli E, Meara E, Platt R. Health and economic impact of surgical site infections diagnosed after hospital discharge. *Emerg Infect Dis* 2003;**9**: 196–203.
38. Noy D, Creedy D. Postdischarge surveillance of surgical site infections: a multi-method approach to data collection. *Am J Infect Control* 2002;**30**: 417–424.
39. Kent P, McDonald M, Harris O, Mason T, Spelman D. Post-discharge surgical wound infection surveillance in a provincial hospital: follow-up rates, validity of data and review of the literature. *ANZ J Surg* 2001;**71**: 583–589.
40. Burns SJ, Dippe SE. Postoperative wound infections detected during hospitalization and after discharge in a community hospital. *Am J Infect Control* 1982;**10**: 60–65.
41. Seaman M, Lammers R. Inability of patients to self-diagnose wound infections. *J Emerg Med* 1991;**9**: 215–219.
42. Anderson DJ, Kaye KS, Classen D, et al. Strategies to prevent surgical site infections in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;**29** Suppl 1:S51–S61.
43. Sands K, Vineyard G, Livingston J, Christiansen C, Platt R. Efficient identification of postdischarge surgical site infections: use of automated pharmacy dispensing information, administrative data, and medical record information. *J Infect Dis* 1999;**179**: 434–441.
44. Chalfine A, Cauet D, Lin WC, et al. Highly sensitive and efficient computer-assisted system for routine surveillance for surgical site infection. *Infect Control Hosp Epidemiol* 2006;**27**: 794–801.
45. Platt R, Kleinman K, Thompson K, et al. Using automated health plan data to assess infection risk from coronary artery bypass surgery. *Emerg Infect Dis* 2002;**8**: 1433–1441.
46. Hirschhorn LR, Currier JS, Platt R. Electronic surveillance of antibiotic exposure and coded discharge diagnoses as indicators of postoperative infection and other quality assurance measures. *Infect Control Hosp Epidemiol* 1993;**14**: 21–28.
47. Bouam S, Girou E, Brun-Buisson C, Karadimas H, Lepage E. An intranet-based automated system for the surveillance of nosocomial infections: prospective validation compared with physicians' self-reports. *Infect Control Hosp Epidemiol* 2003;**24**: 51–55.
48. Burke JP. Surveillance, reporting, automation, and interventional epidemiology. *Infect Control Hosp Epidemiol* 2003;**24**: 10–12.
49. Mayhall CG. *Surgical Infections Including Burns*. Baltimore, MD: Williams & Wilkins; 1993.
50. DS K, AB K. *Postoperative Infections and Antimicrobial Prophylaxis*. 4th ed. New York, NY: Chirchill Livingstone; 1995.
51. Nagachinta T, Stephens M, Reitz B, Polk BF. Risk factors for surgical-wound infection following cardiac surgery. *J Infect Dis* 1987;**156**: 967–973.
52. Weintraub WS, Jones EL, Craver J, Guyton R, Cohen C. Determinants of prolonged length of hospital stay after coronary bypass surgery. *Circulation* 1989;**80**: 276–284.
53. Taylor GJ, Mikell FL, Moses HW, et al. Determinants of hospital charges for coronary artery bypass surgery: the economic consequences of postoperative complications. *Am J Cardiol* 1990;**65**: 309–313.
54. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Am J Infect Control* 1999;**27**: 97–132; quiz 3–4; discussion 96.
55. Bratzler DW, Hunt DR. The surgical infection prevention and surgical care improvement projects: national initiatives to improve outcomes for patients having surgery. *Clin Infect Dis* 2006;**43**: 322–330.
56. Bratzler DW, Houck PM, Richards C, et al. Use of antimicrobial prophylaxis for major surgery: baseline results from The National Surgical Infection Prevention Project. *Arch Surg-Chicago* 2005;**140**: 174–182.
57. Dellinger EP, Hausmann SM, Bratzler DW, et al. Hospitals collaborate to decrease surgical site infections. *Am J Surg* 2005;**190**: 9–15.
58. Haynes AB, Weiser TG, Berry WR, et al. A surgical safety checklist to reduce morbidity and mortality in a global population. *N Engl J Med* 2009;**360**: 491–499.

59. Weiser TG, Haynes AB, Dziekan G, et al. Effect of a 19-item surgical safety checklist during urgent operations in a global patient population. *Ann Surg* 2010;**251**: 976–980.
60. van Klei WA, Hoff RG, van Aarnhem EEHL, et al. Effects of the introduction of the WHO "Surgical Safety Checklist" on in-hospital mortality: a cohort study. *Ann Surg* 2012;**255**: 44–49.
61. Institute for Healthcare Improvement. 2009. Available at: www.ihi.org. Accessed April 22, 2009.
62. Yokoe DS, Mermel LA, Anderson DJ, et al. A compendium of strategies to prevent healthcare-associated infections in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;**29** Suppl 1:S12–S21.
63. Yokoe DS, Classen D. Improving patient safety through infection control: a new healthcare imperative. *Infect Cont Hosp Ep* 2008;**29**:S3–S11.
64. Anderson DJ, Podgorny K, Berrios-Torres SI, et al. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014;**35**: 605–627.
65. Schweizer ML, Chiang HY, Septimus E, et al. Association of a bundled intervention with surgical site infections among patients undergoing cardiac, hip, or knee surgery. *JAMA* 2015;**313**: 2162–2171.
66. Perl TM, Golub JE. New approaches to reduce Staphylococcus aureus nosocomial infection rates: treating S. aureus nasal carriage. *Ann Pharmacother* 1998;**32**:S7–S16.
67. Wenzel RP, Perl TM. The significance of nasal carriage of Staphylococcus aureus and the incidence of postoperative wound infection. *J Hosp Infect* 1995;**31**: 13–24.
68. Kluytmans J, van Belkum A, Verbrugh H. Nasal carriage of Staphylococcus aureus: epidemiology, underlying mechanisms, and associated risks. *Clin Microbiol Rev* 1997;**10**: 505–520.
69. Perl TM, Cullen JJ, Wenzel RP, et al. Intranasal mupirocin to prevent postoperative Staphylococcus aureus infections. *N Engl J Med* 2002;**346**: 1871–1877.
70. Bode LG, Kluytmans JA, Wertheim HF, et al. Preventing surgical-site infections in nasal carriers of Staphylococcus aureus. *N Engl J Med* 2010;**362**: 9–17.
71. Schweizer M, Perencevich E, McDanel J, et al. Effectiveness of a bundled intervention of decolonization and prophylaxis to decrease Gram positive surgical site infections after cardiac or orthopedic surgery: systematic review and meta-analysis. *BMJ* 2013;**346**: f2743.
72. van Rijen M, Bonten M, Wenzel R, Kluytmans J. Mupirocin ointment for preventing Staphylococcus aureus infections in nasal carriers. *Cochrane Database Syst Rev* 2008: CD006216.
73. Surgical Attire. Association of periOperative Registered Nurses. Available at www.aorn.org/guidelines/clinical-resources/clinical-faqs/attire. Accessed March 28, 2016.
74. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery. *Surg Infect* 2013;**14**: 73–156.
75. Zanetti G, Flanagan HL, Jr., Cohn LH, Giardina R, Platt R. Improvement of intraoperative antibiotic prophylaxis in prolonged cardiac surgery by automated alerts in the operating room. *Infect Control Hosp Epidemiol* 2003;**24**: 13–16.
76. Webb ALB, Flagg RL, Fink AS. Reducing surgical site infections through a multidisciplinary computerized process for preoperative prophylactic antibiotic administration. *Am. J. Surg.* 2006;**192**: 663–668.
77. Kanter G, Connelly NR, Fitzgerald J. A system and process redesign to improve perioperative antibiotic administration. *Anesth Analg* 2006;**103**: 1517–1521.
78. Steinberg JP, Braun BI, Hellinger WC, et al. Timing of antimicrobial prophylaxis and the risk of surgical site infections: results from the Trial to Reduce Antimicrobial Prophylaxis Errors. *Ann Surg* 2009;**250**: 10–16.
79. van Kasteren MEE, Mannien J, Ott A, Kullberg BJ, de Boer AS, Gyssens IC. Antibiotic prophylaxis and the risk of surgical site infections following total hip arthroplasty: timely administration is the most important factor. *Clin Infect Dis* 2007;**44**: 921–927.
80. Soriano A, Marco F, Martinez JA, et al. Influence of vancomycin minimum inhibitory concentration on the treatment of methicillin-resistant Staphylococcus aureus bacteremia. *Clin Infect Dis* 2008;**46**: 193–200.
81. Akinyoola AL, Adegbehingbe OO, Odunsi A. Timing of antibiotic prophylaxis in tourniquet surgery. *J Foot Ankle Surg* 2011;**50**: 374–376.
82. Andersson AE, Bergh I, Karlsson J, Eriksson BI, Nilsson K. Traffic flow in the operating room: an explorative and descriptive study on air quality during orthopedic trauma implant surgery. *Am J Infect Control* 2012;**40**: 750–755.
83. Pada S, Perl TM. Operating room myths: what is the evidence for common practices. *Curr Opin Infect Dis* 2015;**28**: 369–374.
84. van der Slegt J, van der Laan L, Veen EJ, Hendriks Y, Romme J, Kluytmans J. Implementation of a bundle of care to reduce surgical site infections in patients undergoing vascular surgery. *PLoS One* 2013;**8**: e71566.
85. Darouiche RO, Wall MJ, Jr., Itani KM, et al. Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. *N Engl J Med* 2010;**362**: 18–26.
86. Swenson BR, Hedrick TL, Metzger R, Bonatti H, Pruett TL, Sawyer RG. Effects of preoperative skin preparation on postoperative wound infection rates: a prospective study of 3 skin preparation protocols. *Infect Control Hosp Epidemiol* 2009;**30**: 964–971.
87. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization: study of wound infection and temperature group. *N Engl J Med* 1996;**334**: 1209–1215.
88. Sessler DI, Akca O. Nonpharmacological prevention of surgical wound infections. *Clin Infect Dis* 2002;**35**: 1397–1404.
89. Melling AC, Ali B, Scott EM, Leaper DJ. Effects of preoperative warming on the incidence of wound infection after clean surgery: a randomised controlled trial. *Lancet* 2001;**358**: 876–880.
90. Latham R, Lancaster AD, Covington JF, Pirolo JS, Thomas CS. The association of diabetes and glucose control with surgical-site infections among cardiothoracic surgery patients. *Infect Cont Hosp Ep* 2001;**22**: 607–612.
91. Dellinger EP. Preventing surgical-site infections: the importance of timing and glucose control. *Infect Control Hosp Epidemiol* 2001;**22**: 604–606.
92. van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med* 2001;**345**: 1359–1367.
93. Kwon S, Thompson R, Dellinger P, Yanez D, Farrohki E, Flum D. Importance of perioperative glycemic control in general surgery: a report from the Surgical Care and Outcomes Assessment Program. *Ann Surg* 2013;**257**: 8–14.

94. Umpierrez GE, Smiley D, Jacobs S, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 surgery). *Diabetes Care* 2011;**34**: 256–261.

95. Hopf HW, Hunt TK, West JM, et al. Wound tissue oxygen tension predicts the risk of wound infection in surgical patients. *Arch Surg* 1997;**132**: 997–1004; discussion 5.

96. Greif R, Akca O, Horn EP, Kurz A, Sessler DI, Grp OR. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. *N Engl J Med* 2000;**342**: 161–167.

97. Bickel A, Gurevits M, Vamos R, Ivry S, Eitan A. Perioperative hyperoxygenation and wound site infection following surgery for acute appendicitis: a randomized, prospective, controlled trial. *Arch Surg* 2011;**146**: 464–470.

98. Rohde JM, Dimcheff DE, Blumberg N, et al. Health care–associated infection after red blood cell transfusion: a systematic review and meta-analysis. *JAMA* 2014;**311**: 1317–1326.

Chapter 15

Surveillance and Prevention of Infections Associated with Vascular Catheters

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1 Introduction

Healthcare-associated bloodstream infections are mostly due to central venous catheters (CVCs) and therefore represent a typical device-associated infection. Often labeled central line-associated bloodstream infection (CLABSI), they reflect the use of vascular catheters in different compartments of the healthcare system. We now know that the proportion of patients with CVCs is highest in intensive care units (ICU) but that the greatest number of CVCs will be encountered outside the ICU, contributing to the majority of catheter-days.[1] These catheters are used for administering fluids and medications, for hemodialysis, and to provide parenteral nutrition. A landmark study by Pronovost and colleagues demonstrated that a large portion of CLABSIs can be prevented combining a handful of evidence-based measures.[2] CLABSI thus became the first healthcare-associated infection (HAI) where the goal of "zero tolerance" was discussed. This chapter will explore the basics on epidemiology, risk factors, and outcomes, and prepare a hospital epidemiologist or infection preventionist with the tools to set up CLABSI surveillance, and to select and implement preventive measures.

Epidemiology

In the United States, approximately 7 million central venous catheters are used each year, and an estimated 250,000 episodes of CLABSI are diagnosed, resulting in a rate of infections per 1,000 catheter days that ranges from below 1 to around 10/1,000 catheter days.[3] The most common pathogens involved in these infections are coagulase-negative staphylococci (CoNS), *Staphylococcus aureus* and others such as enterococci, Gram-negative bacteria, and yeast. Demonstrating an attributable mortality of 2–25 percent (cf. Table 15.1), CLABSI are associated with at least 10,000 deaths annually in the U.S. alone. The estimated cost per CLABSI ranges from $4,000 to $40,000, which may significantly contribute to the financial burden of a healthcare system. Prolonging the length of stay is maybe the most important contributor to costs. Additional complications, such as endocarditis or osteomyelitis, may trigger further expenses.

CLABSI constitute 12–15 percent of all HAI, as demonstrated by the European EPIC and EPIC2 reports.[15,16] In neonatal ICUs, this figure was as high as 37 percent, making CLABSI the predominant neonatal HAI. The CLABSI epidemiology not only differs depending on patient age (cf. Figure 15.1) but also on the type of hospital, the type of ICU, and the country where the surveillance is conducted. In the National Healthcare Safety Network (NHSN) publication from 2015, median incidence rates were as follows: 0.8 CLABSI episodes/1,000 catheter-days for cardiothoracic ICUs; 1.1–1.2 episodes/1,000 for medical ICUs; 1.4 episodes/1,000 for trauma

Table 15.1 Attributable mortality, length of stay, and costs of central line-associated or related bloodstream infections

Author	Year of publication	Reference	Attributable mortality	Attributable length of stay	Attributable costs (US$)
Pittet	1994	(4)	25%	24	41,000
Soufir	1999	(5)	25%	-	-
Digiovine	1999	(6)	4%	7	17,000
Rello	2000	(7)	13%	20	4,000
Pelletier	2000	(8)	14%	-	-
Renaud	2001	(9)	12%	9.5	-
Rosenthal	2003	(10)	25%	12	4,900
Blot	2005	(11)	2%	12	14,000
Stevens	2014	(12)	19%	30	32,000
Goudie	2014	(13)	-	19	55,646

Modified from (14).

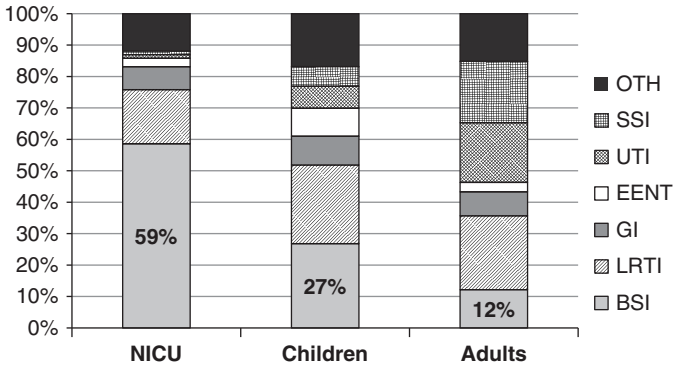

Figure 15.1 Distribution of healthcare-associated infections among adults, children and neonatesin Europe – ECDC point prevalence survey. BSI: Bloodstream infection; LRTI: Lower respiratory tract infection; GI: Gastrointestinal infection; EENT; Eye-ear-nose-throat infection; UTI: Urinary tract infection; SSI: Surgical site infection.

ICUs; 2.9 episodes/1,000 for burn units; and 0.3–1.3 episodes/1,000 for pediatric ICUs.[17] A UK study observed lower infection rates among nonteaching compared to teaching hospitals (2.8/1,000 catheter days versus 5.4/1,000 catheter days).[18] These data most likely reflect case-mix differences across hospital types. Also, ICUs in lower-income countries have reported much higher CLABSI rates compared to those in high-income countries.[19] The International Nosocomial Infection Control Consortium (INICC) report from 2014 identified an incidence density of 4.8/1,000 catheter days in 465 ICUs from 43 countries by using the NHSN CLABSI definition.[20]

Terminology

Different terms are in use for catheter infections. CLABSI is commonly used for surveillance purposes, whereas catheter-related bloodstream infection (CRBSI) requires the catheter tip to be cultured and therefore cannot be established if the catheter is left in place. CRBSI is therefore largely reserved for clinical diagnosis. Surveillance diagnosis and clinical diagnosis should not be confused. Less commonly used descriptors are intravascular catheter-related infections (IV-CRI) and central venous catheter associated bloodstream infection (CVC-BSI). For ease of reading, we will use the acronym CLABSI throughout the chapter.

In addition to BSI, local exit-site infections may be due to an intravascular catheter. In terms of pathogenesis, these derive from pathogens moving into tissues along the outer surface of the catheter. In BSI, however, the pathogenesis can either be from pathogen migration along the outside of the catheter (i.e., mostly earlier BSI) or via the catheter lumen by means of hub contamination or contaminated fluids (i.e., in later infections).

History

The first documented central venous line was a catheter to the right ventricle by Forssmann in 1929. In 1952, the subclavian vein was first used as an access site, and in 1966 the access to the internal jugular vein was pioneered. Early on, mechanical complications, such as fractures and leakage of the catheter, air embolisms, or hub separation were the predominant concerns. However, catheter colonization and CRBSI were soon described and recognized as relevant complications.[21] In response to that, new catheter designs, including the Luer-lock mechanism and catheter cuffs, were developed[22] and catheter materials like silicone and polyurethane were found to be less thrombogenic and less likely to become colonized with pathogens.[23]

In the 1970s, SENIC was the first multicenter observational study to determine rates of different HAIs.[24] The authors observed a reduction in infection rates simply by establishing formal infection prevention and control teams and by feeding back surveillance data. Subsequently, different guidelines on CLABSI prevention were assembled, among which the first CDC HICPAC guideline, published in 2002, stands out.[25] Also, in 2008, the Society for Healthcare Epidemiology of America (SHEA) published a "Compendium of strategies to prevent healthcare-associated infections in acute care hospitals" with the goal to provide a comprehensive set of guidance papers, supported by multiple professional societies. This compendium includes a separate CLABSI section and was updated in 2014.[26]

More recently, the decision taken by the Centers for Medicare and Medicaid Services (CMS) in 2008 not to reimburse hospitals for CLABSIs has highlighted the growing interest in preventing these infections and the attention HAIs and infection prevention receive from a healthcare policy perspective. Outcome surveillance for CLABSI using NHSN definitions with reporting to the CDC has become mandatory in 32 US states as of March 2016.

Catheter Types

The epidemiology of CLABSI varies somewhat with the type of catheter used, as evidenced in a comprehensive review by Maki and colleagues.[27] The incidence rates for CVC, peripherally inserted central catheters (PICC), tunneled CVC, peripheral venous catheters, and implantable port systems were 2.7/1,000 catheter-days, 2.1/1,000, 1.6/1,000, 0.5/1,000, and 0.1/1,000, respectively. PICC lines are often perceived as a safer alternative to nontunneled CVCs. However, the performance of such catheters is not superior to nontunneled CVCs if they are used for the same purpose, as was further demonstrated in a recent nonrandomized intervention study where incidence densities between 638 CVCs and 622 PICC lines were 2.4/1,000 and 2.3/1,000 device-days, respectively.[28]

Peripheral venous catheters (PVC), lastly, are the most frequently used invasive devices in hospitals. Up to 70 percent of patients receive a peripheral venous line during their hospital stay, and conservative estimates suggest that PVC-days account for 15–20 percent of total patient-days in acute care.[29] Only few studies address the problem of PVC-associated BSI, mostly because the incidence density of PVC-BSI is low and thrombophlebitis is a more common problem (cf. Figure 15.2, appendix). Another type of intravascular catheter, the arterial catheter, is not within the scope of this chapter.

Table 15.2 Modifiable risk factors for catheter-associated bloodstream infections

Risk factor	References	Study design	Quality improvement
Duration of catheterization	(32)	NCC	Catheter removal as soon as possible
Femoral access site	(32–34)	RCT	Femoral access site should be avoided
Guidewire exchange	(35, 36)	RCT	No guidewire exchange if CRBSI is suspected
Multilumen catheters	(37)	NCC	Single-lumen catheters should be preferred
Catheter-related thrombosis	(38–40)	NCC	Prophylactic anticoagulation or heparin-coated catheters
Parenteral nutrition	(41–43)	NCC	Encouraging enteral feeding
Reduced nutritional status	(44, 45)	RCT, PPS	Diminishing nutritional risk; optimizing energy supplementation
Unfavorable nurse-to-patient ratio and high workload	(46–50)	NCC	Improving nurse-to-patient ratio
High proportion of pool or agency nurses	(46, 51, 52)	NCC	Reducing employment of agency nurses
Positive organizational culture and safety climate	(46, 53–55)	QRS	Improving the organizational culture (leadership, pathways, work satisfaction)

NCC: Non-controlled cohort; RCT: Randomized-controlled trial; PPS: Point prevalence survey; QRS: qualitative research study.

Risk Factors

To understand how best to address CLABSIs from an infection prevention perspective, one needs to review the risk factors. These factors can be divided into modifiable and nonmodifiable factors. First and foremost, duration of catheterization correlates with risk of CLABSI. Some other factors can easily be influenced, such as catheter site, where the subclavian site is widely accepted to confer lower risk compared to the jugular or femoral veins.[30,31] Other risk factors are colonization of both the insertion site and the catheter hub as well as length of hospital stay prior to catheterization. Nonmodifiable examples of risk factors are gender (females are at decreased risk) and premature birth. See below Table 15.2 for a list of risk factors.

2 How to Start a Surveillance Program for CLABSI

The toolbox for starting a surveillance program includes: 1) applicable surveillance definition, 2) standardized patient data, 3) standardized microbiology results, 4) denominator data (i.e., catheter-days, representing time at risk), 5) a method of calculating infection rates, and 6) a strategy to provide feedback to those involved in patient care as well as those accountable for patient safety. Informatics support for these elements of surveillance is also essential. The main objectives of any surveillance are fourfold: 1) to provide a benchmark within one's own institution over time (i.e., internal benchmarking) and against competing institutions (i.e., external benchmarking), 2) to allow for measuring the effect of preventive strategies, 3) to detect clusters or outbreaks, and 4) provide data for risk management. Surveillance, importantly, is an iterative process that should be simple, feasible, and widely accepted. Data must be representative and available in due time.

One of the important decisions to be made is in which area(s) of the hospital to perform CLABSI surveillance. Given that surveillance is time- and labor-intensive, the most common choices are ICUs and (if present) bone marrow transplant units. Both patient populations are vulnerable, and CLABSI may result in worse outcomes compared to patients in other specialties, and both units use central vascular access extensively. If a certain ward anecdotally appears to have problems with catheter infections, directed surveillance generates baseline data. Hospital-wide CLABSI surveillance is rarely done due to the considerable effort it requires. However, electronic surveillance of laboratory-confirmed bacteremia may include multiple units and floors or even the entire hospital (due to the fact that data are accrued automatically) and helps to detect areas where more intensive surveillance is required.[56]

Traditionally, only inpatients have been subjected to CLABSI surveillance. However, the growing number of catheters used in outpatients may make corresponding surveillance necessary. In particular, peripherally-inserted central catheters (PICCs) may be left in place for weeks to months to provide outpatient antimicrobial therapy (OPAT), ambulatory chemotherapy, or parenteral nutrition. Postdischarge surveillance is required for adequately monitoring PICC lines in outpatients. However, the acquisition of clinical data in outpatients is cumbersome, and surveillance rarely is performed in such settings.

Defining CLABSI

Most hospitals employ the CDC NHSN definition (www.cdc.gov/nhsn/acute-care-hospital/clabsi/index.html), which is also

the basis for the majority of epidemiological research in the field. Slightly different definitions are used in Europe, e.g., in Germany, which has a large surveillance system called Krankenhaus Infektions-Surveillance System (KISS) (www.nrz-hygiene.de/surveillance/kiss/) based on the European Centre for Disease Prevention and Control (ECDC) (http://ecdc.europa.eu/EN/HEALTHTOPICS/HEALTHCARE-ASSOCIATED_INFECTIONS/Pages/index.aspx). Overall, surveillance definitions for CLABSI are more straightforward compared to those for other HAIs such as surgical site infection or ventilator-associated pneumonia.

The CDC surveillance definition of a laboratory-confirmed BSI (LCBI) requires a positive blood culture in a patient where the recovered pathogen cannot be linked to an infection at another body site. If the patient has a CVC in place at the time of the BSI or in the 48 hours before the subsequently positive blood culture was taken, this qualifies as CLABSI. Importantly, there is no minimum required duration of catheterization as part of this definition (www.cdc.gov/nhsn/). Skin contaminants are a diagnostic challenge because true infection can often neither be confirmed nor ruled out. The NHSN definition requires the same common commensal (i.e., diphtheroids [*Corynebacterium* spp. not *C. diphtheriae*], *Bacillus* spp. [not *B. anthracis*], *Propionibacterium* spp., CoNS [including *S. epidermidis*], viridans group streptococci, *Aerococcus* spp., and *Micrococcus* spp.) to be cultured from two or more blood cultures drawn on separate occasions.

From a surveillance perspective, it is important to mention a new subset of CLABSI that was first established in 2013, "mucosal barrier injury laboratory-confirmed bloodstream infection." This "MBI-LCBI" subset takes into account that oncology patients can develop BSI from translocation of gut bacteria (which may be misattributed to the CVC concurrently in place). What proportion of infections in oncology previously labeled as CLABSI are actually MBI-LCBI is currently being debated.[57]

For diagnosing BSI that is due to a central venous catheter, a *clinician*, however, may deem sufficient to find positive blood cultures in a catheterized patient who has no alternative focus of infection. Importantly, physical findings, such as redness around the catheter site, are not reliable in diagnosing BSI related to a CVC.

Diagnosing CLABSI

After adequate skin disinfection, blood cultures should be obtained from both the catheter and a peripheral vein prior to starting antibiotics. Growth of *Staphylococcus aureus*, yeast, or coagulase-negative staphylococci (CoNS) in blood cultures should raise the suspicion of the CVC being the source of the bacteremia (of note, the latter often are contaminants). Also, Gram-negative bacteria are not uncommon agents. If the clinical assessment suggests that the BSI is a consequence of a focus of infection at another body site, this is called secondary BSI and does not qualify as CLABSI. In contrast, primary BSI has no discernible focus or else is considered due to the CVC in place, with a wider range of possible causative agents. If symptoms improve after removal of a catheter, even without any microbiological diagnosis, this is also suggestive for CLABSI. For suspected exit-site infections with drainage, an exit-site culture should be obtained.

Diagnostic approaches (along with laboratory criteria for diagnosis) depend on the capacity of the individual lab and can be classified based on whether the catheter in question is removed or retained.

One traditional method is the semiquantitative approach first demonstrated by Maki et al., where the catheter is removed and its tip (ideally 5 cm) is rolled over an agar plate for culturing ("roll-plate method"). The cut-off for this method is 15 colony-forming units (CFU) and requires the same organism to grow in blood cultures; it exhibits high sensitivity and specificity. Another method involves luminal flushing or sonication in order to obtain quantitative data. A cut-off of 1,000 CFU has been shown to be indicative of infection, particularly in long-term catheters. As both methods above require catheter removal, they should only be pursued if the likelihood of CLABSI is high.

Conversely, one method that does not require catheter removal is to draw blood simultaneously through the catheter in question as well as peripherally and to compare colony counts (CFU have to be 3–5 times higher in catheter blood cultures compared to peripheral blood cultures for a diagnosis of CLABSI).[58] In a meta-analysis, this diagnostic method was found to be the most reliable approach. Also, quantitative cultures can be obtained via the catheter (with a 100 CFU/mL cut-off) and, in contrast, they appear to be the most cost-effective approach.[59] An alternative and third approach is the so-called *differential time to positivity*, where the CVC can also be left in place.[60] Here, blood is obtained from the catheter and from a peripheral vein. If the blood sampling from the catheter shows growth >2 hours earlier than that from the peripheral vein, the catheter is the most likely source of infection. Qualitative methods are not recommended in this context.

Analysis and Feedback of Infection Rates

The standard approach of calculating and feeding back rates is to set the number of infections in relation to the exposure risk, which – in this case – is catheter dwell time. Thus, the rate is usually expressed as infections/1,000 catheter-days. The 95 percent confidence interval provides an estimate of the variation in event rates and allows comparison to other rates. The standardized infection ratio, SIR, is an alternative way to report data. The SIR is a reference value based on the measurement of outcomes in a standard population and adjusted for a number of risk factors. Outcome measures can be compared to this reference for external benchmarking purposes.

For better understanding, infection rates are frequently visualized in the form of curves. These data should be reviewed at set intervals during infection prevention meetings and then be communicated along with editorial notes to healthcare workers (HCWs) on the respective floor or unit. In addition to this communication channel, what has turned out to be essential for making improvements and also obtaining resources to do surveillance, is involving the hospital

Table 15.3 Preventive measures grouped by basic vs. special, behavior vs. technology, and split by the time of use (before, during, or after catheter insertion)

		Best practice procedures	Technology and material
Basic measures	Before	• Correct indication for catheter use • Correct choice of catheter type	
	During	• Hand hygiene • Skin antisepsis with alcohol-based CHG • Maximum sterile barrier precautions • Use of a checklist • Subclavian access site (>jugular ≫ femoral)	• All-inclusive catheter kit/cart • Ultrasound guidance
	After	• Remove catheter when no longer needed • Hand hygiene • Disinfect catheter hubs before accessing • Aseptic technique for all catheter handling • Comply with appropriate changing of tubes and hubs • Skin antisepsis with alcohol-based CHG	
Special measures	Before		• Choice of impregnated catheters if basic measures were not successful
	During		• CHG-impregnated sponges or dressings
	After	• Provide appropriate staffing level	• Antimicrobial locks • Antimicrobial coated connectors • CHG-impregnated sponges or dressings • Daily CHG bathing of the patient • Antimicrobial ointment at the access site in hemodialysis patients

Note. CHG = chlorhexidine gluconate.

leadership and others accountable for HAIs. Feeding back rates is crucial for the success of an ICP program.

The manual collection of catheter-days is relatively time consuming; therefore, electronic algorithms have been studied with the goal of facilitating surveillance.[61,62] These depend on the capacity of electronic medical record systems and are still not widely used.

In addition to measuring infection events and setting them in relation to the population at risk, process measures can be very helpful when trying to determine what can be improved in catheter insertion and care. Process indicators have the advantage of measuring common events (compared to CLABSI being rare events) and providing information about practice (e.g., the compliance with daily catheter rounds or the compliance with disinfection before accessing the catheter hub).

3 Preventive Measures

Before delving into specific measures and their potential effect, it should be restated that the impact of interventions can only be determined when dedicated surveillance is in place. Thus, first of all, the volume of CLABSI should be elicited before planning preventive measures. Also, measures are listed here individually; however, these measures were rarely used as stand-alones but have been grouped into "bundles" and were implemented using a multimodal strategy. We will start by briefly reviewing the most promising measures one by one.

Preventive measures can be divided into measures *before* insertion, *during* insertion, and *after* the catheter has been inserted, when providing catheter care. Also, basic measures can be distinguished from additional or special measures that should only be considered if rates have not dropped when establishing basic measures.[26] An alternative approach is to group measures into "best practice procedures" and "technology and material" (cf. Table 15.3). Typically, the former measures include selection of the access site, hand hygiene, maximal sterile barrier precautions, using aseptic technique for catheter insertion and care, and complying with the recommendations for changing tubes, hubs, and dressings. Typical "technology and material" measures encompass using impregnated catheters, ready-made catheter kits and carts, and antimicrobial locks. A good approach is to first make sure that best practice behavior is in place before moving to technology solutions. However, material such as ergonomic kits or comprehensive carts may help to achieve behavioral change. If preventive measures cannot be introduced institution-wide, efforts should focus on the most vulnerable patients,

including ICU patients, oncology patients, and neonates requiring intensive care (with accompanying unit-based surveillance). Furthermore, hemodialysis patients depending on the type of dialysis catheters represent a population at risk for CLABSI.

Preventive Measures: Best Practice Procedures

Before Insertion

Education: Whoever places a catheter should have adequate training. Ideally, some form of competency assessment and credentialing process accompanies this. There are many ways of providing education and training, but the most promising is the use of simulator training.[63]

Indication and Choice of the Catheter: Importantly, there must be an adequate indication for inserting a catheter, and then a suitable type of catheter must be selected. Administration of nonirritant drugs for a short period of time does not require central access. Administration of irritant drugs for a short duration of time can often be administered via a midline catheter. Prolonged drug therapy should take into account the expected duration and whether the patient stays in the hospital or is treated as an outpatient. In the first case, a regular nontunneled CVC can be used, in the latter scenario, the choice includes PICCs, a tunneled CVC, or a port system.

During Insertion

Hand Hygiene: Hand hygiene is the basis of all actions upon catheter insertion and during catheter care. Surgical hand hygiene (i.e., surgical "scrub") has not been formally shown to be superior to hygienic hand hygiene for catheter insertion.

Skin Antisepsis: Appropriate skin antisepsis is key, both surrounding catheter insertion and during catheter care. The most important factor in terms of effective skin antisepsis is the combination of alcohol (preferably isopropanol) and a substance with prolonged effectiveness, such as CHG, iodine or octenidine. Skin antiseptics must therefore be alcohol-based, except in preterm infants, where alcohol is toxic to the skin. The most commonly selected preparations are alcohol-based CHG, povidone-iodine (PI), and octenidine. A recent randomized controlled trial showed superiority of alcohol-based CHG over alcohol-based PI although the alcohol-composition differed between the two tested products.[64]

Maximum Barrier Precautions: Wearing a cap, a mask, sterile gloves, and a sterile gown together with using a large sterile drape that covers the entire patient elevates CVC insertion to the level of a surgical procedure. Together, these precautions provide an additional layer of security for maintaining a strictly aseptic technique, particularly when insertion is difficult. Maximum barrier precautions have become standard for the insertion of central lines.

Use a Checklist: The use of a checklist during the catheter insertion process has been shown to play a role in CLABSI prevention. However, it must be emphasized that its use was also linked to the presence of a second person, usually a nurse, during the process of CVC insertion. Whether the use of self-assessment checklists by the healthcare worker who inserts the catheter produces a similar effect needs to be determined.

Use an All-Inclusive Catheter Kit/Cart: Having all required material in one place is thought to make the process of inserting a catheter faster. It certainly simplifies the preparation of supplies at the patient side and prevents the operator from moving away from the patient during the procedure.

When Possible, Choose the Subclavian Vein for CVC Insertion and Avoid Femoral Access: Access to the subclavian vein is preferred over the jugular and femoral veins in terms of infection risk (31). This is particularly important in obese patients, where the femoral site is prone to CLABSI due to substantial bacterial colonization. Given the increased use of ultrasound for CVC insertion, the jugular vein has become the predominant access site due to better visualization (65).

Ultrasound Guidance: The use of ultrasound has become standard for CVC insertion in many hospitals and in some countries even is required. While its use to avoid mechanical complications is uncontested, the role in CLABSI prevention is still controversial. This is due to the fact that 1) using ultrasound for CVC insertion needs careful training so that no breach of aseptic technique occurs, and that 2) ultrasound use favors the jugular access, which has been shown to be inferior to the subclavian vein in terms of infection risk.

After Insertion

Catheter maintenance was initially overlooked in the first guidelines as there was little research into optimal maintenance. This topic has since received increasing attention.[66]

Disinfect Catheter Hubs before Accessing: There is good evidence that needleless access hubs must be correctly disinfected before use.[67]

Aseptic Technique for All Catheter Handling: This includes the correct choice of dressing materials and using a no-touch technique so as not to contaminate the catheter.

Comply with Appropriate Changing of Tubes and Hubs: Tubes and hubs must be changed no more frequently than 96 hours, except when they are used for blood products and lipid-containing parenteral nutrition. Semipermeable dressings can be left in place for up to 7 days.

Nurse-to-Patient Ratio: Although there is no evidence-based threshold for nurse-to-patient ratios, neither in the ICU nor in non-ICU wards, unfavorable nurse-to-patient ratios put patients at risk for HAI.[47] Staffing and thus workload of front-line healthcare workers must be adapted to acuity of care.

The Indication Has to Be Checked Daily: Given that duration of use is a risk factor for CLABSI, catheters should only be in place as long as indicated. Leaving CVCs for convenience should be avoided.

Preventive Measures: Technology and Materials

There are special measures that should only be considered if infection rates do not drop despite applying basic measures. Among them is the use of impregnated catheters, antimicrobial-coated connectors, antimicrobial locks, and CHG-

impregnated sponges and dressings. Some of these measures are discussed below.

Best Practice Intervention Studies and the Use of the Bundle Concept

Correct placement of a CVC requires compliance with every single step of the procedure and experience with the insertion technique. The concept of "bundles" has been established with the idea to help the operator remember and comply with a handful of key actions as a minimal standard. The most widely known "bundle" has been reported by the Michigan Keystone project,[2] but other CLABSI best practice interventions have used bundles as a promotion strategy as well. Some best practice intervention studies are listed in Table 15.4. A helpful evaluation of quality improvement interventions has been prepared by Blot and colleagues.[68]

Education and Training

"Team- and task-oriented education and training" and "Use of guidelines in combination with practical education and training" were 2 of 10 key components identified in a systematic review on the organization and management of infection prevention and control (IPC).[46] As a guiding principle, education and training should be hands-on,[84] at the bedside,[82] and/or use skills laboratories.[63,83,85,86] Multidisciplinary focus groups can help IPC programs focus on targets of interest and contribute to improved adherence to hand hygiene protocols and reduced HAI rates.[87,88] Qualitative studies in hand hygiene showed that although formal training is effective, [89] individual experience is perceived to be more important for infection prevention.[90] Education and training programs should be audited against predefined checklists revised over time to take into account local barriers and healthcare worker behavior.[46] Similarly, knowledge tests and competency assessments help to detect gaps and to adjust education and training activities to local needs. Guidelines as stand-alone documents do not change practice,[91] and "knowledge" alone does not change behavior. Physicians showed low adherence to MSB precautions for CVC insertion at a time when evidence for the effectiveness of MSB precautions had been available for more than 10 years and use recommended by several national guidelines.[25,92] Attitudes toward guidelines were more positive among nurses than physicians, and in pediatric more than in adult ICUs.[93] Guidelines are indispensable documents to set the stage for updating procedures, but they must be made "living" by being integrated in practical education and training.[46]

4 How to Implement Preventive Measures

It is one thing to know from the scientific evidence what needs to be done to reduce infection rates and another one to actually implement these measures. Implementation science is the field that attempts to understand and improve implementation of measures in general. In recent years, it has been realized that more focus needs to be placed on how preventive measures are implemented.

Studies on technology and practice change often report only the characteristics of the intervention but rarely comment on implementation. However, even the most effective evidence-based tool or prevention practice may not be applied if serious barriers prevent its implementation process. Hospitals often struggle to implement evidence-based recommendations. IPC programs aiming at changing the behavior of HCWs depend on various aspects. The more tangible factors include infrastructure, resources, ward occupancy, staffing, and available documents. The less tangible factors include "organizational" culture, which is a concept including structure, work organization, work satisfaction, and management. In addition, external factors interfere with decision making and prioritizing projects in the hospital.[94] In this context implementation takes place.

Damschroder and colleagues developed a conceptual model, the Consolidated Framework of Implementation Research (CFIR), which lists[95] five major domains interfering with successful implementation: 1) intervention characteristics, 2) outer setting, 3) inner setting, 4) characteristics of the individuals involved, and 5) the process of implementation. These five domains are neither static nor independent. Multimodality and multidisciplinarity of projects improve the likelihood of implementation success because they take into account the local context and the fact that different HCWs adopt an intervention by being involved in the steps of planning and executing. One of the key aspects of complying with the idea of multimodality and multidisciplinarity is the active participation of HCWs in training their peers.[83] Before, but also during the process of implementation, barriers should be identified, prioritized, and removed.[96] Sustainability of a project can be perceived as an iterative process of implementation, evaluation, and adaptation. For the purpose of facilitating the implementation process, the "4E" framework has been proposed: Engage – Educate – Execute – Evaluate. Resources, personnel, and material, need to be available at sufficient levels and thus, buy-in from the hospital leadership is crucial in making any preventive efforts work. Support is more than lip service. Inconsistency between the management's declared commitment compared with its daily support is negatively perceived by HCWs.[53] Leaders of hospitals who were successful in HAI prevention did: 1) cultivate a culture of clinical excellence and effectively communicated it to staff, 2) focus on overcoming barriers dealing directly with resistant staff or process issues that impeded HAI prevention, 3) inspire their employees, and 4) think strategically while acting locally.[54]

5 Controversial issues

Given the overwhelming success of best practice programs over the past years, the role of technology in the prevention of CLABSI has diminished. However, some products and technologies may contribute to CLABSI prevention and thus need to be discussed.

Table 15.4 Best practice intervention studies in the prevention of catheter-related or catheter-associated bloodstream infections

Study (authors)	Setting	Practice interventions	Implementation strategies	Control/intervention (N/1000 device-days)
Apisarnthanarak (69)	Hospital-wide, single center	Hand hygiene; full barrier precautions at catheter insertion; CHG for skin antisepsis; avoiding the femoral insertion site; removal of unnecessary catheters; optimal catheter care	Lectures; posters; hand hygiene tests	14.0/1.4 (P < 0.001)
Bion (70)	223 ICUs, multicenter	Hand washing; MSB at catheter insertion; checklist during catheter insertion; CHG for skin antisepsis; avoiding the femoral insertion site; CVC maintenance: aseptic access technique, daily site review, and removal of CVCs at earliest opportunity	Training days (data definitions, technical and nontechnical interventions); teleconference calls and internet-based teaching	3.7/1.5 (P < 0.001)
DePalo (71)	23 ICUs, multicenter	Hand washing; full barrier precautions at catheter insertion; CHG for skin-antisepsis; avoiding the femoral insertion site; removal of unnecessary catheters	CUSP	3.7/1.0 (P = 0.003)
Eggimann (72)	1 ICU, single center	Comprehensive intervention addressing material preparation, line insertion, dressing (change), CVC replacement, CVC care, CVC removal, hand hygiene	Slide-shows; practical demonstrations; bedside training	3.1/1.2 (P = 0.04)
Guerin (73)	2 ICUs, single center	Daily inspection of insertion site; site care in case of wet or soiled dressing; documentation of ongoing catheter need; hand hygiene before handling the intravenous system; alcohol scrub of infusion hubs before use	Practice training of catheter insertion; practice training of catheter care	5.7/1.1 (P = 0.004)
Marra (74)	1 ICU, single center	Hand washing; full barrier precautions at catheter insertion; central line cart; CHG for skin antisepsis; avoiding the femoral insertion site; removal of unnecessary catheters	Lectures; monthly feedback of bundle compliance	6.4/3.2 (P < 0.001)
Miller (75)	29 PICUs, multicenter	Hand hygiene; CHG for children ≥2 months; insertion cart; insertion checklist; daily review of line necessity; optimized catheter-care	Support and promotion by senior ICU leader; involvement of quality improvement leaders; workshops; local practice adaptation	5.4/3.1 (P < 0.001)
Palomar (76)	192 ICUs, multicenter	Hand washing; full barrier precautions at catheter insertion; checklist during catheter insertion; CHG for skin-antisepsis; subclavian vein as the preferred insertion site; removal of unnecessary catheters	CUSP; principles of engage, educate, execute, and evaluate	3.1/1.1 (P < 0.001)
Peredo (77)	2 ICUs, single center	Checklist for catheter insertion; CHG for skin antisepsis; avoiding the femoral insertion site; removal of unnecessary catheters	Lectures	6.7/2.4 (P = 0.015)

Table 15.4 (cont.)

Study (authors)	Setting	Practice interventions	Implementation strategies	Control/intervention (N/1000 device-days)
Perez (78)	3 ICUs, single center	Full sterile sheet for catheter insertion; subclavian vein as preferred insertion site; needleless catheter connectors; 2% CHG for skin antisepsis; parenteral nutrition via a multilumen CVC; optimal catheter care	Lectures; before and after knowledge tests	4.2/2.9 (P = 0.030)
Pronovost (2)	90 ICUs, multicenter	Hand washing; full barrier precautions at catheter insertion; checklist during catheter insertion; CHG for skin antisepsis; avoiding the femoral insertion site; removal of unnecessary catheters	CUSP	7.7/1.1 (P < 0.001)
Schulman (79)	18 NICUs, multicenter	Hand hygiene; central line kit or cart for catheter insertion; MSB; checklist for catheter insertion; CHG for skin antisepsis; optimized catheter care; checklist for catheter care; daily evaluation of catheter exit site; aseptic technique for catheter handling; "scrub the hub"; daily review of line necessity	State-wide workshops; periodic surveys and conference calls	3.5/2.1 (P < 0.001)
Venkatram (80)	1 ICU, single center	Hand hygiene; full barrier precautions at catheter insertion; checklist during catheter insertion; CHG for skin-antisepsis; preferring subclavian access; daily review of line necessity	Lectures	10.7/1.7 (P < 0.001)
Weber (81)	8 ICUs, single center	Hand washing; full barrier precautions at catheter insertion; checklist for catheter insertion; customized CVC insertion kits; alcohol-based CHG for skin antisepsis; avoiding the femoral insertion site; removal of unnecessary catheters	Lectures; repeated practice training for CVC insertion and care	8.9/2.4 (P < 0.001)
Zingg (82)	5 ICUs	Hand hygiene; optimized catheter dressing; no-touch technique for CVC manipulation; preparation of infusates; optimized catheter care	Tool preparation guided by frontline healthcare workers' perceptions bed-side training; lectures	3.9/1.0 (P < 0.01)
Zingg (83)	Hospital-wide, single center	Comprehensive intervention addressing CVC insertion, CVC care (dressing change, preparation of drugs/infusates), CVC removal, hand hygiene	Skills laboratories training for doctors; modular E-learning using a train-the-trainer system for nurses; optimized insertion set; trolleys for CVC insertion	2.3/0.7 (P < 0.001)

CHG: Chlorhexidine gluconate; CLABSI: central line-associated bloodstream infection; CRBSI: catheter-related bloodstream infection; CUSP: comprehensive unit-based safety program; CVC: central venous catheter; ICU: intensive care unit; MSB: maximum sterile barrier; NICU: neonatal intensive care unit; PICU: pediatric intensive care unit

Impregnated Catheters

Despite abundant literature on this topic, impregnated catheters are not being used consistently.[97] Many studies that tested impregnated catheters were of poor quality and only few included catheters with dwell-times longer than 12 days.[98] This is relevant as the effectiveness of CHG–silver sulfadiazine (CHG/SS) may not last for longer than one week.[99] Antibiotic-coated catheters (e.g., minocycline-rifampicin) have been shown to be more effective than CHG/SS CVCs and to significantly reduce CRBSI. A meta-analysis of eight randomized controlled trials on minocycline-rifampicin-impregnated catheters calculated a CRBSI reduction of more than 75 percent.[100] Most of the studies included in the meta-analysis, however, were sponsored by industry. Most importantly, the additional benefit of CHG/SS catheters may be limited once compliance with best practice procedures has improved.[101] Anti-infective catheters should not be recommended for prolonged catheter use and may only have a role when CLABSI rates continue to be above the institutional goal despite established best practice procedures.[102,103]

Chlorhexidine-Impregnated Dressings

Two randomized multicenter trials in France achieved significant CRBSI reductions after introducing CHG-impregnated sponges or CHG dressings.[104,105] CHG-impregnated sponges were also effective in oncology where CVCs remained in place for prolonged dwell times of >14 days.[106] The CRBSI IDs decreased from 7.2/1,000 device-days down to 3.8/1,000 ($P = 0.02$).

Antimicrobial Lock Solutions

Lock solutions serve either therapeutic or preventive purposes. For therapeutic use, the most recent clinical practice guidelines issued by the Infectious Diseases Society of America (IDSA) recommend antibiotic lock therapy for catheter salvage in uncomplicated CRBSI due to CoNS and enterococci.[107]

Ethanol works well *in vitro*,[108,109] and ethanol locks have been promoted as a simple means to prevent CLABSI. Some studies revealed favorable results with high ethanol concentrations (70 percent) in patients with long-dwelling catheters,[110,111] but others produced conflicting findings. A recent systematic review also identified a number of potential hazards with ethanol locks, such as structural changes of catheters *in vitro*, elution of molecules from the catheter polymers *in vitro*, systemic toxicity in clinical studies, increased catheter occlusion in clinical studies, and breaches in catheter integrity in clinical studies.[112] Urokinase was repeatedly reported to be a successful salvage therapy in children with tunneled long-dwelling catheters,[113,114] and was recently proposed as CRBSI prevention strategy.[115] However, it was only effective for CoNS in adults, and further studies are required to prove efficacy and safety of urokinase in this area. Lastly, a novel lock solution using a combination of 7 percent sodium citrate, 0.15 percent methylene blue, 0.15 percent methyl-paraben, and 0.015 percent propyl-paraben performed well in patients with hemodialysis catheters;[116] the 201 catheters that were locked with this product were significantly less at risk for CRBSI compared to the 206 controls that were locked with unfractionated heparin (0.24 vs. 0.82 per 1,000 catheter days; $P = 0.005$).

Bathing Patients with Chlorhexidine-Containing Solutions

Daily bathing of ICU patients with CHG cloths has reduced bacteremia due to vancomycin-resistant enterococci in an ICU[117] and a long-term care facility.[118] The results were confirmed in a cross-over cluster-randomized trial in 9 ICUs,[119] although HABSI rates during control and intervention periods were high (6.6/1,000 vs. 4.8/1,000 catheter-days, respectively). A cluster-randomized study in 43 hospitals with 74 ICUs tested three interventions: 1) screening and isolation of MRSA patients (without further measures); 2) targeted decolonization of identified MRSA patients; and 3) universal decolonization with mupirocin and CHG body wash of all ICU patients. BSI from any pathogen decreased most significantly by using the above-mentioned third intervention (6.1 vs. 3.6/1,000 catheter-days, respectively).[120] Even in neonates, CHG bathing was effective.[121] CLABSI rates only decreased in the population eligible for bathing (birth weight >1,000 g and/or age ≥28 days), but not in others. As CHG is used for hand hygiene, preoperative skin preparation, and now bathing patients in the ICU,[117,122,123] emerging resistance of this substance should be closely monitored due to extensive use.[124]

Ultrasound Guidance

Ultrasound-guided catheter insertion has been found to reduce CRBSI (from 16 percent to 10 percent) compared to the so-called landmark technique.[125] However, ultrasound had no effect in settings with lower CLABSI rates (incidence density: 2.1/1,000 device-days).[65,126] This is most likely due to ultrasound competing with best practice procedures.[126]

6 Conclusions

CLABSI is the most extensively studied device-associated infection and is largely preventable. It is also one of the four most frequent healthcare-associated infections and therefore a frequent target of surveillance programs. Given the fact that hospitals are no longer being reimbursed for CLABSIs by CMS, this may be the first surveillance project that was installed at your hospital (or it may the first you need to tackle). Most CVCs are placed outside the ICU although the percentage of patients with vascular access is highest in the ICU. In neonates, of note, CLABSI is the most common HAI. With bundles of preventive measures the CLABSI rate can be reduced dramatically.

Appendix

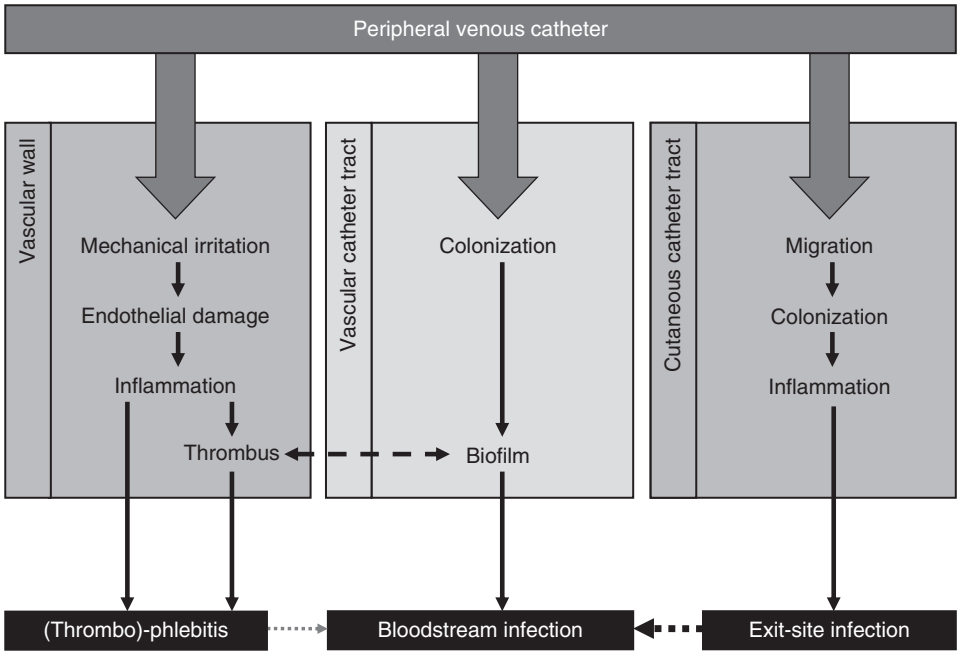

Figure 15.2 Overview of mechanisms for emerging thrombophlebitis, peripheral venous catheter-associated bloodstream infection and catheter exit-site infection (published in Zingg et al).[29]

References

1. Climo M, Diekema D, Warren DK, et al. Prevalence of the use of central venous access devices within and outside of the intensive care unit: results of a survey among hospitals in the prevention epicenter program of the Centers for Disease Control and Prevention. *Infect Control Hosp Epidemiol.* 2003;**24** (12):942–945.
2. Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med.* 2006;**355** (26):2725–2732.
3. Raad I, Hanna H, Maki D. Intravascular catheter-related infections: advances in diagnosis, prevention, and management. *Lancet infectious diseases.* 2007;**7** (10):645–657.
4. Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infection in critically ill patients: excess length of stay, extra costs, and attributable mortality. *JAMA.* 1994;**271** (20):1598–1601.
5. Soufir L, Timsit JF, Mahe C, Carlet J, Regnier B, Chevret S. Attributable morbidity and mortality of catheter-related septicemia in critically ill patients: a matched, risk-adjusted, cohort study. *Infect Control Hosp Epidemiol.* 1999;**20** (6):396–401.
6. Digiovine B, Chenoweth C, Watts C, Higgins M. The attributable mortality and costs of primary nosocomial bloodstream infections in the intensive care unit. *Am J Respir Crit Care Med.* 1999;**160**(3):976–981.
7. Rello J, Ochagavia A, Sabanes E, et al. Evaluation of outcome of intravenous catheter-related infections in critically ill patients. *Am J Respir Crit Care Med.* 2000;**162**(3 Pt 1):1027–1030.
8. Pelletier SJ, Crabtree TD, Gleason TG, Pruett TL, Sawyer RG. Bacteremia associated with central venous catheter infection is not an independent predictor of outcomes. *J Am Coll Surg.* 2000;**190**(6):671–680; discussion 80–81.
9. Renaud B, Brun-Buisson C. Outcomes of primary and catheter-related bacteremia: a cohort and case-control study in critically ill patients. *Am J Respir Crit Care Med.* 2001;**163** (7):1584–1590.
10. Rosenthal VD, Guzman S, Migone O, Crnich CJ. The attributable cost, length of hospital stay, and mortality of central line–associated bloodstream infection in intensive care departments in Argentina: a prospective, matched analysis. *Am J Infect Control.* 2003;**31** (8):475–480.
11. Blot SI, Depuydt P, Annemans L, et al. Clinical and economic outcomes in critically ill patients with nosocomial catheter-related bloodstream infections. *Clin Infect Dis.* 2005;**41**(11): 1591–1508.
12. Stevens V, Geiger K, Concannon C, Nelson RE, Brown J, Dumyati G. Inpatient costs, mortality and 30-day re-admission in patients with central-line-associated bloodstream infections. *Clin Microbiol Infect.* 2014;**20**(5):O318–0324.
13. Goudie A, Dynan L, Brady PW, Rettiganti M. Attributable cost and length of stay for central line-associated bloodstream infections. *Pediatrics.* 2014;**133**(6):e1525–1532.
14. Zingg W, Cartier-Fassler V, Walder B. Central venous catheter-associated infections. *Best Pract Res Clin Anaesthesiol.* 2008;**22**(3):407–421.
15. Vincent JL, Bihari DJ, Suter PM, et al. The prevalence of nosocomial infection in intensive care units in Europe: results of the European Prevalence of Infection in Intensive Care (EPIC) Study. EPIC International Advisory Committee. *JAMA.* 1995;**274**(8):639–644.
16. Vincent JL, Rello J, Marshall J, et al. International study of the prevalence and outcomes of infection in intensive

care units. *JAMA.* 2009;**302**(21):2323–2329.

17. Dudeck MA, Edwards JR, Allen-Bridson K, et al. National Healthcare Safety Network report, data summary for 2013: device-associated Module. *Am J Infect Control.* 2015;**43**(3):206–221.
18. Coello R, Charlett A, Ward V, et al. Device-related sources of bacteraemia in English hospitals: opportunities for the prevention of hospital-acquired bacteraemia. *J Hosp Infect.* 2003;**53**(1):46–57.
19. Rosenthal VD, Maki DG, Salomao R, et al. Device-associated nosocomial infections in 55 intensive care units of 8 developing countries. *Ann Intern Med.* 2006;**145**(8):582–591.
20. Rosenthal VD, Maki DG, Mehta Y, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary of 43 countries for 2007–2012: device-associated module. *Am J Infect Control.* 2014;**42**(9):942–56.
21. Mostert JW, Kenny GM, Murphy GP. Safe placement of central venous catheter into internal jugular veins. *Arch Surg.* 1970;**101**(3):431–432.
22. Peters JL, Mehtar S, Vallis CJ, Kenning BR. Central venous catheter design and maintenance complications. *Br J Anaesth.* 1979;**51**(8):805–806.
23. Pottecher T, Forrler M, Picardat P, Krause D, Bellocq JP, Otteni JC. Thrombogenicity of central venous catheters: prospective study of polyethylene, silicone and polyurethane catheters with phlebography or post-mortem examination. *Eur Journal Anaesthesiol.* 1984;**1**(4):361–365.
24. Haley RW, Quade D, Freeman HE, Bennett JV. The SENIC Project: Study on the efficacy of nosocomial infection control (SENIC Project), Summary of study design. *Am J Epidemiol.* 1980;**111**(5):472–85.
25. O'Grady NP, Alexander M, Dellinger EP, et al. Guidelines for the prevention of intravascular catheter-related infections. Centers for Disease Control and Prevention. *MMWR Recommendations and Reports.* 2002;**51**(RR-10):1–29.
26. Marschall J, Mermel LA, Fakih M, et al. Strategies to prevent central line–associated bloodstream infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol.* 2014;**35** Suppl 2:S89–S107.
27. Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. *Mayo Clinic Pro.* 2006;**81**(9):1159–11571.
28. Al Raiy B, Fakih MG, Bryan-Nomides N et al. Peripherally inserted central venous catheters in the acute care setting: a safe alternative to high-risk short-term central venous catheters. *Am J Infect Control.* 2010;**38**(2):149–153.
29. Zingg W, Pittet D. Peripheral venous catheters: an under-evaluated problem. *Int J Antimicrob Agents.* 2009;**34** Suppl 4:S38–S42.
30. Parienti JJ, Thirion M, Megarbane B, et al. Femoral vs. jugular venous catheterization and risk of nosocomial events in adults requiring acute renal replacement therapy: a randomized controlled trial. *JAMA.* 2008;**299**(20):2413–2422.
31. Parienti JJ, Mongardon N, Megarbane B, et al. Intravascular complications of central venous catheterization by insertion site. *N Engl J Med.* 2015;**373**(13):1220–1229.
32. Richet H, Hubert B, Nitemberg G, et al. Prospective multicenter study of vascular-catheter-related complications and risk factors for positive central-catheter cultures in intensive care unit patients. *J Clin Microbiol.* 1990;**28**(11):2520–2525.
33. Goetz AM, Wagener MM, Miller JM, Muder RR. Risk of infection due to central venous catheters: effect of site of placement and catheter type. *Infect Control Hosp Epidemiol.* 1998;**19**(11):842–845.
34. Merrer J, De Jonghe B, Golliot F, et al. Complications of femoral and subclavian venous catheterization in critically ill patients: a randomized controlled trial. *JAMA.* 2001;**286**(6):700–707.
35. Cobb DK, High KP, Sawyer RG, et al. A controlled trial of scheduled replacement of central venous and pulmonary-artery catheters. *N Engl J Med.* 1992;**327**(15):1062–1068.
36. Cook D, Randolph A, Kernerman P, et al. Central venous catheter replacement strategies: a systematic review of the literature. *Crit Care Med.* 1997;**25**(8):1417–1424.
37. Zurcher M, Tramer MR, Walder B. Colonization and bloodstream infection with single- versus multi-lumen central venous catheters: a quantitative systematic review. *Anesth Analg.* 2004;**99**(1):177–182.
38. Timsit JF, Farkas JC, Boyer JM, et al. Central vein catheter-related thrombosis in intensive care patients: incidence, risks factors, and relationship with catheter-related sepsis. *Chest.* 1998;**114**(1):207–213.
39. Abdelkefi A, Ben Othman T, Kammoun L, et al. Prevention of central venous line-related thrombosis by continuous infusion of low-dose unfractionated heparin, in patients with haemato-oncological disease: a randomized controlled trial. *Thromb Haemost.* 2004;**92**(3):654–661.
40. Abdelkefi A, Achour W, Ben Othman T, et al. Use of heparin-coated central venous lines to prevent catheter-related bloodstream infection. *J Support Oncol.* 2007;**5**(6):273–278.
41. Zingg W, Posfay-Barbe KM, Pfister RE, Touveneau S, Pittet D. Individualized catheter surveillance among neonates: a prospective, 8-year, single-center experience. *Infect Control Hosp Epidemiol.* 2011;**32**(1):42–49.
42. Opilla MT, Kirby DF, Edmond MB. Use of ethanol lock therapy to reduce the incidence of catheter-related bloodstream infections in home parenteral nutrition patients. *JPEN J Parenter Enteral Nutr.* 2007;**31**(4):302–305.
43. Chen HS, Wang FD, Lin M, Lin YC, Huang LJ, Liu CY. Risk factors for central venous catheter-related infections in general surgery. *J Microbiol Immunol Infect = Wei mian yu gan ran za zhi.* 2006;**39**(3):231–236.
44. Heidegger CP, Berger MM, Graf S, et al. Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: a randomised controlled clinical trial. *Lancet.* 2013;**381**(9864):385–393.
45. Thibault R, Makhlouf AM, Kossovsky MP, et al. Healthcare-associated infections are associated with insufficient dietary intake: an observational cross-sectional study. *PloS one.* 2015;**10**(4):e0123695.
46. Zingg W, Holmes A, Dettenkofer M, et al. Hospital organisation, management, and structure for prevention of health-care-associated infection: a systematic review and expert consensus. *Lancet Infect Dis.* 2015;**15**(2):212–224.
47. Fridkin SK, Pear SM, Williamson TH, Galgiani JN, Jarvis WR. The role of understaffing in central venous catheter-associated bloodstream infections. *Infect Control Hosp Epidemiol.* 1996;**17**(3):150–158.
48. Virtanen M, Kurvinen T, Terho K, et al. Work hours, work stress, and collaboration among ward staff in

relation to risk of hospital-associated infection among patients. *Med Care*. 2009;**47**(3):310–318.

49. Pittet D, Simon A, Hugonnet S, Pessoa-Silva CL, Sauvan V, Perneger TV. Hand hygiene among physicians: performance, beliefs, and perceptions. *Ann Intern Med*. 2004;**141**(1):1–8.
50. Cimiotti JP, Haas J, Saiman L, Larson EL. Impact of staffing on bloodstream infections in the neonatal intensive care unit. *Arch Pediatr Adolesc Med*. 2006;**160**(8):832–836.
51. Alonso-Echanove J, Edwards JR, Richards MJ, et al. Effect of nurse staffing and antimicrobial-impregnated central venous catheters on the risk for bloodstream infections in intensive care units. *Infect Control Hosp Epidemiol*. 2003;**24**(12):916–925.
52. Robert J, Fridkin SK, Blumberg HM, et al. The influence of the composition of the nursing staff on primary bloodstream infection rates in a surgical intensive care unit. *Infect Control Hosp Epidemiol*. 2000;**21**(1):12–17.
53. Elder NC, Brungs SM, Nagy M, Kudel I, Render ML. Intensive care unit nurses' perceptions of safety after a highly specific safety intervention. *Qual Safety Health Care*. **17**(1):25–30. 2008.
54. Saint S, Kowalski CP, Banaszak-Holl J, Forman J, Damschroder L, Krein SL. The importance of leadership in preventing healthcare-associated infection: results of a multisite qualitative study. *Infect Control Hosp Epidemiol*. 2010;**31**(9):901–907.
55. Sinuff T, Cook D, Giacomini M, Heyland D, Dodek P. Facilitating clinician adherence to guidelines in the intensive care unit: a multicenter, qualitative study. *Crit Care Med*. 2007;**35**(9):2083–2089.
56. Snyders RE, Goris AJ, Gase KA, Leone CL, Doherty JA, Woeltje KF. Increasing the reliability of fully automated surveillance for central line-associated bloodstream infections. *Infect Control Hosp Epidemiol*. 2015;**36**(12):1396–1400.
57. Metzger KE, Rucker Y, Callaghan M, et al. The burden of mucosal barrier injury laboratory-confirmed bloodstream infection among hematology, oncology, and stem cell transplant patients. *Infect Control Hosp Epidemiol*. 2015;**36**(2):119–124.
58. Safdar N, Fine JP, Maki DG. Meta-analysis: methods for diagnosing intravascular device-related bloodstream infection. *Ann Intern Med*. 2005;**142**(6):451–466.
59. Siegman-Igra Y, Anglim AM, Shapiro DE, Adal KA, Strain BA, Farr BM. Diagnosis of vascular catheter-related bloodstream infection: a meta-analysis. *J Clin Microbiol*. 1997;**35**(4):928–936.
60. Blot F, Nitenberg G, Chachaty E, et al. Diagnosis of catheter-related bacteraemia: a prospective comparison of the time to positivity of hub-blood versus peripheral-blood cultures. *Lancet*. 1999;**354**(9184):1071–1077.
61. Woeltje KF, Butler AM, Goris AJ, et al. Automated surveillance for central line-associated bloodstream infection in intensive care units. *Infect Control Hosp Epidemiol*. 2008;**29**(9):842–846.
62. Hota B, Lin M, Doherty JA, et al. Formulation of a model for automating infection surveillance: algorithmic detection of central-line associated bloodstream infection. *J Am Med Informatics Assoc: JAMIA*. 2010;**17**(1):42–48.
63. Khouli H, Jahnes K, Shapiro J, et al. Performance of medical residents in sterile techniques during central vein catheterization: randomized trial of efficacy of simulation-based training. *Chest*. 2011;**139**(1):80–87.
64. Mimoz O, Lucet JC, Kerforne T, et al. Skin antisepsis with chlorhexidine-alcohol versus povidone iodine-alcohol, with and without skin scrubbing, for prevention of intravascular-catheter-related infection (CLEAN): an open-label, multicentre, randomised, controlled, two-by-two factorial trial. *Lancet*. 2015;**386**(10008):2069–2077.
65. Cartier V, Haenny A, Inan C, Walder B, Zingg W. No association between ultrasound-guided insertion of central venous catheters and bloodstream infection: a prospective observational study. *J Hosp Infect*. 2014;**87**(2):103–108.
66. Dumyati G, Concannon C, van Wijngaarden E, et al. Sustained reduction of central line-associated bloodstream infections outside the intensive care unit with a multimodal intervention focusing on central line maintenance. *Am J Infect Control*. 2014;**42**(7):723–730.
67. Gueri K, Wagner J, Rains K, Bessesen M. Reduction in central line–associated bloodstream infections by implementation of a postinsertion care bundle. *Am J Infect Control*. 2010;**38**(6):430–433.
68. Blot K, Bergs J, Vogelaers D, Blot S, Vandijck D. Prevention of central line–associated bloodstream infections through quality improvement interventions: a systematic review and meta-analysis. *Clin Infect Dis*. 2014;**59**(1):96–105.
69. Apisarnthanarak A, Thongphubeth K, Yuekyen C, Warren DK, Fraser VJ. Effectiveness of a catheter-associated bloodstream infection bundle in a Thai tertiary care center: a 3-year study. *Am J Infect Control*. 2010;**38**(6):449–455.
70. Bion J, Richardson A, Hibbert P, et al. "Matching Michigan": a 2-year stepped interventional programme to minimise central venous catheter-blood stream infections in intensive care units in England. *BMJ Qual Safety*. 2013;**22**(2):110–123.
71. DePalo VA, McNicoll L, Cornell M, Rocha JM, Adams L, Pronovost PJ. The Rhode Island ICU collaborative: a model for reducing central line-associated bloodstream infection and ventilator-associated pneumonia statewide. *Qual Saf Health Care*. 2010;**19**(6):555–561.
72. Eggimann P, Harbarth S, Constantin MN, Touveneau S, Chevrolet JC, Pittet D. Impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care. *Lancet*. 2000;**355**(9218):1864–8.
73. Guerin K, Wagner J, Rains K, Bessesen M. Reduction in central line–associated bloodstream infections by implementation of a postinsertion care bundle. *Am J Infect Control*. **38**(6):430–3. 2010.
74. Marra AR, Cal RG, Durao MS, Correa L, Guastelli LR, Moura DF, Jr., et al. Impact of a program to prevent central line-associated bloodstream infection in the zero tolerance era. *Am J Infect Control*. 2010.
75. Miller MR, Griswold M, Harris JM, et al. Decreasing PICU catheter-associated bloodstream infections: NACHRI's quality transformation efforts. *Pediatrics*. **125**(2):206–213. 2010.
76. Palomar M, Alvarez-Lerma F, Riera A, et al. Impact of a national multimodal intervention to prevent catheter-related bloodstream infection in the ICU: the Spanish experience. *Crit Care Med*. 2013;**41**(10):2364–2372.
77. Peredo R, Sabatier C, Villagra A, et al. Reduction in catheter-related bloodstream infections in critically ill patients through a multiple system

intervention. *Eur J Clin Microbiol Infect Dis*. 2010;**29**(9):1173–1177.

78. Perez Parra A, Cruz Menarguez M, Perez Granda MJ, Tomey MJ, Padilla B, Bouza E. A simple educational intervention to decrease incidence of central line-associated bloodstream infection (CLABSI) in intensive care units with low baseline incidence of CLABSI. *Infect Control Hosp Epidemiol*. 2010;**31**(9):964–967.
79. Schulman J, Stricof R, Stevens TP, et al. Statewide NICU central-line-associated bloodstream infection rates decline after bundles and checklists. *Pediatrics*. 2011;**127**(3):436–444.
80. Venkatram S, Rachmale S, Kanna B. Study of device use adjusted rates in health care–associated infections after implementation of "bundles" in a closed-model medical intensive care unit. *J Crit Care*. 2010;**25**(1):174 e11–e18.
81. Weber DJ, Brown VM, Sickbert-Bennett EE, Rutala WA. Sustained and prolonged reduction in central line-associated bloodstream infections as a result of multiple interventions. *Infect Control Hosp Epidemiol*. 2010;**31**(8):875–877.
82. Zingg W, Imhof A, Maggiorini M, Stocker R, Keller E, Ruef C. Impact of a prevention strategy targeting hand hygiene and catheter care on the incidence of catheter-related bloodstream infections. *Crit Care Med*. 2009;**37**(7):2167–2173; quiz 80.
83. Zingg W, Cartier V, Inan C, et al. Hospital-wide multidisciplinary, multimodal intervention programme to reduce central venous catheter–associated bloodstream infection. *PLoS One*. 2014;**9**(4):e93898.
84. Sherertz RJ, Ely EW, Westbrook DM, et al. Education of physicians-in-training can decrease the risk for vascular catheter infection. *Ann Intern Med*. 2000;**132**(8):641–648.
85. Barsuk JH, Cohen ER, Feinglass J, McGaghie WC, Wayne DB. Use of simulation-based education to reduce catheter-related bloodstream infections. *Arch Intern Med*. 2009;**169**(15):1420–1423.
86. Evans LV, Dodge KL, Shah TD, et al. Simulation training in central venous catheter insertion: improved performance in clinical practice. *Acad Med*. 2010;**85**(9):1462–1469.
87. Marra AR, Guastelli LR, de Araujo CM, et al. Positive deviance: a new strategy for improving hand hygiene compliance. *Infect Control Hosp Epidemiol*. 2010;**31**(1):12–20.
88. Joshi SC, Diwan V, Tamhankar AJ, et al. Qualitative study on perceptions of hand hygiene among hospital staff in a rural teaching hospital in India. *J Hosp Infect*. 2012;**80**(4):340–344.
89. Turnberg W, Daniell W, Simpson T, et al. Personal healthcare worker (HCW) and work-site characteristics that affect HCWs' use of respiratory-infection control measures in ambulatory healthcare settings. *Infect Control Hosp Epidemiol*. 2009;**30**(1):47–52.
90. Nicol PW, Watkins RE, Donovan RJ, Wynaden D, Cadwallader H. The power of vivid experience in hand hygiene compliance. *J Hosp Infect* **72**(1):36–42. 2009.
91. Larson EL, Quiros D, Lin SX. Dissemination of the CDC's Hand Hygiene Guideline and impact on infection rates. *Am J Infect Control*. 2007;**35**(10):666–675.
92. Raad, II, Hohn DC, Gilbreath BJ, et al. Prevention of central venous catheter–related infections by using maximal sterile barrier precautions during insertion. *Infect Control Hosp Epidemiol*. 1994;**15**(4 Pt 1):231–238.
93. Quiros D, Lin S, Larson EL. Attitudes toward practice guidelines among intensive care unit personnel: a cross-sectional anonymous survey. *Heart Lung*. **36**(4):287–297. 2007:Aug.
94. Haustein T, Gastmeier P, Holmes A, et al. Use of benchmarking and public reporting for infection control in four high-income countries. *Lancet Infect Dis*. 2011;**11**(6):471–481.
95. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci*. 2009;**4**:50.
96. Gurses AP, Murphy DJ, Martinez EA, Berenholtz SM, Pronovost PJ. A practical tool to identify and eliminate barriers to compliance with evidence-based guidelines. *Jt Comm J Qual Patient Saf*. 2009;**35**(10):526–532, 485.
97. Hansen S, Schwab F, Behnke M, et al. National influences on catheter-associated bloodstream infection rates: practices among national surveillance networks participating in the European HELICS project. *J Hosp Infect*. 2009;**71**(1):66–73.
98. Hockenhull JC, Dwan KM, Smith GW, et al. The clinical effectiveness of central venous catheters treated with anti-infective agents in preventing catheter-related bloodstream infections: a systematic review. *Crit Care Med*. 2009;**37**(2):702–12.
99. Walder B, Pittet D, Tramer MR. Prevention of bloodstream infections with central venous catheters treated with anti-infective agents depends on catheter type and insertion time: evidence from a meta-analysis. *Infect Control Hosp Epidemiol*. 2002;**23**(12):748–756.
100. Falagas ME, Fragoulis K, Bliziotis IA, Chatzinikolaou I. Rifampicin-impregnated central venous catheters: a meta-analysis of randomized controlled trials. *J Antimicrob Chemother*. 2007;**59**(3):359–369.
101. Cherry-Bukowiec JR, Denchev K, Dickinson S, et al. Prevention of catheter-related blood stream infection: back to basics? *Surg Infect (Larchmt)*. 2011;**12**(1):27–32.
102. Marschall J, Mermel LA, Classen D, et al. Strategies to prevent central line–associated bloodstream infections in acute care hospitals. *Infect Control Hosp Epidemiol*. 2008;**29** Suppl 1:S22–30.
103. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Am J Infect Control*. 2011;**39**(4 Suppl 1):S1–S34.
104. Timsit JF, Schwebel C, Bouadma L, et al. Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: a randomized controlled trial. *JAMA*. 2009;**301**(12):1231–1241.
105. Timsit JF, Mimoz O, Mourvillier B, et al. Randomized controlled trial of chlorhexidine dressing and highly adhesive dressing for preventing catheter-related infections in critically ill adults. *Am J Respir Crit Care Med*. 2012;**186**(12):1272–1278.
106. Ruschulte H, Franke M, Gastmeier P, et al. Prevention of central venous catheter related infections with chlorhexidine gluconate impregnated wound dressings: a randomized controlled trial. *Ann Hematol*. 2009;**88**(3):267–272.
107. Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter–related

infection: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2009;**49**(1):1–45.

108. Sherertz RJ, Boger MS, Collins CA, Mason L, Raad, II. Comparative in vitro efficacies of various catheter lock solutions. *Antimicrob Agents Chemother*. 2006;**50**(5):1865–868.
109. Takla TA, Zelenitsky SA, Vercaigne LM. Effectiveness of a 30% ethanol/4% trisodium citrate locking solution in preventing biofilm formation by organisms causing haemodialysis catheter-related infections. *J Antimicrob Chemother*. 2008;**62**(5):1024–1026.
110. Cober MP, Kovacevich DS, Teitelbaum DH. Ethanol-lock therapy for the prevention of central venous access device infections in pediatric patients with intestinal failure. *JPEN J Parenter Enteral Nutr*. 2010;**35**(1):67–73.
111. Jones BA, Hull MA, Richardson DS, et al. Efficacy of ethanol locks in reducing central venous catheter infections in pediatric patients with intestinal failure. *J Pediatr Surg*. 2010;**45**(6):1287–1293.
112. Mermel LA, Alang N. Adverse effects associated with ethanol catheter lock solutions: a systematic review. *J Antimicrob Chemother*. 2014;**69**(10):2611–2619.
113. Dillon PW, Jones GR, Bagnall-Reeb HA, Buckley JD, Wiener ES, Haase GM. Prophylactic urokinase in the management of long-term venous access devices in children: a Children's Oncology Group study. *J Clin Oncol*. 2004;**22**(13):2718–2723.
114. Kalmanti M, Germanakis J, Stiakaki E, et al. Prophylaxis with urokinase in pediatric oncology patients with central venous catheters. *Pediatr Hematol Oncol*. 2002;**19**(3):173–179.
115. van Rooden CJ, Schippers EF, Guiot HF, et al. Prevention of coagulase-negative staphylococcal central venous catheter–related infection using urokinase rinses: a randomized double-blind controlled trial in patients with hematologic malignancies. *J Clin Oncol*. 2008;**26**(3):428–433.
116. Maki DG, Ash SR, Winger RK, Lavin P. A novel antimicrobial and antithrombotic lock solution for hemodialysis catheters: a multi-center, controlled, randomized trial. *Crit Care Med*. 2011;**39**(4):613–620.
117. Climo MW, Sepkowitz KA, Zuccotti G, et al. The effect of daily bathing with chlorhexidine on the acquisition of methicillin-resistant Staphylococcus aureus, vancomycin-resistant Enterococcus, and healthcare-associated bloodstream infections: results of a quasi-experimental multicenter trial. *Crit Care Med*. 2009;**37**(6):1858–18565.
118. Munoz-Price LS, Hota B, Stemer A, Weinstein RA. Prevention of bloodstream infections by use of daily chlorhexidine baths for patients at a long-term acute care hospital. *Infect Control Hosp Epidemiol*. 2009;**30**(11):1031–1035.
119. Climo MW, Yokoe DS, Warren DK, et al. Effect of daily chlorhexidine bathing on hospital-acquired infection. *N Engl J Med*. 2013;**368**(6):533–42.
120. Huang SS, Septimus E, Kleinman K, et al. Targeted versus universal decolonization to prevent ICU infection. *N Engl J Med.* 2013;**368**(24):2255–65.
121. Quach C, Milstone AM, Perpete C, Bonenfant M, Moore DL, Perreault T. Chlorhexidine bathing in a tertiary care neonatal intensive care unit: impact on central line–associated bloodstream infections. *Infect Control Hosp Epidemiol*. 2014;**35**(2):158–163.
122. Pittet D, Hugonnet S, Harbarth S, et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. *Infection Control Programme*.[Erratum appears in *Lancet* 2000 Dec 23–30;**356**(9248):2196]. Lancet. 2000;**356**(9238):1307–1312.
123. Darouiche RO, Wall MJ, Jr., Itani KM, et al. Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. *N Engl J Med*. 2010;**362**(1):18–26.
124. Batra R, Cooper BS, Whiteley C, Patel AK, Wyncoll D, Edgeworth JD. Efficacy and limitation of a chlorhexidine-based decolonization strategy in preventing transmission of methicillin-resistant Staphylococcus aureus in an intensive care unit. *Clin Infect Dis*. 2010;**50**(2):210–217.
125. Karakitsos D, Labropoulos N, De Groot E, et al. Real-time ultrasound-guided catheterisation of the internal jugular vein: a prospective comparison with the landmark technique in critical care patients. *Crit Care*. 2006;**10**(6):R162.
126. Zingg W, Cartier V, Walder B. No association between ultrasound-guided insertion of central venous catheters and bloodstream infection: a prospective observational study. *J Hosp Infect*. 2015.

Chapter 16

Control of Gram-Positive Multidrug-Resistant Pathogens

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Antibiotic-resistant pathogens are a significant and increasingly important threat to human health with an estimated 2 million infections and 23,000 deaths due to antibiotic-resistant pathogens per year in the United States.[1] Patients with infections due to antibiotic-resistant pathogens have healthcare costs that are $6,000–$30,000 higher than those for patients infected with antibiotic-susceptible organisms.[2] Healthcare settings are crucial pivot points in the initial development of antibiotic-resistance traits and the clonal expansion of antibiotic-resistant pathogens via person-to-person transmission. Healthcare epidemiologists are increasingly involved in programs to reinforce prudent use of antimicrobial agents and to control epidemic and endemic transmission of multidrug-resistant organisms (MDROs). This chapter is intended as a brief overview of the major issues regarding control of transmission of Gram-positive MDROs.

Definition

MDROs are often defined as organisms that are resistant to more than 1 class of antimicrobial agents. Although the names of the most common MDROs, such as methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant enterococci (VRE), imply resistance to only one antibiotic, these pathogens are often resistant to all but a few available antimicrobial agents.

Prevalence and Significance

Unfortunately, encountering MDROs such as MRSA and VRE has become common, particularly in the inpatient setting. MRSA was first observed in Europe approximately 50 years ago, concomitant with the introduction of antistaphylococcal penicillins. During the 1970s and 1980s, outbreaks of MRSA occurred in hospitals throughout the world. The prevalence of methicillin resistance among *S. aureus* isolates steadily increased in US healthcare facilities during the 1990s and early 2000s.[3] The most recent data published by the Centers for Disease Control and Prevention (CDC) cite *S. aureus* as the most common pathogen causing healthcare-associated infections (HAI) with 48.2 percent of strains methicillin-resistant.[4] In the early 2000s, an explosive growth of MRSA infections in the outpatient setting was described, driven by the rise of what has been termed community-associated MRSA (CA-MRSA).[5] CA-MRSA has become highly prevalent with more invasive MRSA infections occurring in community-dwelling patients than in hospitalized patients.[6] However, despite the rise of CA-MRSA, the majority of patients who develop an MRSA infection outside of the hospital continue to have traditional risk factors such as a recent hospital stay, receipt of hemodialysis, or residence in a long-term care facility (LTCF).[6] While the prevalence of methicillin resistance remains high in *S. aureus*, the actual incidence of MRSA infections has been in decline for nearly a decade.[7] A multicenter US survey of invasive healthcare-associated MRSA infections found the incidence of both hospital and community-onset MRSA declined 9.4 percent and 5.7 percent per year respectively between 2005 and 2008.[8]

Enterococci were the second most common pathogens causing HAI in the US between 2009 and 2010, and resistance to vancomycin remains highly prevalent in *E. faecium*.[4] While the number of hospitalizations for treatment of VRE infections doubled between 2003 and 2006, vancomycin resistance rates have remained relatively stable with vancomycin resistance noted in >80 percent of *E. faecium* but only 8.5 percent in *E. faecalis*.[4] Although penicillin-resistant pneumococci may be considered gram-positive MDROs, they rarely result in HAI and will not be considered further in this chapter.

Antibiotic resistance is associated with less favorable clinical outcomes.[10] Kollef et al.[10] found that infection-related mortality was 2.37 times more likely in intensive care unit (ICU) patients where antimicrobial treatment was inadequate (not active against the pathogen), and this was most commonly because the causal pathogen was antibiotic-resistant ($P < .001$). With regard to Gram-positive MDROs, numerous investigators have documented their clinical significance. Compared to patients with infections due to methicillin-susceptible *S. aureus* (MSSA), patients with infections due to MRSA have significantly greater mortality, length of hospital stay, and hospital costs.[11–14] For example, Engemann et al. studied staphylococcal surgical site infections and found that patients infected with MRSA compared to MSSA were 3.4 times as likely to die, and excess hospital charges were $13,901 per infection.[11] It remains unclear as to whether these differences are due to intrinsic differences in the virulence of the microbes, differences in the underlying host, variation in antimicrobial agent efficacy, or some combination of these factors. For example, after controlling for other prognostic factors such as age, comorbidity, and severity of illness, Yaw and colleagues found no mortality difference in patients with MRSA and MSSA bacteremia.[15] Although similar observations have been made regarding the significance of VRE, conclusions drawn from these findings are even less clear-cut, owing to multiple confounding variables that often exist among patients infected with VRE. Edmond et al.[16] observed an attributable mortality of

37 percent and a risk ratio for mortality of 2.3 in a comparison between patients with VRE bacteremia and matched control subjects. Bhavnani et al.[17] noted that VRE bacteremia, when compared with vancomycin-susceptible enterococcal bacteremia, was associated with an increased clinical failure rate (60 percent vs. 40 percent of patients; P <.001) and all-cause mortality (52 percent vs. 27 percent of patients; P <.001). Finally, in a prospective, multicenter study, vancomycin resistance was an independent predictor of mortality among patients with enterococcal bacteremia.[18] However, investigators in several similar studies involving various patient cohorts noted that vancomycin resistance was not associated with differences in outcomes.[19–21] Despite these conflicting findings, there is general agreement that antibiotic-resistant pathogens are problematic because they limit the number of therapeutic choices, require more costly and potentially more toxic antimicrobial agents, and increase the costs associated with performance of surveillance cultures and placement of patients in isolation.

Mechanism of Resistance and Reservoir for Transmission

MRSA

Methicillin resistance in *S. aureus* is due to the production of an alternate penicillin-binding protein, PBP2a, which is the product of the *mecA* gene. PBP 2a has a low affinity for beta-lactam antibiotics and generates stable peptidoglycan products in the presence of inhibitory concentrations of β-lactam antibiotics.[22] Recently, a divergent *mecA* homologue, termed *mecC*, was described in Europe.[23] This mechanism of methicillin resistance was primarily described in livestock strains of *S. aureus*, but occasional transmission to humans has been noted. The genetic elements encoding methicillin resistance are carried on the staphylococcal chromosome cassette (SCCmec), which is a large chromosomal element typically containing the *mecA* gene, regulators, and usually a variety of other resistance-conferring genes. Until recently, genetic transfer of SCCmec from strain to strain had been a very rare event, and thus the worldwide spread of MRSA was almost exclusively due to clonal expansion of a few strains with this genetic background via person- to-person spread. Transmission of MRSA has traditionally been associated with the healthcare system, and previously almost all cases of colonization or infection with MRSA could be traced back to the subject's treatment at an inpatient care facility, receipt of hemodialysis, stay at a long-term care facility, or receipt of home infusion therapy.[24]

However, in recent years, CA-MRSA strains have been recovered from persons without risk factors for MRSA acquisition. These strains carry a smaller, more mobile and less physiologically burdensome chromosomal element (most often SCCmec type IV). This genetic element usually carries only the *mecA* gene with no other resistance determinants, differentiating it from genetic elements traditionally found in hospital strains of MRSA, which are usually multidrug resistant.[25,26] More recently, multidrug-resistant CA-MRSA strains have been described, and the overall prevalence of drug resistance in CA-MRSA has risen.[27] The most prevalent strain of CA-MRSA is the USA300 strain, and its expansion has radically altered the epidemiologic characteristics of MRSA. It has even replaced MSSA as the most common cause of purulent skin and soft-tissue infections.[28] The rapid expansion of the USA300 strain, its entry into the hospital setting, and its acquisition of increasing drug resistance has blurred the line between community and hospital strains, making differentiating strain types difficult using traditional epidemiologic or phenotypic methods. In San Francisco, 43.5 percent of hospital-onset *S. aureus* infections during 2004 and 2005 were due to the USA300 strain.[29] From 2000 through 2006, investigators at a large inner-city hospital observed that the percentage of hospital-onset MRSA bloodstream infections due to genotypic CA-MRSA increased from 24 percent to 49 percent.[30]

Despite the emergence of CA-MRSA, the major MRSA reservoir still consists of patients with significant contact with the healthcare system, and the organism is usually spread in healthcare facilities via contact with healthcare workers and, to a lesser extent, with medical fomites, such as stethoscopes, blood-pressure cuffs, thermometers, and environmental surfaces, such as bed rails and tables. It should be emphasized that the majority of carriers of MRSA are asymptomatically colonized. The most common site of MRSA colonization is the anterior nares, but other sites, such as axillae, the rectum, the throat, wounds, and implanted devices, may also become colonized.[31] There is evidence that transmission of CA-MRSA strains might be less dependent on nasal colonization and more dependent on fomite or skin-to-skin contact.

Other concerning developments involving *S. aureus* are reported increases in the minimum inhibitory concentration (MIC) of vancomycin (sometimes referred to as "MIC creep"), the emergence of vancomycin-intermediate strains (VISA) and vancomycin-heteroresistant strains (hVISA), and the detection of vancomycin-resistant *S. aureus* (VRSA). While some single center studies have described rising vancomycin MIC values for MRSA strains, more recent multicenter data have not confirmed the presence of MIC creep.[32–34] The clinical significance of vancomycin MICs that are elevated but still susceptible (>1 and ≤2 mg/mL) has been a topic of much investigation and little consensus. While some studies have suggested that these MIC values are associated with increased treatment failure and mortality in both MRSA and MSSA, a recent large meta-analysis including over 8,000 episodes of *S. aureus* bloodstream infection found no association of higher vancomycin MIC values with an increase in mortality.[35–37] Subpopulations of *S. aureus* with vancomycin susceptibilities in the intermediate range have also been described. These strains have been designated as hVISA, and their detection by standard microbiologic methods is difficult, prompting changes in the criteria for interpreting the vancomycin MIC.[38,39] The mechanism behind this decreased susceptibility is a thickening of the bacterial cell wall and biomatrix;[40] hVISA strains may be associated with treatment failure and prolonged bacteremia. Complete resistance to vancomycin in *S. aureus*

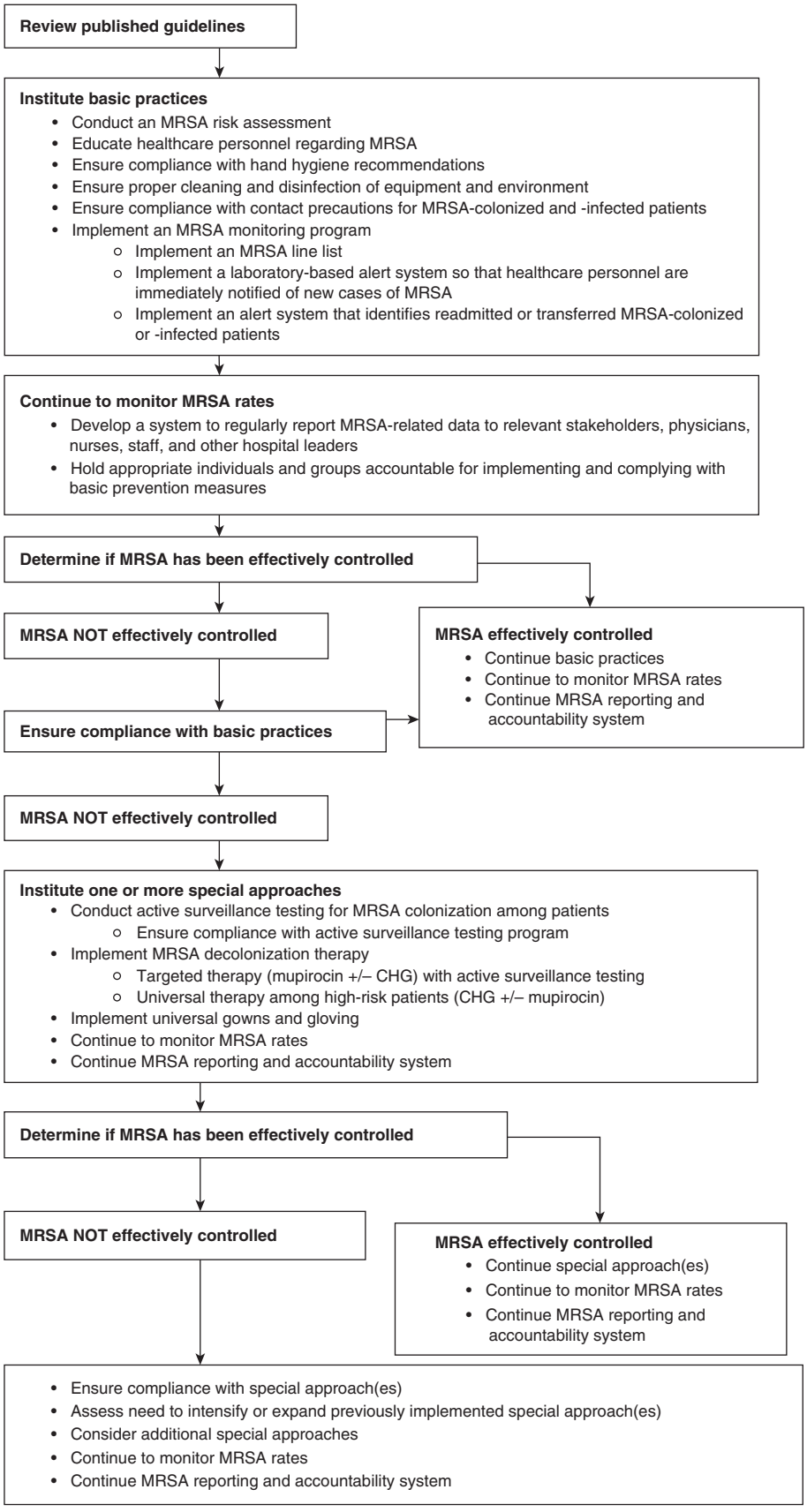

Figure 16.1 Suggested approach to the control of methicillin-resistant *Staphylococcus aureus*. Reproduced from Calfee et al.[45]

isolates occurs via acquisition of the *vanA* gene from VRE species. These isolates have been surprisingly rare, and their transmission to other patients has not been documented; however, with the continued heavy use of vancomycin, resistance is expected to increase in all forms.[41]

VRE

Vancomycin resistance in *E. faecalis* and *E. faecium* is primarily due to the acquisition of *vanA* or *vanB* gene clusters, which encode enzymes responsible for the production of peptidoglycan precursors with reduced affinity for glycopeptides. The resistance genes are carried on mobile genetic elements that are readily transferable between enterococcal strains.

In the United States, VRE is almost always linked to persons with significant contact with the healthcare system. Transmission of VRE in the US typically occurs via healthcare workers and medical fomites. In Europe, the prevalence of VRE varies by country, and the epidemiology of VRE is somewhat different than in the US. Until 1997, avoparcin, a glycopeptide, was widely used as a growth promoter in farm animals, and transmission by food products played a significant role in VRE acquisition. However, this mode of acquisition appears to have diminished dramatically in response to the prohibition of avoparcin as a growth promoter, and VRE transmission in Europe is now similar to transmission in the US.[42,43] The natural ecologic niche of enterococci is the gut, and VRE can be readily recovered from cultures of rectal swab specimens or stool specimens from colonized persons.

Control Measures

Infection control efforts to limit the spread of gram-positive MDROs must be considered in a larger context and should be part of a comprehensive, system-wide program directed at antimicrobial resistance. Such programs should be strongly supported by hospital administration and should include educational efforts with facility-wide and unit-specific scopes. It must also be recognized that the major driving factors in the emergence of antibiotic resistance are overuse and inappropriate use of antimicrobial agents.[44] Control of antibiotic use and antimicrobial stewardship is discussed in detail in Chapter 19. Efforts to reduce selective pressure through more prudent use of antimicrobials should be coupled with primary measures to prevent infection, such as vaccination programs and campaigns to prevent HAIss. Finally, the rigorous use of standard infection control precautions to prevent transmission of resistant pathogens from both identified and unidentified carriers is essential.

Comprehensive statements from the Society for Healthcare Epidemiology of America (SHEA) and the CDC regarding control of gram-positive MDROs have been promulgated.[45,46] The CDC Hospital Infection Control Practices Advisory Committee (HICPAC) document was published in 2006 and covers infection control considerations in a variety of healthcare settings for a broad range of potential pathogens, including gram-positive MDROs.[46] The SHEA compendium publication was updated in 2014 and focuses exclusively on MRSA, although the principles are generally applicable to other Gram-positive organisms such as VRE.[45] While these publications differ in a number of areas, both the SHEA MRSA guidelines and the CDC MDRO guidelines advocate a tiered approach to Gram-positive MDRO control. They strongly advocate for the effective implementation of basic practices, such as hand hygiene, contact isolation, and proper disinfection of equipment and environmental surfaces, coupled with monitoring of MDROs and education regarding how to prevent their spread. If vigorous application of basic control measures is ineffective in decreasing the prevalence of a target MDRO or an MDRO has been identified in a highly vulnerable patient population or unit (e.g., neonatal ICU, burn unit), more intensive interventions should be used. Additional measures potentially include implementation of an active surveillance culture program, targeted or universal decolonization procedures using mupirocin and/or chlorhexidine (CHG), and the use of universal contact precautions, with continual assessment of their effectiveness until control of the target organism is achieved. Figure 16.1[45] outlines the major steps in controlling the transmission of MRSA. Key issues in a comprehensive program to limit the spread of Gram-positive MDROs are discussed below.

Basic Practices

Risk Assessment

The SHEA guideline recommends a risk assessment be performed focusing on the opportunity for pathogen transmission, facility-resistant pathogen burden, and rate of transmission and/or infection.[45] The findings of the risk assessment should be used to define a control strategy including how and where to implement control measures.

Surveillance

Surveillance is critical to the control of MDROs because it allows for identification of emerging pathogens, monitoring of epidemiologic trends, and assessment of the effectiveness of interventions. Creation of facility-wide antimicrobial susceptibility results such as an antibiogram is a simple way to monitor MDROs, and these should be both facility- and unit-specific. A specific program for MRSA monitoring that includes the ability to rapidly identify and track patients colonized or infected with MRSA is recommended in the SHEA guidelines.[45] Additionally, it is recommended that a system be in place to notify infection control personnel when a culture positive for MRSA is reported and to identify patients transferred or admitted who have previously been colonized or infected with MRSA.[45] Starting in 2015, acute care facilities were required to report all hospital-onset MRSA bacteremia through NHSH allowing for comparison to other facilities.[47] Reporting of VRE and non-bacteremia MRSA to NHSN is also available, but not required. A full description of laboratory methods to detect Gram-positive MDROs and the role of the clinical microbiology laboratory in infection control efforts is beyond the

scope of this chapter, and the interested reader is referred to recent reviews.[48,49] A variety of molecular-based assays and more efficient chromogenic agar culture-based methods to detect MRSA have been introduced to the market. The cost-effectiveness of these laboratory techniques and their impact on surveillance and prevention programs is an area of intense study and is discussed further in the section on active surveillance.

Isolation Precautions

Standard Precautions

Standard precautions should be used during all encounters with patients. The CDC HICPAC guidelines recognize that colonization with MDROs is frequently undetected and emphasize the role of standard precautions.[46] Hand hygiene is a cornerstone of standard precautions, and its value should not be underemphasized. Healthcare workers should be encouraged to use an approved alcohol-based hand rub for routine hand disinfection and to wash their hands with soap and water whenever their hands are visibly soiled with blood or body fluids.[50] Numerous tools for improving hand hygiene are available from the CDC and the World Health Organization (WHO).[51]

Contact Isolation Precautions

Both the SHEA and CDC/HICPAC guidelines recommend that patients known to be or strongly suspected of harboring a gram-positive MDRO be cared for in contact isolation precautions.[45,46] While this has long been standard practice, some have begun to question the relative value of contact isolation, and application of contact isolation will be further discussed later in this chapter.[52] When contact precautions are utilized, patients should be housed to provide spatial separation to reduce the risk of transmission. The most effective means of accomplishing this goal is to mandate use of private rooms for persons infected or colonized with Gram-positive MDROs. When this is not practical, patients harboring the same species of Gram-positive MDRO may be cohorted with one another to provide a physical barrier between colonized or infected patients and patients who do not harbor MDROs. There are conflicting data regarding the detrimental effects of contact precautions on a patient's mental and physical well-being.[53,54] While a recent randomized trial found significantly fewer patient visits by healthcare workers in units using universal contact precautions compared to those where contact precautions were only applied when patients were colonized or infected with resistant pathogens, there was no difference in adverse events between groups.[55] When contact precautions are used, efforts should be made to monitor for and counteract potential adverse effects.

Barrier Precautions: Gloves, Gowns, and Masks

Gloves should be worn as part of standard precautions whenever it can be reasonably anticipated that contact with blood, mucous membranes, potentially infectious material, or colonized skin will occur.[56] The use of gloves is recommended when caring for a person infected or colonized with a Gram-positive MDRO. It should be stressed to healthcare workers that gloves should be changed between contact with different patients and, for a single patient, between performance of a contamination-prone task (e.g., repositioning a patient, changing diapers, and emptying a bedpan) and a task involving a clean site (e.g., manipulation of an intravenous catheter and performance of an intramuscular injection).[50] In addition, use of gloves does not obviate the need for hand hygiene, and hands should be disinfected following the removal of gloves.[50]

Gowns should be worn as part of standard precautions to protect uncovered skin and prevent soiling of clothing during patient-care activities that are likely to generate splashes or sprays of blood or body fluids.[56] Questions have been raised regarding the need for gowns in the routine care of patients asymptomatically colonized with Gram-positive MDROs. Data to support the use of gowns include the fact that colonization or infection with Gram-positive MDROs often results in widespread contamination of the patient and their environment.[57–59] Contact with either often results in contamination of healthcare workers' hands and clothing, and gown use has been associated with both protection from contamination and improved control of Gram-positive MDROs.[57,60–63] Masks are not generally recommended unless used as part of standard precautions during any splash-generating procedure, care of an open tracheostomy, or when transmission from a heavily colonized source (e.g., burn wounds) is likely.[46]

As MDRO Gram-positive pathogens such as MRSA and VRE have transitioned from epidemic to endemic pathogens in both the inpatient and ambulatory arena, there has been increasing debate regarding the utility of contact precautions.[61] The SHEA guidelines rate the quality of evidence supporting routine use of contact isolation as moderate, and a recent review evaluating literature published after 2002 concluded that there is a lack of strong evidence to either support or reject contact precautions for patients colonized with Gram-positive MDROs.[45,51] Studies that have evaluated the topic are difficult to interpret as they frequently have combined contact precautions with other control strategy changes (active surveillance +/– decolonization, etc.), and no study has directly compared contact precautions with standard precautions alone. Interestingly, a recent survey of the SHEA research network found that >90 percent of respondents used contact precautions for MDRO gram positives, but 30 facilities were identified that did not employ or had recently discontinued routine contact precaution for these pathogens.[51] If contact precautions are discontinued, close monitoring of the rate of infection due to MDRO Gram-positive organisms is warranted.

Equipment

Numerous studies have documented that medical devices (stethoscopes, thermometers, tourniquets, glucose monitors, etc.) can become contaminated with Gram-positive MDROs during patient care activities.[64–67] Furthermore, contaminated equipment has been linked with the transmission of Gram-

positive MDROs to patients.[66,67] Therefore, noncritical patient care equipment should be dedicated to a single patient. If use of nondedicated equipment is unavoidable, items should be carefully cleaned and disinfected between use involving different patients.

Environmental Measures

As previously mentioned, patients harboring Gram-positive MDROs can widely contaminate the patient care environment, including clothes, linens, bed rails, wheelchairs, bedside tables, patient care equipment, doorknobs, faucet handles, telephone handsets, and computer keyboards.[45,46,57,59,61,68] In addition, Gram-positive MDROs are quite hardy, resist desiccation, and remain viable on inanimate surfaces for days to months, and their presence in the environment predisposes patients to colonization.[69,70] Therefore, it is important to include the environmental services department in a comprehensive program to combat the spread of Gram-positive MDROs. Environmental services workers should be educated, and procedures should be implemented to ensure consistent cleaning and disinfection, particularly of surfaces most likely to be touched, such as bed rails, doorknobs, and faucet handles.[45,46] Lack of adherence to prescribed facility procedures is associated with continued environmental contamination, and to combat this, a system that monitors adherence to protocols is desirable.[45,46] The use of education, feedback, and enforcement of standard cleaning policies can result in significant reductions in environmental contamination without significant financial burden.[71–73] MRSA and VRE are rapidly killed by standard, low-level disinfectants, but cleaning and disinfection must be performed with careful attention to the adequacy of cleaning, the dilution of the disinfectant, and the duration of disinfectant contact with environmental surfaces to be effective.[74] Recent literature suggests that developing systems that provide feedback regarding the adequacy of cleaning to environmental services workers can result in marked improvements in the effectiveness of cleaning.[71,73,75]

Environmental cleaning, even when aggressively promoted, is unlikely to be 100 percent efficacious as it is difficult to completely eliminate MDRO pathogens from the environment. A variety of supplemental methods of environmental disinfection such as vaporized hydrogen peroxide, ultraviolet irradiation, and antimicrobial-impregnated surfaces have shown promise, but data on their effectiveness are very limited.[76–78] As these technologies are expensive and unproven, they are considered supplemental and should only be employed when MDRO pathogens continue to spread despite documentation of compliance with basic control practices including environmental cleaning. Environmental cultures are recommended only when there is epidemiologic evidence suggesting that an environmental source is responsible for transmission.[46]

Discontinuation of Contact Isolation Precautions

Indications for the discontinuation of contact isolation are controversial, and both the CDC guidelines and the SHEA guidelines consider this an unresolved issue awaiting more definitive studies.[45,46] It is clear that patients may harbor MDRO Gram-positive pathogens for prolonged periods of time, and exposure to repeated courses of antimicrobials or residing in MDRO-rich environments (hospitals, dialysis units, long-term care facilities) makes those colonized particularly unlikely to rid themselves of MRSA and VRE. Discontinuation of contact precautions has typically relied upon having two or more negative screening cultures from the site of colonization (nares with *S. aureus*, rectal area with VRE). Unfortunately, screening may not detect persons with low-level VRE colonization, cultures may be only intermittently positive, and VRE may reemerge when patients are exposed to antimicrobials.[79–81] Similarly, colonization with MRSA may not be detected when screening only one anatomic site, may be persistent or intermittent, and may be difficult to detect in persons with low-level colonization or intermittent shedding.[82–84] A common practice is to consider patients colonized with an MDRO until results of 3 surveillance cultures performed over the 1–2-week period after completion of antimicrobial therapy are negative.[45,46] The use of protocols that actively screen colonized patients for contact precaution removal have been associated with earlier discontinuation of contact precautions, particularly when coupled with polymerase chain reaction (PCR)–based screening.[85]

Education

Education of healthcare workers is important when implementing control strategies as a method to encourage behavior change. Healthcare workers should be educated regarding risk factors, routes of transmission, outcomes associated with infection, and selected institutional prevention strategies along with compliance with these strategies.[45, 46] Additionally, patients and their families should be educated as a means of reducing anxiety, improving satisfaction, and promoting adherence to institutional control policies.[46]

Intensive Interventions

Active Surveillance

As previously mentioned, the majority of patients harboring MRSA or VRE are asymptomatically colonized, and case finding based solely on detection of Gram-positive MDROs from routinely submitted clinical specimens will not detect the majority of asymptomatic carriers.[45,88,89] Active screening will detect asymptomatically colonized individuals and presumably allow improved application of various control practices such as contact isolation or decolonization. Despite this well-reasoned theory, the application of active surveillance has produced mixed results, and there is much controversy regarding its effectiveness in controlling Gram-positive MDROs. Both the SHEA and CDC guidelines recognize the significance of patients who are asymptomatically colonized with Gram-positive MDROs and recommend consideration of active surveillance cultures as part of a multifaceted program targeted at the control of MDROs when adherence to basic practices has

been unsuccessful at controlling MDRO spread.[45,46] The exact circumstances in which active surveillance cultures should be used are not well-defined but should be specifically tailored to individual facilities and/or high-risk populations.

A number of quasi-experimental studies combining active surveillance with other control measures in high-risk and/or high-prevalence settings have found the introduction of active surveillance to be associated with decreased rates of either MDRO acquisition or clinical infection.[87,90–92] For example, an observational cohort study performed in 3 hospitals found that use of active surveillance cultures reduced MRSA infections by nearly 70 percent.[87] Similarly, the introduction of active surveillance in all 153 Veterans Affairs hospitals was associated with a decrease in healthcare-associated MRSA infections both in the ICU (62 percent decrease) and outside the ICU (45 percent decrease).[93] Conversely, a single-institution crossover cohort trial involving surgical patients found that PCR-based active surveillance did not decrease the incidence of health care-associated MRSA infections.[94] Recently, three randomized trials have evaluated the role of active surveillance in preventing the spread of Gram- positive MDROs in the ICU.[95–97] A multicenter, cluster-randomized trial compared universal gloving to active surveillance with subsequent initiation of contact precautions in those who were colonized.[95] ICU days in contact precautions were significantly greater with active surveillance (51 percent vs. 38 percent, $P < 0.001$), but no difference in acquisition or infection with either MRSA or VRE was noted.[95] Derde and colleagues randomized 13 ICUs to culture or PCR-based screening for MDROs after an initial program to improve hand hygiene and implement CHG bathing.[96] The addition of active surveillance in an environment where compliance was high with both of these practices did not decrease acquisition of MDROs. Finally,[97] Huang, et al. randomized 73 ICUs in 43 hospitals to MRSA screening and isolation; screening, isolation, and decolonization of MRSA carriers; or universal decolonization without screening. Both decolonization strategies were more effective than screening and isolation with universal decolonization being the most effective strategy for decreasing both MRSA detection from clinical cultures and bloodstream infections of any type.[97] These studies suggest that active surveillance likely has limited efficacy in nonoutbreak settings, particularly where there is high compliance with horizontal infection control measures such as hand hygiene and CHG bathing.

If active surveillance is felt to be necessary, many factors must be taken into account when starting a program. The first consideration is the additional support needed to implement the program: both personnel to collect samples and to process them in the microbiology laboratory, and also the means to communicate the findings and measure compliance with the screening procedures. Other important considerations are where to implement the program, which patients to screen (e.g., patients in the ICU, patients with a high risk of infection or all patients), when to perform the screening (on admission to the prescribed unit is considered the minimum), and which anatomic sites to screen. The anterior nares is the most frequent culture-positive site for MRSA, but screening only the nares has been noted to miss up to 27 percent of carriers.[98] The anterior nares should always be included in MRSA screening, and other sites, such as open wounds, perirectal areas, throat, or foreign bodies, may also be included to increase yield. VRE screening is typically accomplished using rectal swabs. It is imperative that a screening program be part of a multifaceted effort to control the transmission of MDROs. Simply identifying colonized patients without adherence to isolation, hand hygiene, and environmental disinfection procedures is unlikely to be effective.

Multiple laboratory methods are available for screening, including culture-based techniques and molecular assays. Traditional culture methods require an interval of at least 48 hours, but newer chromogenic media yield findings in 24 hours.[99] Molecular assays offer the advantage of being very rapid (2 hours or less, if tests are run continuously and not batched) and highly sensitive and specific, but they are limited by their cost and the lack of a pathogen that is available for typing and evaluating epidemiologic associations. Two randomized trials found that use of PCR compared to culture-based screening significantly shortened time-to-results reporting and time to isolation, but neither was able to associate this improvement with a decrease in MRSA acquisition.[100,101] The preferred test for a given facility should be determined by considering a number of factors, including the performance characteristics of the test, the turnaround time, the laboratory's capabilities, the number of specimens anticipated, and the cost. How patients should be managed while they await screening results should be determined, and it is reasonable to manage patients empirically by placing them in contact isolation until negative results of active surveillance cultures are available. Finally, compliance with screening recommendations, isolation precautions, and communication of results should be monitored.

Universal Gown and Glove Use

Another potential strategy for controlling the spread of Gram-positive MDROs is the use of gowns and gloves for all patient and patient environmental contact. Small studies have suggested that this strategy may decrease the transmission of MDROs, although as previously mentioned, there is concern for potential patient harm through decreased caregiver visits, depression, etc. The SHEA guidelines suggest that universal contact precautions (gown and glove use) may be considered as a supplemental strategy when adequate control of MDROs is not achieved with basic interventions.[45] The strongest evidence to support this practice comes from a randomized trial performed in 20 ICUs, which compared universal gown and glove use for all patient contact to use only in patients known to be colonized with MRSA or VRE.[55] While there was no difference in the composite outcome of both MRSA and VRE acquisition, MRSA acquisition was significantly lower in the universal precautions group as were healthcare personnel visits in the patient room.

Decolonization and Chlorhexidine Bathing

Decolonization is an important part of efforts to decrease transmission and infection due to antibiotic-resistant Gram-positive pathogens, particularly MRSA.[45] Recent studies have begun to discern the relative importance of decolonization compared to other control measures, as well as appropriate patient populations in which to utilize decolonization, comparative effectiveness of different decolonization regimens, and cost-effectiveness. Decolonization as a strategy to prevent surgical site infection is discussed in Chapter 14.

Decolonization is the administration of antimicrobials, most commonly topical preparations such as CHG or mupirocin with or without systemic agents, in order to suppress or eliminate microbial carriage. Decolonization can be coupled with an active surveillance culture program to target only persons known to harbor pathogens (e.g., patients with positive MRSA screening cultures), or it can be administered to defined clinical populations at higher risk of infections (e.g., ICU patients or patients with central venous catheters) or to all patients (e.g., universal decolonization).

Decolonization has long been used to curtail outbreaks and has been employed both in a targeted or more generalized fashion.[102–104] Recent studies have concentrated on the usefulness of decolonization for control of Gram-positive pathogens in adult ICU patients. Several small or single-center studies have examined the effect of bathing all ICU patients in CHG and observed beneficial effects on transmission or infection due to MRSA and/or VRE.[105–108] However, not all institutions have noted such a beneficial effect.[109] In a multicenter before/after trial and a follow-up multicenter crossover trial, Climo and colleagues convincingly demonstrated the utility of CHG bathing with either impregnated washcloths or bed baths in diminishing the transmission of MRSA and VRE in the ICU.[110,111] Huang and colleagues evaluated whether targeted or universal decolonization was more effective in ICU patients in a 43 hospital, cluster-randomized study.[97] They noted that universal application of nasal mupirocin and CHG bathing was more effective in reducing transmission of MRSA than either targeted decolonization or screening and isolation.[97] However, the relative importance of mupirocin vs. CHG was not examined. Using interrupted time-series analysis, Derde and colleagues further documented the utility of universal decolonization of ICU patients using CHG bathing in 13 ICUs, where CHG bathing coupled with improved hand hygiene significantly reduced the acquisition of antibiotic-resistant pathogens, particularly MRSA.[96] It should be noted that many of these studies also demonstrated a significant beneficial impact on the incidence of central line–associated bloodstream infections.

Less experience with decolonization regimens is available outside the ICU. CHG bathing, with or without mupirocin, has been shown to have a beneficial effect on transmission or infection due to Gram-positive pathogens in the following patient settings: surgical ward,[112] rehabilitation facility,[113] general medicine ward,[114] and whole hospital.[115] The role of decolonization in pediatric patients is less well-studied and its benefit less clear.[116–119]

Numerous questions and controversies remain regarding the role of decolonization in controlling resistant Gram-positive pathogens. First, the most effective regimen for decolonization is not defined, and the relative benefit of mupirocin, CHG, and systemic antibiotics is poorly characterized. Although the nasal application of mupirocin is a widely utilized for preventing MRSA infection, it appears that the USA 300 strain of MRSA, responsible for numerous community and hospital outbreaks, frequently colonizes other body sites (skin, groin, axilla, perirectal region), and therefore nasal mupirocin would not be expected to be effective in such circumstances.[120] Recovery of MRSA from the oropharynx or perirectal region predicts the failure of topical decolonization regimens.[121] However, the use of systemic antibiotics to decolonize the gastrointestinal tract increases the risk of toxicity. Second, there is concern that use of decolonization regimens will promote the emergence of resistance. Mupirocin resistance has paralleled the increased use of mupirocin in a number of reports.[122] Similarly, CHG resistance has been observed and has been associated with failure of decolonization.[123,124] Third, the cost-effectiveness of various decolonization regimens needs to be better studied. Fourth, the use of decolonization outside the ICU and in pediatric patients should be better defined. Finally, the value of decolonization in MRSA patient contacts (e.g., family members) and in healthcare providers should be ascertained.

Practice Settings

Consensus exists that patients in acute care settings (e.g., ICUs, burn units, and inpatient wards) are at high risk for the development of HAIs and that comprehensive measures should be implemented to prevent healthcare-associated acquisition and transmission of Gram-positive MDROs.[45,46] However, it is less clear what measures should be practiced in ambulatory care, long-term care, or home care settings. While transmission of Gram-positive MDROs can occur in any healthcare setting, interventions to control the spread of Gram-positive MDROs likely have greater effectiveness and long-term impact in high-risk settings. CDC infection prevention guidelines for the ambulatory setting emphasize standard precautions as the foundation for prevention of the spread of resistant pathogens.[125] In long-term care facilities the general principles for control of Gram-positive MDROs are similar and should include monitoring and reporting, education, environmental cleaning, and fastidious standard precautions. CDC and SHEA guidelines for infection control in long-term care facilities recommend that contact precautions be modified based upon the health and functionality of a resident colonized or infected with a Gram-positive MDRO.[46,126] They suggest that contact precautions be reserved for patients colonized with Gram-positive MDROs who are totally dependent on healthcare personnel and that standard precautions are acceptable for relatively healthy patients unless contact is expected with uncontrolled respiratory secretions, pressure ulcers, draining wounds, stool, or ostomy bags.[46,126] Similar recommendations should be followed in the ambulatory care setting, although this issue is unresolved.

Conclusion

Antimicrobial resistance among Gram-positive pathogens is a significant and unresolved problem. The fearful specter of a "post-antibiotic era" in which drug development does not keep pace with the emergence of antimicrobial resistance is a realistic possibility. Therefore, efforts to control the spread of Gram-positive MDROs are of paramount importance. Infection control efforts should be part of a comprehensive program that includes antimicrobial stewardship and primary infection prevention measures. The foundation of programs directed at the prevention of transmission of gram-positive MDROs is the vigorous application of standard precautions and hand hygiene. When these practices, along with contact isolation and appropriate environmental disinfection, are inadequate to control MDROs, more intensive practices should be implemented. When, how, and which of these practices to implement remains a much debated topic with facilities being able to choose from a menu of options including: active surveillance using either PCR- or culture-based methods, decolonization tied to active surveillance or applied to all or selected patients, or the universal use of contact precautions. These practices should be tailored to each hospital, unit, and patient group based on an institutional risk assessment. Finally, costs and feasibility of each of the measures are important to consider. While advanced measures are particularly important for preventing infections in high-risk populations, they should be used as broadly as possible and practical.

While many challenges remain regarding control of gram-positive MDROs, it is encouraging to note that current infection control efforts appear to have resulted in significant patient benefit. Despite the continued expansion of CA-MRSA, healthcare-associated MRSA acquisition and infection rates appear to be declining. Illustrating this, national CDC data noted that the prevalence of MRSA increased from 48 percent in1997 to 65 percent in 2007, but the incidence of MRSA central-line associated bloodstream infections decreased almost 50 percent during the same period.[7] Additionally, the incidence of invasive healthcare-associated MRSA infections, in particular bloodstream infections, has been declining for a number of years.[6,8] Although the reasons for this decrease were not assessed, it is reasonable to speculate that it was due to efforts to prevent central line–associated bloodstream infections, such as implementing use of full sterile barrier precautions, CHG skin disinfection, and a "checklist" approach. This highlights the continued need for emphasis on the basics of infection control, such as hand hygiene, environmental disinfection, limiting the number of fomites, and infection prevention efforts aimed at preventing device-associated infections and surgical site infections. These practices will limit transmission and infection due to a variety of pathogens, whereas measures that are specific to a single pathogen may detract from such general efforts.

Despite these advances, there remain major gaps in our knowledge regarding the pathogenesis of disease, factors that influence colonization and infection by gram-positive MDROs, how best to apply new techniques in rapid MDRO detection, how to interpret new typing technologies such as whole genome sequencing, and the most effective and cost-effective means to eliminate or block MDRO colonization and transmission.

References

1. Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2013. Available at: www.cdc.gov/drugresistance/threat-report-2013/. Accessed January 4, 2016.
2. Cosgrove SE. The relationship between antimicrobial resistance and patient outcomes: mortality, length of hospital stay, and health care costs. *Clin Infect Dis*. 2006;**42** Suppl 2:S82–S89.
3. National Nosocomial Infections Surveillance System. National nosocomial infections surveillance (NNIS) system report, data summary from January 1992 to June 2002, issued August 2002. *Am J Infect Control*. 2002;**30**(8):458–475.
4. Sievert DM, Ricks P, Edwards JR, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the national healthcare safety network at the Centers for Disease Control and Prevention, 2009–2010. *Infect Control Hosp Epidemiol*. 2013;**34**(1):1–14.
5. Tattevin P, Schwartz BS, Graber CJ, et al. Concurrent epidemics of skin and soft tissue infection and bloodstream infection due to community-associated methicillin-resistant Staphylococcus aureus. *Clin Infect Dis*. 2012;**55**(6):781–788.
6. Dantes R, Mu Y, Belflower R, et al. National burden of invasive methicillin-resistant Staphylococcus aureus infections, United States, 2011. *JAMA Intern Med*. 2013;**173**(21):1970–1978.
7. Burton DC, Edwards JR, Horan TC, et al. Methicillin-resistant Staphylococcus aureus central line-associated bloodstream infections in US intensive care units, 1997–2007. *JAMA*. 2009;**301**(7):727–736.
8. Kallen AJ, Mu Y, Bulens S, et al. Health care-associated invasive MRSA infections, 2005–2008. *JAMA*. 2010;**304**(6):641–648.
9. Roberts RR, Hota B, Ahmad I, et al. Hospital and societal costs of antimicrobial-resistant infections in a Chicago teaching hospital: implications for antibiotic stewardship. *Clin Infect Dis*. 2009;**49**(8):1175–1184.
10. Kollef MH, Sherman G, Ward S, et al. Inadequate antimicrobial treatment of infections: a risk factor for hospital mortality among critically ill patients. *Chest*. 1999;**115**(2):462–474.
11. Engemann JJ, Carmeli Y, Cosgrove SE, et al. Adverse clinical and economic outcomes attributable to methicillin resistance among patients with Staphylococcus aureus surgical site infection. *Clin Infect Dis*. 2003;**36**(5):592–598.
12. Cosgrove SE, Qi Y, Kaye KS, et al. The impact of methicillin resistance in Staphylococcus aureus bacteremia on patient outcomes: Mortality, length of stay, and hospital charges. *Infect Control Hosp Epidemiol*. 2005;**26**(2):166–174.
13. Cosgrove SE, Sakoulas G, Perencevich EN, et al. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible Staphylococcus aureus bacteremia: a meta-analysis. *Clin Infect Dis*. 2003;**36**(1):53–59.

14. Rubin RJ, Harrington CA, Poon A, et al. The economic impact of Staphylococcus aureus infection in new york city hospitals. *Emerg Infect Dis*. 1999;**5**(1):9–17.
15. Yaw LK, Robinson JO, Ho KM. A comparison of long-term outcomes after methicillin-resistant and methicillin-sensitive Staphylococcus aureus bacteraemia: an observational cohort study. *Lancet Infect Dis*. 2014;**14** (10):967–975.
16. Edmond MB, Ober JF, Dawson JD, et al. Vancomycin-resistant enterococcal bacteremia: natural history and attributable mortality. *Clin Infect Dis*. 1996;**23**(6):1234–1239.
17. Bhavnani SM, Drake JA, Forrest A, et al. A nationwide, multicenter, case-control study comparing risk factors, treatment, and outcome for vancomycin-resistant and -susceptible enterococcal bacteremia. *Diagn Microbiol Infect Dis*. 2000;**36** (3):145–158.
18. Vergis EN, Hayden MK, Chow JW, et al. Determinants of vancomycin resistance and mortality rates in enterococcal bacteremia. a prospective multicenter study. *Ann Intern Med*. 2001;**135**(7):484–492.
19. Cheah AL, Spelman T, Liew D, et al. Enterococcal bacteraemia: factors influencing mortality, length of stay and costs of hospitalization. *Clin Microbiol Infect*. 2013;**19**(4):E181–E189.
20. Garbutt JM, Ventrapragada M, Littenberg B, et al. Association between resistance to vancomycin and death in cases of enterococcus faecium bacteremia. *Clin Infect Dis*. 2000;**30** (3):466–472.
21. Erlandson KM, Sun J, Iwen PC, et al. Impact of the more-potent antibiotics quinupristin-dalfopristin and linezolid on outcome measure of patients with vancomycin-resistant enterococcus bacteremia. *Clin Infect Dis*. 2008;**46** (1):30–36.
22. Chambers HF. Methicillin-resistant staphylococci. *Clin Microbiol Rev*. 1988;**1**(2):173–186.
23. Garcia-Alvarez L, Holden MT, Lindsay H, et al. Methicillin-resistant Staphylococcus aureus with a novel mecA homologue in human and bovine populations in the UK and Denmark: a descriptive study. *Lancet Infect Dis*. 2011;**11**(8):595–603.
24. Salgado CD, Farr BM, Calfee DP. Community-acquired methicillin-resistant Staphylococcus aureus: a meta-analysis of prevalence and risk factors. *Clin Infect Dis*. 2003;**36** (2):131–139.
25. Naimi TS, LeDell KH, Como-Sabetti K, et al. Comparison of community- and health care–associated methicillin-resistant Staphylococcus aureus infection. *JAMA*. 2003;**290** (22):2976–2984.
26. Said-Salim B, Mathema B, Braughton K, et al. Differential distribution and expression of panton-valentine leucocidin among community-acquired methicillin-resistant Staphylococcus aureus strains. *J Clin Microbiol*. 2005;**43** (7):3373–3379.
27. Diep BA, Chambers HF, Graber CJ, et al. Emergence of multidrug-resistant, community-associated, methicillin-resistant Staphylococcus aureus clone USA300 in men who have sex with men. *Ann Intern Med*. 2008;**148**(4):249–257.
28. Kaplan SL, Hulten KG, Gonzalez BE, et al. Three-year surveillance of community-acquired Staphylococcus aureus infections in children. *Clin Infect Dis*. 2005;**40**(12):1785–1791.
29. Liu C, Graber CJ, Karr M, et al. A population-based study of the incidence and molecular epidemiology of methicillin-resistant Staphylococcus aureus disease in San Francisco, 2004–2005. *Clin Infect Dis*. 2008;**46** (11):1637–1646.
30. Popovich KJ, Weinstein RA, Hota B. Are community-associated methicillin-resistant Staphylococcus aureus (MRSA) strains replacing traditional nosocomial MRSA strains? *Clin Infect Dis*. 2008;**46**(6):787–794.
31. Currie A, Davis L, Odrobina E, et al. Sensitivities of nasal and rectal swabs for detection of methicillin-resistant Staphylococcus aureus colonization in an active surveillance program. *J Clin Microbiol*. 2008;**46**(9):3101–3103.
32. Sader HS, Fey PD, Limaye AP, et al. Evaluation of vancomycin and daptomycin potency trends (MIC creep) against methicillin-resistant Staphylococcus aureus isolates collected in nine U.S. medical centers from 2002 to 2006. *Antimicrob Agents Chemother*. 2009;**53**(10):4127–4132.
33. Steinkraus G, White R, Friedrich L. Vancomycin MIC creep in non-vancomycin-intermediate Staphylococcus aureus (VISA), vancomycin-susceptible clinical methicillin-resistant S. aureus (MRSA) blood isolates from 2001–2005. *J Antimicrob Chemother*. 2007;**60** (4):788–794.
34. Wang G, Hindler JF, Ward KW, et al. Increased vancomycin MICs for Staphylococcus aureus clinical isolates from a university hospital during a 5-year period. *J Clin Microbiol*. 2006;**44** (11):3883–3886.
35. Holmes NE, Turnidge JD, Munckhof WJ, et al. Antibiotic choice may not explain poorer outcomes in patients with Staphylococcus aureus bacteremia and high vancomycin minimum inhibitory concentrations. *J Infect Dis*. 2011;**204**(3):340–347.
36. Kalil AC, Van Schooneveld TC, Fey PD, et al. Association between vancomycin minimum inhibitory concentration and mortality among patients with Staphylococcus aureus bloodstream infections: a systematic review and meta-analysis. *JAMA*. 2014;**312** (15):1552–1564.
37. Soriano A, Marco F, Martinez JA, et al. Influence of vancomycin minimum inhibitory concentration on the treatment of methicillin-resistant Staphylococcus aureus bacteremia. *Clin Infect Dis*. 2008;**46**(2):193–200.
38. Tenover FC, Moellering RC, Jr. The rationale for revising the clinical and laboratory standards institute vancomycin minimal inhibitory concentration interpretive criteria for Staphylococcus aureus. *Clin Infect Dis*. 2007;**44**(9):1208–1215.
39. Maor Y, Hagin M, Belausov N, et al. Clinical features of heteroresistant vancomycin-intermediate Staphylococcus aureus bacteremia versus those of methicillin-resistant S. aureus bacteremia. *J Infect Dis*. 2009;**199**(5):619–624.
40. Cui L, Ma X, Sato K, et al. Cell wall thickening is a common feature of vancomycin resistance in Staphylococcus aureus. *J Clin Microbiol*. 2003;**41**(1):5–14.
41. Sievert DM, Rudrik JT, Patel JB, et al. Vancomycin-resistant Staphylococcus aureus in the United States, 2002–2006. *Clin Infect Dis*. 2008;**46**(5):668–674.
42. Wegener H. Ending the use of antimicrobial growth promotes is making a difference. *ASM News*. 2003;**69**(9:)443–448.
43. Werner G, Coque TM, Hammerum AM, et al. Emergence and spread of vancomycin resistance among enterococci in Europe. *Eur Surveill*. 2008;**13**(47):19046.
44. Centers for Disease Control and Prevention. About antimicrobial

resistance. Available at: www.cdc.gov/drugresistance/about.html. Accessed January 4, 2016.

45. Calfee DP, Salgado CD, Milstone AM, et al. Strategies to prevent methicillin-resistant Staphylococcus aureus transmission and infection in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol*. 2014;**35**(7):772–796.
46. Centers for Disease Control and Prevention. Management of multidrug-resistant organisms in healthcare settings. Available at: www.cdc.gov/hicpac/mdro/mdro_0.html. Accessed January 4, 2016.
47. Centers for Disease Control and Prevention. Surveillance for C. difficile, MRSA, and other drug-resistant infections. Available at: www.cdc.gov/nhsn/acute-care-hospital/cdiff-mrsa/index.html. Accessed January 5, 2016.
48. Struelens MJ, Hawkey PM, French GL, et al. Laboratory tools and strategies for methicillin-resistant Staphylococcus aureus screening, surveillance and typing: state of the art and unmet needs. *Clin Microbiol Infect*. 2009;**15**(2):112–119.
49. Malhotra-Kumar S, Haccuria K, Michiels M, et al. Current trends in rapid diagnostics for methicillin-resistant Staphylococcus aureus and glycopeptide-resistant enterococcus species. *J Clin Microbiol*. 2008;**46**(5):1577–1587.
50. Boyce JM PD, Healthcare Infection Control Practices Advisory Committee, HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Guideline for hand hygiene in health-care settings. recommendations of the healthcare infection control practices advisory committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. *MMWR Recomm Rep*. 2002;Oct 25;**51**(RR-16):1–45.
51. Centers for Disease Control and Prevention. Guideline for hand hygiene in health-care settings. Available at: www.cdc.gov/handhygiene/training.html. Accessed January 5, 2016.
52. Morgan DJ, Murthy R, Munoz-Price LS, et al. Reconsidering contact precautions for endemic methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococcus. *Infect Control Hosp Epidemiol*. 2015;**36**(10):1163–1172.
53. Stelfox HT, Bates DW, Redelmeier DA. Safety of patients isolated for infection control. *JAMA*. 2003;**290**(14):1899–1905.
54. Day HR, Perencevich EN, Harris AD, et al. Do contact precautions cause depression? A two-year study at a tertiary care medical centre. *J Hosp Infect*. 2011;**79**(2):103–107.
55. Harris AD, Pineles L, Belton B, et al. Universal glove and gown use and acquisition of antibiotic-resistant bacteria in the ICU: a randomized trial. *JAMA*. 2013;**310**(15):1571–1580.
56. Occupational exposure to bloodborne pathogens–OSHA. final rule. *Fed Regist*. 1991;**56**(235):64004–64182.
57. Boyce JM, Potter-Bynoe G, Chenevert C, et al. Environmental contamination due to methicillin-resistant Staphylococcus aureus: possible infection control implications. *Infect Control Hosp Epidemiol*. 1997;**18**(9):622–627.
58. Smith TL, Iwen PC, Olson SB, et al. Environmental contamination with vancomycin-resistant enterococci in an outpatient setting. *Infect Control Hosp Epidemiol*. 1998;**19**(7):515–518.
59. Hardy KJ, Oppenheim BA, Gossain S, et al. A study of the relationship between environmental contamination with methicillin-resistant Staphylococcus aureus (MRSA) and patients' acquisition of MRSA. *Infect Control Hosp Epidemiol*. 2006;**27**(2):127–132.
60. Snyder GM, Thom KA, Furuno JP, et al. Detection of methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci on the gowns and gloves of healthcare workers. *Infect Control Hosp Epidemiol*. 2008;**29**(7):583–589.
61. Puzniak LA, Leet T, Mayfield J, et al. To gown or not to gown: The effect on acquisition of vancomycin-resistant enterococci. *Clin Infect Dis*. 2002;**35**(1):18–25.
62. Srinivasan A, Song X, Ross T, et al. A prospective study to determine whether cover gowns in addition to gloves decrease nosocomial transmission of vancomycin-resistant enterococci in an intensive care unit. *Infect Control Hosp Epidemiol*. 2002;**23**(8):424–428.
63. Williams C, McGraw P, Schneck EE, et al. Impact of universal gowning and gloving on health care worker clothing contamination. *Infect Control Hosp Epidemiol*. 2015;**36**(4):431–437.
64. Vajravelu RK, Guerrero DM, Jury LA, et al. Evaluation of stethoscopes as vectors of Clostridium difficile and methicillin-resistant Staphylococcus aureus. *Infect Control Hosp Epidemiol*. 2012;**33**(1):96–98.
65. de Gialluly C, Morange V, de Gialluly E, et al. Blood pressure cuff as a potential vector of pathogenic microorganisms: a prospective study in a teaching hospital. *Infect Control Hosp Epidemiol*. 2006;**27**(9):940–943.
66. Livornese LL, Jr, Dias S, Samel C, et al. Hospital-acquired infection with vancomycin-resistant enterococcus faecium transmitted by electronic thermometers. *Ann Intern Med*. 1992;**117**(2):112–116.
67. Brooks S, Khan A, Stoica D, et al. Reduction in vancomycin-resistant enterococcus and Clostridium difficile infections following change to tympanic thermometers. *Infect Control Hosp Epidemiol*. 1998;**19**(5):333–336.
68. Sexton T, Clarke P, O'Neill E, et al. Environmental reservoirs of methicillin-resistant Staphylococcus aureus in isolation rooms: Correlation with patient isolates and implications for hospital hygiene. *J Hosp Infect*. 2006;**62**(2):187–194.
69. Neely AN, Maley MP. Survival of enterococci and staphylococci on hospital fabrics and plastic. *J Clin Microbiol*. 2000;**38**(2):724–726.
70. Drees M, Snydman DR, Schmid CH, et al. Prior environmental contamination increases the risk of acquisition of vancomycin-resistant enterococci. *Clin Infect Dis*. 2008;**46**(5):678–685.
71. Carling PC, Parry MM, Rupp ME, et al. Improving cleaning of the environment surrounding patients in 36 acute care hospitals. *Infect Control Hosp Epidemiol*. 2008;**29**(11):1035–1041.
72. Hayden MK, Bonten MJ, Blom DW, et al. Reduction in acquisition of vancomycin-resistant enterococcus after enforcement of routine environmental cleaning measures. *Clin Infect Dis*. 2006;**42**(11):1552–1560.
73. Rupp ME, Fitzgerald T, Sholtz L, et al. Maintain the gain: program to sustain performance improvement in environmental cleaning. *Infect Control Hosp Epidemiol*. 2014;**35**(7):866–868.
74. Sehulster L, Chinn RY, CDC, et al. Guidelines for environmental infection control in health-care facilities: recommendations of CDC and the healthcare infection control practices advisory committee (HICPAC). *MMWR Recomm Rep*. 2003;**52** (RR-10):1–42.

75. Carling PC, Parry MF, Bruno-Murtha LA, et al. Improving environmental hygiene in 27 intensive care units to decrease multidrug-resistant bacterial transmission. *Crit Care Med*. 2010;**38** (4):1054–1059.
76. Passaretti CL, Otter JA, Reich NG, et al. An evaluation of environmental decontamination with hydrogen peroxide vapor for reducing the risk of patient acquisition of multidrug-resistant organisms. *Clin Infect Dis*. 2013;**56**(1):27–35.
77. Nerandzic MM, Thota P, Sankar CT, et al. Evaluation of a pulsed xenon ultraviolet disinfection system for reduction of healthcare-associated pathogens in hospital rooms. *Infect Control Hosp Epidemiol*. 2015;**36** (2):192–197.
78. Salgado CD, Sepkowitz KA, John JF, et al. Copper surfaces reduce the rate of healthcare-acquired infections in the intensive care unit. *Infect Control Hosp Epidemiol*. 2013;**34**(5):479–486.
79. Byers KE, Anglim AM, Anneski CJ, et al. Duration of colonization with vancomycin-resistant enterococcus. *Infect Control Hosp Epidemiol*. 2002;**23** (4):207–211.
80. Donskey CJ, Hoyen CK, Das SM, et al. Recurrence of vancomycin-resistant enterococcus stool colonization during antibiotic therapy. *Infect Control Hosp Epidemiol*. 2002;**23**(8):436–440.
81. Henard S, Lozniewski A, Aissa N, et al. Evaluation of the duration of vanA vancomycin-resistant enterococcus faecium carriage and clearance during a large-scale outbreak in a region of eastern France. *Am J Infect Control*. 2011;**39**(2):169–171.
82. Scanvic A, Denic L, Gaillon S, et al. Duration of colonization by methicillin-resistant Staphylococcus aureus after hospital discharge and risk factors for prolonged carriage. *Clin Infect Dis*. 2001;**32**(10):1393–1398.
83. Harbarth S, Liassine N, Dharan S, et al. Risk factors for persistent carriage of methicillin-resistant Staphylococcus aureus. *Clin Infect Dis*. 2000;**31** (6):1380–1385.
84. Marschall J, Muhlemann K. Duration of methicillin-resistant Staphylococcus aureus carriage, according to risk factors for acquisition. *Infect Control Hosp Epidemiol*. 2006;**27** (11):1206–1212.
85. Shenoy ES, Kim J, Rosenberg ES, et al. Discontinuation of contact precautions for methicillin-resistant Staphylococcus aureus: a randomized controlled trial comparing passive and active screening with culture and polymerase chain reaction. *Clin Infect Dis*. 2013;**57**(2):176–184.
86. Robicsek A, Beaumont JL, Paule SM, et al. Universal surveillance for methicillin-resistant Staphylococcus aureus in 3 affiliated hospitals. *Ann Intern Med*. 2008;**148**(6):409–418.
87. Girou E, Pujade G, Legrand P, et al. Selective screening of carriers for control of methicillin-resistant Staphylococcus aureus (MRSA) in high-risk hospital areas with a high level of endemic MRSA. *Clin Infect Dis*. 1998;**27**(3):543–550.
88. Huang SS, Rifas-Shiman SL, Pottinger JM, et al. Improving the assessment of vancomycin-resistant enterococci by routine screening. *J Infect Dis*. 2007;**195**(3):339–346.
89. Huang SS, Yokoe DS, Hinrichsen VL, et al. Impact of routine intensive care unit surveillance cultures and resultant barrier precautions on hospital-wide methicillin-resistant Staphylococcus aureus bacteremia. *Clin Infect Dis*. 2006;**43**(8):971–978.
90. Marshall C, Richards M, McBryde E. Do active surveillance and contact precautions reduce MRSA acquisition? A prospective interrupted time series. *PLoS One*. 2013;**8**(3):e58112.
91. Jain R, Kralovic SM, Evans ME, et al. Veterans Affairs initiative to prevent methicillin-resistant Staphylococcus aureus infections. *N Engl J Med*. 2011;**364**(15):1419–1430.
92. Harbarth S, Fankhauser C, Schrenzel J, et al. Universal screening for methicillin-resistant Staphylococcus aureus at hospital admission and nosocomial infection in surgical patients. *JAMA*. 2008;**299** (10):1149–1157.
93. Huskins WC, Huckabee CM, O'Grady NP, et al. Intervention to reduce transmission of resistant bacteria in intensive care. *N Engl J Med*. 2011;**364**(15):1407–1418.
94. Derde LP, Cooper BS, Goossens H, et al. Interventions to reduce colonisation and transmission of antimicrobial-resistant bacteria in intensive care units: an interrupted time series study and cluster randomised trial. *Lancet Infect Dis*. 2014;**14**(1):31–39.
95. Huang SS, Septimus E, Kleinman K, et al. Targeted versus universal decolonization to prevent ICU infection. *N Engl J Med*. 2013;**368** (24):2255–2265.
96. Eveillard M, de Lassence A, Lancien E, et al. Evaluation of a strategy of screening multiple anatomical sites for methicillin-resistant Staphylococcus aureus at admission to a teaching hospital. *Infect Control Hosp Epidemiol*. 2006;**27**(2):181–184.
97. Cherkaoui A, Renzi G, Francois P, et al. Comparison of four chromogenic media for culture-based screening of meticillin-resistant Staphylococcus aureus. *J Med Microbiol*. 2007;**56** (Pt 4):500–503.
98. Jeyaratnam D, Whitty CJ, Phillips K, et al. Impact of rapid screening tests on acquisition of meticillin resistant Staphylococcus aureus: cluster randomised crossover trial. *BMJ*. 2008;**336**(7650):927–930.
99. Roisin S, Laurent C, Denis O, et al. Impact of rapid molecular screening at hospital admission on nosocomial transmission of methicillin-resistant Staphylococcus aureus: Cluster randomised trial. *PLoS One*. 2014;**9**(5): e96310.
100. Dacre J, Emmerson AM, Jenner EA. Gentamicin-methicillin-resistant Staphylococcus aureus: epidemiology and containment of an outbreak. *J Hosp Infect*. 1986;**7**(2):130–136.
101. Meier PA, Carter CD, Wallace SE, et al. A prolonged outbreak of methicillin-resistant Staphylococcus aureus in the burn unit of a tertiary medical center. *Infect Control Hosp Epidemiol*. 1996;**17**(12):798–802.
102. Saiman L, Cronquist A, Wu F, et al. An outbreak of methicillin-resistant Staphylococcus aureus in a neonatal intensive care unit. *Infect Control Hosp Epidemiol*. 2003;**24**(5):317–321.
103. Vernon MO, Hayden MK, Trick WE, et al. Chlorhexidine gluconate to cleanse patients in a medical intensive care unit: the effectiveness of source control to reduce the bioburden of vancomycin-resistant enterococci. *Arch Intern Med*. 2006;**166** (3):306–312.
104. Karki S, Cheng AC. Impact of non-rinse skin cleansing with chlorhexidine gluconate on prevention of healthcare-associated infections and colonization with multi-resistant organisms: a systematic review. *J Hosp Infect*. 2012;**82**(2):71–84.
105. Ridenour G, Lampen R, Federspiel J, et al. Selective use of intranasal mupirocin and chlorhexidine bathing and the incidence of methicillin-resistant Staphylococcus

aureus colonization and infection among intensive care unit patients. *Infect Control Hosp Epidemiol*. 2007;**28**(10):1155–1161.

106. Evans HL, Dellit TH, Chan J, et al. Effect of chlorhexidine whole-body bathing on hospital-acquired infections among trauma patients. *Arch Surg*. 2010;**145**(3):240–246.
107. Noto MJ, Domenico HJ, Byrne DW, et al. Chlorhexidine bathing and health care-associated infections: a randomized clinical trial. *JAMA*. 2015;**313**(4):369–378.
108. Climo MW, Sepkowitz KA, Zuccotti G, et al. The effect of daily bathing with chlorhexidine on the acquisition of methicillin-resistant Staphylococcus aureus, vancomycin-resistant enterococcus, and healthcare-associated bloodstream infections: results of a quasi-experimental multicenter trial. *Crit Care Med*. 2009;**37**(6):1858–1865.
109. Climo MW, Yokoe DS, Warren DK, et al. Effect of daily chlorhexidine bathing on hospital-acquired infection. *N Engl J Med*. 2013;**368**(6):533–542.
110. Lee AS, Cooper BS, Malhotra-Kumar S, et al. Comparison of strategies to reduce meticillin-resistant Staphylococcus aureus rates in surgical patients: a controlled multicentre intervention trial. *BMJ Open*. 2013;**3**(9):e003126–003126.
111. Widner A, Nobles DL, Faulk C, et al. The impact of a "search and destroy" strategy for the prevention of methicillin-resistant Staphylococcus aureus infections in an inpatient rehabilitation facility. *PM R*. 2014;**6**(2):121–6; quiz 126.
112. Kassakian SZ, Mermel LA, Jefferson JA, et al. Impact of chlorhexidine bathing on hospital-acquired infections among general medical patients. *Infect Control Hosp Epidemiol*. 2011;**32**(3):238–243.
113. Rupp ME, Cavalieri RJ, Lyden E, et al. Effect of hospital-wide chlorhexidine patient bathing on healthcare-associated infections. *Infect Control Hosp Epidemiol*. 2012;**33**(11):1094–1100.
114. Wang X, Panchanathan S, Chowell G. A data-driven mathematical model of CA-MRSA transmission among age groups: evaluating the effect of control interventions. *PLoS Comput Biol*. 2013;**9**(11):e1003328.
115. Popoola VO, Budd A, Wittig SM, et al. Methicillin-resistant Staphylococcus aureus transmission and infections in a neonatal intensive care unit despite active surveillance cultures and decolonization: challenges for infection prevention. *Infect Control Hosp Epidemiol*. 2014;**35**(4):412–418.
116. Delaney HM, Wang E, Melish M. Comprehensive strategy including prophylactic mupirocin to reduce Staphylococcus aureus colonization and infection in high-risk neonates. *J Perinatol*. 2013;**33**(4):313–318.
117. Milstone AM, Elward A, Song X, et al. Daily chlorhexidine bathing to reduce bacteraemia in critically ill children: a multicentre, cluster-randomised, crossover trial. *Lancet*. 2013;**381**(9872):1099–1106.
118. Kumar N, David MZ, Boyle-Vavra S, et al. High Staphylococcus aureus colonization prevalence among patients with skin and soft tissue infections and controls in an urban emergency department. *J Clin Microbiol*. 2015;**53**(3):810–815.
119. Buehlmann M, Frei R, Fenner L, et al. Highly effective regimen for decolonization of methicillin-resistant Staphylococcus aureus carriers. *Infect Control Hosp Epidemiol*. 2008;**29**(6):510–516.
120. Hetem DJ, Bonten MJ. Clinical relevance of mupirocin resistance in Staphylococcus aureus. *J Hosp Infect*. 2013;**85**(4):249–256.
121. Lee AS, Macedo-Vinas M, Francois P, et al. Impact of combined low-level mupirocin and genotypic chlorhexidine resistance on persistent methicillin-resistant Staphylococcus aureus carriage after decolonization therapy: a case-control study. *Clin Infect Dis*. 2011;**52**(12):1422–1430.
122. Batra R, Cooper BS, Whiteley C, et al. Efficacy and limitation of a chlorhexidine-based decolonization strategy in preventing transmission of methicillin-resistant Staphylococcus aureus in an intensive care unit. *Clin Infect Dis*. 2010;**50**(2):210–217.
123. Centers for Disease Control and Prevention. Guide to infection prevention for outpatient settings: minimum expectations for safe care. Available at: www.cdc.gov/HAI/settings/outpatient/outpatient-care-guidelines.html. Accessed January 22, 2016.
124. Smith PW, Bennett G, Bradley S, et al. SHEA/APIC guideline: infection prevention and control in the long-term care facility. *Am J Infect Control*. 2008;**36**(7):504–535.

Chapter 17

Control of Gram-Negative Multidrug-Resistant Pathogens

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1.0 Introduction

In 2014, the World Health Organization declared antimicrobial resistance an international crisis that requires urgent action.[1] During the past decade, the incidence of multidrug-resistant Gram-negatives (MDRGNs) has reached unprecedented levels, affecting the practice of medicine in virtually all healthcare settings. Their dissemination will likely only continue with the rise in international migration and medical tourism. Compounding the problem is the stagnation in the pharmaceutical industry in developing new antibiotics against MDRGNs because of significant economic, scientific, and regulatory barriers. To address these sobering facts, global efforts to improve the detection and limit the spread of MDRGNs are needed.

2.0 Defining MDRGNs

Efforts to characterize and enumerate multidrug-resistance have been hampered in part by the lack of standardized definitions. Promotion of standard MDRGN definitions by public health agencies and expert societies could enable more accurate prevalence estimates. A cross-sectional survey conducted in 2012 to 2013 described substantial variation in definitions of multidrug-resistance for Gram-negative organisms across healthcare institutions.[2] In response to the wide variation in definitions used to characterize multidrug-resistance in the medical literature, a group of international experts came together through a joint initiative by the European Centre for Disease Prevention and Control and the United States Centers for Disease Control and Prevention (CDC), to create a standardized international terminology to describe acquired resistance profiles in Enterobacteriaceae, *Pseudomonas aeruginosa*, and *Acinetobacter* spp.[3] These definitions are used in the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) publication in 2014 entitled "ESCMID Guidelines for the Management of the Infection Control Measures to Reduce Transmission of Multidrug-Resistant Gram-Negative Bacteria in Hospitalized Patients."[4] More recently, in 2015, the US CDC's National Healthcare and Safety Network (NHSN) published "antimicrobial resistant phenotypic" definitions for various epidemiologically important MDR organisms. These definitions require nonsusceptibility to one or more antimicrobials in three or more antimicrobial classes, and are used for surveillance purposes in US healthcare facilities (Table 17.1).[5] The Clinical and Laboratory Standards Institute (CLSI) establishes recommendations followed by most clinical microbiology laboratories in the US as to what constitutes "susceptibility" and "nonsusceptibility" of specific organisms to specific antibiotics.[6] The European Committee on Antimicrobial Susceptibility Testing (EUCAST) does the same for the European Union.[7] Changes in CLSI and EUCAST recommendations should be reviewed with the clinical microbiology laboratory at least annually.

3.0 Select Epidemiologically Important Gram-Negative Pathogens

This section will outline some of the most clinically important Gram-negative pathogens, including extended-spectrum β-lactamases (ESBLs), carbapenem-resistant Enterobacteriaceae (CRE), multidrug-resistant *P. aeruginosa*, and multidrug-resistant *Acinetobacter baumanii*. A report from the CDC's NHSN described antimicrobial resistance patterns for healthcare-associated infections across intensive care units (ICUs) submitted to the NHSN during 2009–2010.[8] Pooled data evaluating multidrug-resistance from central line–associated bloodstream infections, catheter-associated urinary tract infections, and ventilator-associated pneumonia were as follows: *A. baumannii* (67 percent), *Escherichia coli* (2 percent), *Enterobacter* spp. (3 percent), *Klebsiella* spp. (16 percent), *and P. aeruginosa* (15 percent).

The clinical microbiology laboratory plays a pivotal role in generating and disseminating data related to MDRGNs (see Chapter 23). To ensure that infection prevention teams can act upon these data in a timely manner, it is important for the infection prevention team and the clinical microbiology laboratory director to periodically review MDRGN definitions, surveillance practices, standardized mechanisms of notification of results in real time, and practices of units with unacceptable rates of MDRGN colonization or infection.

3.1 Extended-spectrum β-lactamases (ESBLs): Currently, there are over 1300 β-lactamases present.[9] The Ambler classification system differentiates β-lactamases based on molecular structure. ESBLs are categorized in Class A of the Ambler classification scheme. These enzymes are produced exclusively by Gram-negative organisms, primarily *E. coli, K. pneumoniae, K. oxytoca*, and *Proteus mirabilis*. As these organisms are generally found in the intestinal tract, common infections caused by ESBL-producing pathogens include intra-abdominal infections and urinary tract infections. ESBLs confer resistance to most β-lactam antibiotics, including penicillins, cephalosporins, and aztreonam. ESBLs are not able to effectively inactivate

Table 17.1 National Healthcare Safety Network surveillance definitions for antimicrobial resistance[1]

Pathogen	Definition
Carbapenem-resistant Enterobacteriaceae	Any *Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae*, or *Enterobacter* spp. that has tested resistant to at least one of the following: doripenem, ertapenem, imipenem, or meropenem
Multidrug-resistant *Pseudomonas aeruginosa*	*Pseudomonas aeruginosa* that has tested either intermediate or resistant to at least 1 drug in at least 3 of the following 5 categories: 1. Extended-spectrum cephalosporins (cefepime, ceftazidime) 2. Fluoroquinolones (ciprofloxacin, levofloxacin) 3. Aminoglycosides (amikacin, gentamicin, tobramycin) 4. Carbapenems (imipenem, meropenem, doripenem) 5. Piperacillin/piperacillin-tazobactam
Multidrug-resistant *Acinetobacter* spp.	Any *Acinetobacter* spp. that has tested either intermediate or resistant to at least 1 drug in at least 3 of the following 6 categories: - Extended-spectrum cephalosporins (cefepime, ceftazidime) - Fluoroquinolones (ciprofloxacin, levofloxacin) - Aminoglycosides (amikacin, gentamicin, tobramycin) - Carbapenems (imipenem, meropenem, doripenem) - Piperacillin/piperacilin-tazobactam - Ampicillin/sulbactam

[1] www.cdc.gov/nhsn/pdfs/ps-analysis-resources/phenotype_definitions.pdf.

the cephamycins (e.g., cefoxitin and cefotetan) or the carbapenems. Their *in vitro* growth may be inhibited by β-lactamase inhibitor antibiotics (e.g., -tazobactam, -clavulanate). The CLSI does not require that diagnostic laboratories perform confirmatory testing of Gram-negative organisms for ESBLs, so antibiotic susceptibility patterns are often used as surrogates to suggest their presence. Without standardized testing, the actual prevalence of organisms producing ESBLs in the United States is unknown and likely underestimated. In a sample of over 5000 *E. coli, Klebsiella* spp., and *P. mirabilis* isolates collected from 72 US hospitals, 12 percent were identified as ESBL-producing.[10] The prevalence by species was as follows: *K. pneumoniae* (16 percent), *E. coli* (12 percent), *K. oxytoca* (10 percent), and *P. mirabilis* (5 percent). The ESBL family is heterogenous and includes CTX-M type, SHV-type, and TEM-type ESBLs. CTX-M are the most common ESBLs found in the United States.[10] The successful proliferation of CTX-M ESBLs is related to the dissemination of CTX-M encoding genes on mobile genetic elements that have inserted themselves into highly successful lineages, most notably *E. coli* sequence type 131 (ST131).[11]

3.2 Carbapenem-Resistant Enterobacteriaceae (CRE): The NHSN reported that approximately 12 percent of all *Klebsiella* isolates recovered in 2009–2010[8] were carbapenem resistant, compared with slightly less than 1 percent in 2000.[12] These organisms have become increasingly prevalent in the US and are endemic in the Northeast.[13] In 2013, the CDC assigned the highest threat level to CRE, declaring that they require urgent public health attention. CRE infections are associated with mortality upwards of 60 percent in some reports.[14–18] The most common Enterobacteriaceae exhibiting carbapenem resistance are *K. pneumoniae* followed by *Enterobacter* spp.[8]

Resistance to carbapenems develops by one of two general mechanisms: enzymatic or non-enzymatic mechanisms. The former involves production of carbapenemases, enzymes that hydrolyze the β-lactam ring of carbapenem antibiotics. The latter includes production of ESBLs and/or AmpC cephalosporinases in conjunction with decreases in membrane permeability. Carbapenemase-producing Enterobacteriaceae have largely been responsible for the rapid worldwide spread of CRE owing to easily transferred mobile genetic elements (e.g., plasmids, transposons) that encode carbapenemase genes.[19,20] Carbapenemase-encoding genes are especially successful when they become established in organism strains particularly adept at clonal expansion (e.g. bla_{KPC} gene in sequence type 258 of *K. pneumoniae*).[19,21] These genes can then easily be passed to neighboring bacterial species (Figure 17.1).

Ambler class A carbapenemases include chromosomally as well as plasmid-encoded carbapenemases, the most common of which is *K. pneumoniae* carbapenemase (KPC). KPC production accounts for 80 percent of carbapenem resistance in the United States and is considered endemic in the northeastern US.[13,22] Ambler class B carbapenemases include the Verona integron–encoded metallo-β-lactamase (VIM), the imipenemase (IMP) metallo-β-lactamase, and the New Delhi metallo-beta-lactamases (NDM).[23] VIM and IMP have historically been linked to the Mediterranean region and Asia, although they have been isolated to a lesser frequency worldwide, including in the US.[20] NDM is endemic to the Indian subcontinent and accounts for as many as 50 percent of CRE isolates in this region.[20,23]

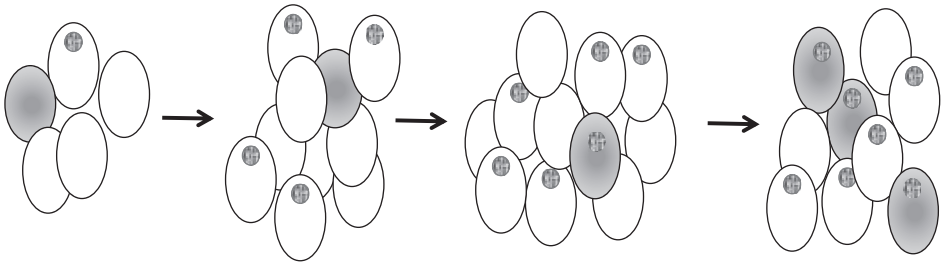

Figure 17.1 Expansion of a *Klebsiella pneumoniae* clone harboring a plasmid containing a carbapenemase-encoding gene that has successfully integrated into Enterobacter cloacae.

Ambler class D carbapenemases are oxacillinases, notably OXA-48. Class D carbapenemases are most frequently identified in *A. baumannii*. OXA-48 was originally associated with the Middle East and North Africa, but like other groups of carbapenemases, have been isolated in several other geographic regions worldwide, including the United States.[24] As these resistance mechanisms continue to spread between species and regions, it is anticipated that organism and geographic distinctions for the various carbapenemases will eventually disappear.

As of January 2015, the CDC defines CRE as organisms resistant to any carbapenem[25] (Table 17.1). Although specifically identifying carbapenemases is not mandatory, it is encouraged when Enterobacteriaceae isolates are suspicious for carbapenemase production.[6] At the present time, most clinical microbiology laboratories do not distinguish enzymatic and non-enzymatic mechanisms of carbapenem resistance. However, determining whether a carbapenem-resistant organism is carbapenemase-producing has important infection control implications as these resistance mechanisms can spread rapidly between patients, leading to devastating consequences. Rapid patient-to-patient spread of noncarbapenemase carbapenem-resistant organisms has not been observed. In addition, without specifically identifying carbapenemase-producers, approximately 50 percent of patients with carbapenem-resistant isolates could unnecessarily be placed on contact isolation precautions.[26]

Available phenotypic tests to identify carbapenemases include the modified Hodge test (Class A and D), metallo-β-lactamase Etest (Class B), and rapid chromogenic assays such as the Carba NP test (Class A and B). The modified Hodge test is a culture-based assay to detect the release of carbapenemases into agar media. Concerns with this assay include (a) limited sensitivity and specificity in detecting carbapenemases (<80 percent for both), (b) low to moderate inter-reader reliability in interpreting results, and (c) turn-around time from culture collection to detection of carbapenemases of approximately 72–96 hours.[27] The Carba NP test has a sensitivity of approximately 90 percent, with lower sensitivity attributed to inconclusive results or false negative results with OXA-type carbapenemases.[28,29] Its specificity approaches 100 percent, which when coupled with the ease of use and rapid turn-around time (within 2 hours), makes it an attractive alternative to the modified Hodge test.[27–29]

3.3 Multidrug-Resistant *Pseudomonas aeruginosa:* *P. aeruginosa* can be recovered from all body sites and is a common cause of healthcare-associated pneumonia. Although still predominantly implicated in infections in patients with previous healthcare exposure, extensive antibiotic use, indwelling hardware, or immunocompromising conditions, it is being increasingly recognized as a cause of community-acquired infections, including folliculitis or otitis externa from swimming pools and hot tubs,[30] puncture wound osteomyelitis,[31] and endocarditis in intravenous drug users.[32] *P. aeruginosa* is intrinsically resistant to a number of antibiotics and can acquire additional resistance during antibiotic therapy. Acquired resistance can be mediated by a number of mechanisms, including degrading enzymes (e.g., AmpC cephalosporinases, carbapenemases), loss or alteration of outer membrane porins, and upregulation of efflux pumps.[33] Aside from evaluating for nonsusceptibility to multiple classes of antibiotics (Table 17.1), there is no commercially available, rapid diagnostic assay to detect the most common mechanisms of resistance for *P. aeruginosa*.

3.4 Multidrug-Resistant *Acinetobacter baumannii*: Similar to *P. aeruginosa, A. baumannii* is a leading cause of healthcare-associated pneumonia, particularly in ICU patients.[34] It is also an important cause of skin and soft tissue infections in military personnel returning from deployment and in victims of natural disasters (e.g., earthquakes).[35] *A. baumannii* has the ability to accumulate diverse mechanisms of resistance, leading to the emergence of isolates nonsusceptible to most or all available antibiotics. Hospital outbreaks with *A. baumannii* can be dramatic and widespread. For example, an outbreak of OXA-40 carbapenemase-producing *A. baumannii* in the Chicago area in 2005 impacted at least seven acute care facilities and two long-term care facilities, and over 90 patients.[36] *A. baumannii* outbreaks can occasionally be traced to contaminated respiratory and ventilator equipment.[37] Prolonged colonization may contribute to the endemicity of *A. baumannii* observed after such outbreaks.[37] In a cross-sectional evaluation of the period prevalence of MDR *A. baumanii* in mechanically ventilated patients in the state of Maryland in 2009–2010, 27 percent of patients were found to be colonized with this pathogen, in a nonoutbreak setting,[38] suggesting its increasing prominence in chronically ventilated patients and in the ICU setting.

4.0 Hospital and Patient-Level Factors Contributing to the Transmission of MDRGNs

There is a long list of causal factors that may be driving the emergence and spread of Gram-negative, antibiotic-resistant bacteria. Figure 17.2 illustrates the complicated interaction among many of these factors. The two most important parameters for deciding which infection prevention and antibiotic stewardship options should be implemented for the control of MDRGNs are 1) the organism-specific proportion of antibiotic resistance attributable to antibiotic use and 2) the organism-specific attributable fraction due to lapses in infection control practices. The ability to quantify both parameters could lead to answers to the following questions:

1. Should I implement contact precautions for patients colonized with MDRGNs?
2. Should I obtain active surveillance cultures to detect patients colonized with MDRGNs?
3. Should I cohort patients colonized with MDRGNs?
4. Should I focus more effort on infection control interventions aimed at decreasing the amount of patient-to-patient transmission or on antimicrobial stewardship interventions aimed at decreasing the emergence of antibiotic resistance?
5. How aggressively should I initiate targeted interventions for cleaning and disinfecting the environment?

However, at present, accurate estimates of these parameters are lacking for many MDRGNs in the nonoutbreak setting for several reasons.[39] First, because transmissions of MDRGNs are relatively uncommon events, any study designed to demonstrate efficacy requires sample sizes that are often prohibitively large to achieve the power needed for definitive conclusions. Second, many studies implement a number of interventions in parallel making it difficult to determine the relative contribution of individual interventions. Third, many of the available data come from quasi-experimental studies that have some epidemiological methodological issues often not accounted for in analyses (see Chapter 6). Fourth, without genomic data, the relatedness between potentially transmitted organisms may not be clear. Despite the limitations of the existing literature, common sense infection control practices suggest that failure to identify and isolate patients harboring highly drug resistant organisms can lead to transmission to other vulnerable patients, potentially leading to significant morbidity and mortality. This is supported by the high colonization rate of healthcare workers contaminating their hands and clothing when caring for patients with MDRGNs.[43,46] With hand hygiene compliance rates still being nowhere near 100 percent, in our opinion these data support the use of contact precautions in preventing the spread of MDRGNs in healthcare facilities.

4.1 Role of the Healthcare Worker in the Transmission of MDRGNs: The healthcare worker is often believed to be the predominant mechanism of patient-to-patient transmission of MDRGNs in the hospital setting. The hands of healthcare providers, their apparel, and their personal medical equipment can become contaminated with antibiotic-resistant bacteria and contribute to the subsequent transfer of organisms between patients. One study demonstrated that nearly 25 percent of healthcare workers practicing usual care in the ICU become contaminated with organisms during their shift.[40] A number of studies have demonstrated that healthcare workers become colonized on a frequent basis with antibiotic-resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE).[41,42] Less work has been done to determine the role of gloves and gowns in protecting healthcare workers caring for patients harboring MDRGNs from colonization. ICU data

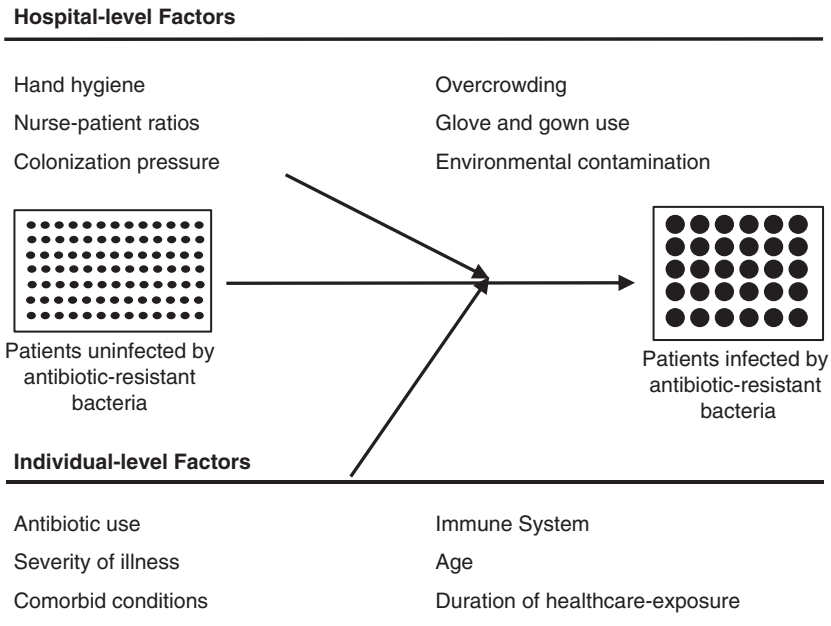

Figure 17.2 Interaction among causal factors contributing to antibiotic resistance in gram-negative bacteria.

indicate that approximately 39 percent of healthcare workers contaminate their gowns or gloves after contact with patients colonized with MDR *A. baumanii*.[43] This is in contrast to approximately an 8 percent gown or glove contamination rate after caring for patients colonized with MDR *P. aeruginosa*.[43] These results highlight the potential for contact precautions to reduce transmission of MDRGNs between patients. They also suggest that differential rates of transmission across Gram-negative organisms exist.

Available data suggest a large portion of ESBL-producing *Klebsiella* spp. and a lesser proportion of ESBL-producing *E. coli* are transmitted by patient-to-patient spread. Harris and colleagues evaluated ESBL-producing *E. coli* and ESBL-producing *Klebsiella* spp. in a large cohort.[44,45] These investigators used active surveillance cultures to determine bacterial acquisition, pulsed-field gel electrophoresis (PFGE) to determine the genetic relatedness of isolates, and analysis of data sets that overlapped in time to help determine epidemiologic relatedness. For ESBL-producing *Klebsiella* spp., it was determined that 52 percent of acquisitions in the ICU setting were due to patient-to-patient transmission.[44] In contrast, for ESBL-producing *E. coli*, it was determined that 13 percent of acquisitions in the ICU setting were due to patient-to-patient transmission.[45]

Although differences in the risk of patient transmission by organism species exists, it is unclear if there are differences within the same species depending on the resistance mechanisms present. As an example, the healthcare provider contamination rate of *Klebsiella* species does not differ between patients colonized with KPC-producing organisms and those colonized with non-KPC-producing organisms.[46]

Poor compliance with contact precautions, unrecognized colonized patients not on contact precautions, and differing use of contact precautions contributes to ongoing transmission of MDRGNs.[47] Integrating microbiology data, electronic health record alerts, and automated orders can ensure a rapid and comprehensive system for isolating patients without oversight by infection prevention personnel. One study found that automated reminders recommending contact precautions for patients with drug-resistant pathogens improved initiation of contact precautions from 33 percent to 89 percent for patients harboring drug-resistant pathogens, with a decreased median time to contact precautions of almost 17 hours.[48]

Most studies have evaluated the spread of MDRGNs in the epidemic setting,[49–53] the results of which have highlighted the importance of bundled strategies in preventing transmission.[54] In 2007, the Israel Ministry of Health initiated a nationwide intervention aimed at containing the spread of CRE, primarily driven by the rapid dissemination of a single clone of *K. pneumoniae*.[50,55] During the intervention, healthcare-associated CRE acquisition declined from a monthly high of 55.5 to 11.7 cases per 100,000 patient-days. The Israeli experience suggests that MDRGN containment can occur with a strategy that includes patient isolation, dedicated staffing, and active surveillance. One of the most important lessons from this experience is that infection prevention guidelines are most effective when applied uniformly across healthcare facilities and developed by a centralized public health authority with the power to oversee and enforce their implementation.

4.2 Role of the Environment in the Transmission of MDRGNs: In the last decade, a growing body of research highlights the importance of the environment in transmission of MDR organisms. Numerous studies indicate that having a prior room occupant with MDRGN colonization or infection increases the risk of transmission to a subsequent patient.[56–58] These data suggest that inadequate terminal cleaning of the room upon discharge of the colonized or infected patient leads to transmission events to future occupants.

Studies involving patients colonized with MDRGNs have demonstrated that their immediate environment is frequently contaminated with the same bacteria.[59,60] Although most Gram-negative organisms remain viable on inanimate surfaces for only short periods, *A. baumannii* is relatively resistant to desiccation and may remain viable for extended periods of time. Under experimental conditions, *A. baumannii* was shown to persist on dry surfaces for up to 33 days in one study and for 4 months in another study.[61] *A. baumannii* has been isolated from a variety of environmental surfaces throughout the hospital, including patient beds, bed rails, bedside tables, curtains, sinks, counter tops, and floors.[62–64] One study demonstrated recovery of *A. baumannii* from a bed rail 9 days after a patient infected with the same strain was discharged from that room.[63] Furthermore, several outbreaks due to *A. baumannii* have been linked to an environmental reservoir.[57,63–65]

Nonfermentative bacteria, like *P. aeruginosa*, have often been linked to water reservoirs in the hospital.[66,67] *Pseudomonas* spp. can be found in hospital water and are known to exist in biofilms in faucets and faucet aerators. Potable water itself may be a source, although *P. aeruginosa* isolates recovered from potable water in healthcare settings are rarely MDR unless faucets or faucet aerators are contaminated. However, the relative importance of faucets and hospital water supplies as modes of patient-to-patient transmission in the endemic setting is still not clear.

In addition to environmental cleaning, the importance of appropriate cleaning, disinfection, and sterilization of devices has become increasingly recognized as an important mode of transmission of drug-resistant pathogens. Reprocessed endoscopes contaminated with CRE have been implicated in a number of CRE transmissions[68–70] (see Chapter 8).

4.3 Role of Colonization Pressure in the Transmission of MDRGNs: An influx of patients colonized with MDRGNs with a history of exposure to the healthcare system provides sources for the continued spread of MDRGNs (i.e., increased colonization pressure).[39] Moreover, inpatients exposed to these unidentified carriers can asymptomatically acquire these strains and became a secondary source of transmission. Using CRE as a case study, only a minority of patients colonized with CRE will have positive clinical cultures.[71] A study at a US hospital found that approximately one-third of all positive CRE patients were first identified by screening cultures.[71] An outbreak of carbapenem-resistant *K. pneumoniae* at the National Institutes of Health Clinical Center that led to 18

affected patients and 6 deaths demonstrated that active surveillance was critical in identifying previously unrecognized patients colonized with CRE in the outbreak setting.[49] Whole-genome-sequencing of isolates in this outbreak revealed that the most important transmitters of CRE were asymptomatic carriers and not clinically infected patients.[72] As there is no currently available assay that screens for all epidemiologically relevant MDRGNs, the decision on which organisms to target should be based on local epidemiology.

4.4 Role of Antibiotic Use in the Emergence of MDRGNs. Since the time of penicillin, the introduction of each new antibiotic class has been followed by the emergence of resistance both to that class and often simultaneously to other antibiotic classes. For example, routine fluoroquinolone prophylaxis in patients undergoing urologic procedures is an important driver of not only fluoroquinolone resistance but also of ESBL-producing Enterobacteriaceae.[73] The emergence of broad-spectrum resistance among Gram-negative organisms is particularly concerning since therapeutic options are scarce, and for some infections no effective antibiotic agents are available.[74,75]

An estimated 50 percent of antibiotic use in healthcare facilities is estimated to be unnecessary.[76] The goal of antimicrobial stewardship programs is to ensure that all patients with appropriate indications for antibiotics receive the right drug, at the right dose, for the right duration of time.[77] Antimicrobial stewardship programs can ensure judicious and optimal antibiotic use through both restrictive (i.e., formulary restriction, prior-approval authorization) and persuasive (i.e., institutional guidelines, postprescription review with feedback) techniques[77] (see Chapter 19). Data suggest that decreased rates of antibiotic resistance to specific antibiotics correlates with decreased use of those agents, providing support for the notion that interventions to optimize antibiotic use are necessary for the control of antibiotic resistance.[78–83] This association was confirmed in a Cochrane Database systematic review, which demonstrated that reductions in excessive antibiotic prescribing to hospitalized patients through antimicrobial stewardship programs reduced subsequent antimicrobial resistance.[84]

5.0 Decolonization of Patients Harboring MDRGNs

Compared to decolonization regimens established for MRSA, decolonization practices and benefits for MDRGNs are less clear. Decontamination of the upper respiratory and digestive tracts attempts to reduce infection in critically ill patients by decreasing organism burden at these sites. Methods include oropharyngeal decontamination with antiseptics (e.g., chlorhexidine gluconate [CHG]) and selective decontamination of the oropharyngeal and digestive tracts with nonabsorbable antibiotics. A number of studies have indicated that selective oral and digestive tract decontamination reduces rates of bacteremia and mortality in ICU patients, although the overall benefit appears modest.[85–88] Concern about the long-term effects of prophylactic antibiotics on antimicrobial resistance has precluded widespread acceptance of these practices, particularly in North America. Selective decontamination has not been adopted in most US institutions. Low rates of antibiotic resistance in the Netherlands, where the largest trials were conducted, limit the generalizability of findings to areas more endemic for MDRGNs.

CHG is an antiseptic with broad-spectrum activity against a host of organisms, including highly drug-resistant Gram-negative organisms. Daily CHG bathing has been shown to decrease CRE skin colonization.[89] Large studies have shown a benefit of CHG bathing in reducing the risk of hospital-acquired bloodstream infections and colonization with MRSA and/or VRE, although the effects differed from study to study with a predominant effect being on skin contaminants.[90–93] Although studies specifically focusing on the role of CHG bathing in preventing MDRGN transmission have not been conducted, various bundles that have been successful in reducing MDRGN transmission have included daily CHG bathing.[53,94] However, the concern for development of CHG resistance by Gram-negative organisms has tempered some of the enthusiasm for the potential role of daily CHG bathing.[95–98]

6.0 Important Healthcare Facility Reservoirs of MDRGNs beyond the Acute Care Setting

The community has been shown to be an important setting for the spread of ESBL-producing organisms. A study from a Swiss healthcare facility found that transmission rates of ESBL *E. coli* and *K. pneumoniae* were approximately 5 percent and 8 percent, respectively.[99] These same investigators found that transmission rates in households were approximately 25 percent for both organisms.[99] Transmission of ESBLs appears more efficient among household contacts. One report describes two young children from the same household who presented to medical care for the treatment of ESBL infections. On further evaluation, all 6 household members were identified as carrying the same *E. coli* ST131 strain.[100] A substantial proportion of community-onset ESBL *E. coli* infections have been identified in patients with no discernable healthcareexposures.[101]

Post–acute care facilities, including long-term acute care hospitals (LTACHs), long-term care facilities (LTCFs), and nursing homes are playing an increasingly important role in the healthcare continuum. LTACHs provide care for "medically complex" patients with acute medical needs and are characterized by high rates of both indwelling device and antibiotic utilization. In a study of 45 LTACHs, carbapenem and vancomycin use were higher than the 50th percentile for acute care hospital ICU use.[102] The multimorbidity of the population, prolonged durations of stay, and significant rates of device and antibiotic use establishes the perfect milieu for antibiotic resistance in the post–acute care setting. This is exacerbated by the convergence of high-risk patients from many different healthcare facilities and seems to be particularly concerning for MDRGNs. In an LTCF in the Boston region evaluating over 1600 clinical isolates, MDRGNs were

recovered from 11 percent of patients, compared to MRSA and VRE in 6 percent and 1 percent of residents, respectively.[103] In one freestanding LTACH, approximately 50 percent of *K. pneumoniae* isolates were identified as carbapenem-resistant, with solid organ or stem-cell transplantation, mechanical ventilation, fecal incontinence, and recent antibiotic exposure identified as independent risk factors for colonization or infection with carbapenem-resistant *K. pneumoniae*.[104] LTACH residence has been well-established as a risk factor for CRE, with 30 percent of residents demonstrating colonization with CRE in a point prevalence study of Chicago-area LTACHs.[105] Furthermore, colonization may persist for prolonged periods. In a study evaluating 33 patients in an LTACH colonized with MDRGNs, the median duration of colonization was 144 days.[106] As patients are frequently transferred between LTACHs and acute care facilities, they increase the MDRGN colonization pressure in the respective facilities. Without interventions aimed at controlling the MDRGN reservoir at LTACHs, containment efforts in the acute care setting may be undermined. A standardized, rigorous method of reviewing current and past history of MDR organism colonization or infection when care is transferred between post–acute care and acute care facilities is essential to limiting dissemination of these organisms.

7.0 Current Infection Control Practices and Guidelines Relative to MDRGNs

In the past several years, there have been a number of comprehensive documents advising healthcare facilities on best practices to control the spread of MDRGNs.[4,107–109] The Healthcare Infection Control Practices Advisory Committee (HICPAC) published a guideline in 2007 on the use of isolation precautions to prevent transmission of infectious agents in healthcare settings.[108] There are also recommendations published by HICPAC on the management of MDR organisms in healthcare settings.[107] These publications provide guidance regarding the following: (a) education of healthcare workers; (b) surveillance for targeted MDR organisms; (c) application of infection control precautions during patient care; (d) environmental cleaning and disinfection measures; (e) decolonization practices; and (f) the judicious use of antibiotics.

The CDC recently published a document entitled "Guidance for Control of Carbapenem-Resistant Enterobacteriaceae (CRE)," which recommends certain core measures for all acute and long-term care facilities to decrease the transmission of CRE.[109] These core measures address (1) hand hygiene; (2) contact precautions; (3) patient and staff cohorting; (4) use of invasive devices; (5) antimicrobial stewardship; and (6) active surveillance. To highlight a few core measures, active surveillance of patients transferred from facilities known to have outbreaks of CRE and patients hospitalized within the previous 6 months in countries outside the US where CRE are endemic is recommended. For patients in these categories, preemptive contact precautions pending the results of screening cultures should be considered, and all patients colonized or infected with CRE should be placed on contact precautions. Based on limited data indicating that the duration of colonization with CRE can be prolonged for up to several months,[110,111] the CDC was unable to provide recommendations for the timing of contact precaution discontinuation.

The European Society of Clinical Microbiology and Infectious Diseases (ESCMID) published a document in 2014 entitled "ESCMID Guidelines for the Management of the Infection Control Measures to Reduce Transmission of Multidrug-Resistant Gram-Negative Bacteria in Hospitalized Patients."[4] These evidence-based guidelines were developed after an extensive review of the published literature on infection prevention strategies aimed at reducing the transmission of MDRGNs, and include standard recommendations for all acute care facilities and enhanced recommendations when there is evidence of ongoing transmission of MDRGNs. These guidelines include a discussion of the following topics with regard to their role in decreasing MDRGN transmission: (1) hand hygiene; (2) contact precautions; (3) active surveillance; (4) environmental cleaning; and (5) antimicrobial stewardship.

8.0 Conclusions

The rising prevalence of MDRGNs poses significant challenges for healthcare facilities worldwide. The uniform use of standard precautions and hand hygiene remains the cornerstone of control measures to prevent transmission of organisms between patients. However, in the case of MDRGNs, we believe that enhanced infection control efforts, including contact precautions, are necessary to curb their spread. It is imperative that surveillance of, and prevention of transmission of drug-resistant organisms within healthcare facilities be prioritized by infection prevention teams. Further research studies using sophisticated study designs such as cluster-randomized trials and randomized controlled trials are needed to understand the relative contributions of individual infection prevention strategies in reducing the transmission of specific MDRGNs.

References

1. World Health Organization (WHO). www.who.int/drugresistance/documents/surveillancereport/en/. Accessed November 12, 2015.
2. Drees M, Pineles L, Harris AD, Morgan DJ. Variation in definitions and isolation procedures for multidrug-resistant Gram-negative bacteria: a survey of the Society for Healthcare Epidemiology of America Research Network. *Infect Control Hosp Epidemiol.* Apr 2014;**35**(4):362–366.
3. Magiorakos AP, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect.* Mar 2012;**18**(3):268–281.
4. Tacconelli E, Cataldo MA, Dancer SJ, et al. ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients. *Clin Microbiol Infect.* 2014;**20** Suppl 1:1–55.

5. World Health Organization (WHO). www.cdc.gov/nhsn/pdfs/ps-analysis-resources/phenotype_definitions.pdf. Accessed November 12, 2015.
6. Clinical and Laboratory Standards Institute (CLSI). Performance standards for antimicrobial susceptibility testing; approved standard. *Twenty-fourth informational supplement. CLSI Document M100-S24*. Wayne, PA: CLSI 2014.
7. www.eucast.org/clinical_breakpoints/. Accessed November 12, 2015.
8. Sievert DM, Ricks P, Edwards JR, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009–2010. *Infect Control Hosp Epidemiol*. 2013;**34**(1):1–14.
9. Bush K. The ABCD's of B-lactamase nomenclature. *J Infect Chemother*. 2013; **19**(4):549–559.
10. Castanheira M, Farrell SE, Krause KM, Jones RN, Sader HS. Contemporary diversity of beta-lactamases among Enterobacteriaceae in the nine U.S. census regions and ceftazidime-avibactam activity tested against isolates producing the most prevalent beta-lactamase groups. *Antimicrob Agents Chemother*. 2014;**58** (2):833–838.
11. D'Andrea MM, Arena F, Pallecchi L, Rossolini GM. CTX-M-type beta-lactamases: a successful story of antibiotic resistance. *Int J Med Microbiol*. Aug 2013;**303**(6–7):305–317.
12. Hidron AI, Edwards JR, Patel J, et al. NHSN annual update: antimicrobial-resistant pathogens associated with healthcare-associated infections: annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007. *Infect Control Hosp Epidemiol*. Nov 2008;**29** (11):996–1011.
13. Guh AY, Bulens SN, Mu Y, et al. Epidemiology of carbapenem-resistant enterobacteriaceae in 7 US communities, 2012–2013. *JAMA*. 2015;**314**(14):1479–1487.
14. Perez F, Van Duin D. Carbapenem-resistant Enterobacteriaceae: a menace to our most vulnerable patients. *Cleve Clin J Med*. Apr 2013;**80**(4):225–233.
15. Centers for Disease Control and Prevention (CDC). Vital signs: carbapenem-resistant Enterobacteriaceae. *MMWR*. 2013;**62** (9):165–170.
16. Borer A, Saidel-Odes L, Riesenberg K, et al. Attributable mortality rate for carbapenem-resistant Klebsiella pneumoniae bacteremia. *Infect Control Hosp Epidemiol*. 2009;**30**(10):972–976.
17. Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-resistant Enterobacteriaceae: epidemiology and prevention. *Clin Infect Dis*. 2011;**53** (1):60–67.
18. Satlin MJ, Jenkins SG, Walsh TJ. The global challenge of carbapenem-resistant Enterobacteriaceae in transplant recipients and patients with hematologic malignancies. *Clin Infect Dis*. 2014;**58**(9):1274–1283.
19. Munoz-Price LS, Poirel L, Bonomo RA, et al. Clinical epidemiology of the global expansion of Klebsiella pneumoniae carbapenemases. *Lancet Infect Dis*. 2013; **13**(9):785–96.
20. Nordmann P, Naas T, Poirel L. Global spread of Carbapenemase-producing Enterobacteriaceae. *Emerg Infect Dis*. 2011;**17**(10):1791–1798.
21. Kitchel B, Rasheed JK, Patel JB, et al. Molecular epidemiology of KPC-producing Klebsiella pneumoniae isolates in the United States: clonal expansion of multilocus sequence type 258. *Antimicrob Agents Chemother*. 2009;**53**(8):3365–3370.
22. Kaiser RM, Castanheira M, Jones RN, Tenover F, Lynfield R. Trends in Klebsiella pneumoniae carbapenemase-positive K. pneumoniae in US hospitals: report from the 2007–2009 SENTRY Antimicrobial Surveillance Program. *Diagn Microbiol Infect Dis*. Jul 2013;**76** (3):356–360.
23. Kumarasamy KK, Toleman MA, Walsh TR, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *Lancetl Infect Dis*. 2010;**10**(9):597–602.
24. Mathers AJ, Hazen KC, Carroll J, et al. First clinical cases of OXA-48-producing carbapenem-resistant Klebsiella pneumoniae in the United States: the "menace" arrives in the New World. *J Clin Microbiol*. 2013; **51**(2) 680–683.
25. Centers for Disease Control (CDC). www.cdc.gov/hai/organisms/cre/definition.html. Accessed October 19, 2015.
26. Chea N, Bulens SN, Kongphet-Tran T, et al. Improved phenotype-based definition for identifying carbapenemase producers among carbapenem-resistant Enterobacteriaceae. *Emerg Infect Dis*. 2015;**21**(9):1611–1616.
27. Hrabak J, Chudackova E, Papagiannitsis CC. Detection of carbapenemases in Enterobacteriaceae: a challenge for diagnostic microbiological laboratories. *Clin Microbiol Infect*. Sep 2014;**20**(9):839–853.
28. Hombach M, von Gunten B, Gastelberg C, et al. Evaluation of the RAPIDEC® CARBA NP test for the detection of carbapenemases in Enterobacteriaceae. *J Clin Microbiol* 2015 Sep **30**. pii: JCM.02327–15. Epub ahead of print.
29. Nordmann P, Poirel L, Dortet L. Rapid detection of carbapenemase-producing Enterobacteriaceae. *Emerg Infect Dis*. 2012;**18**(9):1503–1507.
30. Pseudomonas dermatitis/folliculitis associated with pool and hot tubs: Colorado and Maine, 1999–2000. *MMW*. 2000;**49**(48):1087–1091.
31. Dixon RS, Sydnor CH. Puncture wound pseudomonal osteomyelitis of the foot. *J Foot Ankle Surg*. 1993; **32**(4):434–442.
32. Wieland M, Lederman MM, Kline-King C, et al. Left-sided endocarditis due to Pseudomonas aeruginosa: a report of 10 cases and review of the literature. *Medicine (Baltimore)*. May 1986; **65**(3):180–189.
33. Livermore DM. Multiple mechanisms of antimicrobial resistance in Pseudomonas aeruginosa: our worst nightmare? *Clin Infect Dis*. 2002; **34** (5):634–640.
34. Maragakis LL and Perl TM. Acinetobacter baumannii: epidemiology, antimicrobial resistance, and treatment options. *Clin Infect Dis* 2008;**46**(8):1254–1263.
35. Acinetobacter baumannii infections among patients at military medical facilities treating injured U.S. service members, 2002–2004. *MMWR*. 2004;**53** (45):1063–1066.
36. Lolans K, Rice TW, Munoz-Price LS, Quinn JP. Multicity outbreak of carbapenem-resistant Acinetobacter baumannii isolates producing the carbapenemase OXA-40. *Antimicrob Agents Chemother*. 2006;**50** (9):2941–2945.
37. Munoz-Price LS, Arheart K, Nordmann P, et al. Eighteen years of experience with Acinetobacter baumannii in a tertiary care hospital. *Crit Care Med*. Dec 2013;**41** (12):2733–2742.
38. Thom KA, Maragakis LL, Richards K, et al. Assessing the burden of

Acinetobacter baumannii in Maryland: a statewide cross-sectional period prevalence survey. *Infect Control Hosp Epidemiol*. Sep 2012;**33**(9):883–888.

39. Harris AD, McGregor JC, Furuno JP. What infection control interventions should be undertaken to control multidrug-resistant gram-negative bacteria? *Clin Infect Dis* Sept 2006:**43** Suppl 2:S57–S61.
40. Williams C, McGraw P, Schneck EE, et al. Impact of universal gowning and gloving on health care worker clothing contamination. *Infect Control Hosp Epidemiol*. 2015;**36**(4):431–437.
41. Hayden MK, Blom DW, Lyle EA, Moore CG, Weinstein RA. Risk of hand or glove contamination after contact with patients colonized with vancomycin-resistant enterococcus or the colonized patients' environment. *Infect Control Hosp Epidemiol*. 2008;**29** (2):149–154.
42. Snyder GM, Thom KA, Furuno JP, et al. Detection of methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci on the gowns and gloves of healthcare workers. *Infect Control Hosp Epidemiol*. 2008;**29**(7):583–589.
43. Morgan DJ, Liang SY, Smith CL, et al. Frequent multidrug-resistant Acinetobacter baumannii contamination of gloves, gowns, and hands of healthcare workers. *Infect Control Hosp Epidemiol*. 2010;**31** (7):716–721.
44. Harris AD, Perencevich EN, Johnson JK, et al. Patient-to-patient transmission is important in extended-spectrum beta-lactamase-producing Klebsiella pneumoniae acquisition. *Clin Infect Dis*. 2007;**45** (10):1347–1350.
45. Harris AD, Kotetishvili M, Shurland S, et al. How important is patient-to-patient transmission in extended-spectrum beta-lactamase Escherichia coli acquisition. *Am J Infect Contrl*. 2007;**35**(2):97–101.
46. Rock C, Thom KA, Masnick M, Johnson JK, Harris AD, Morgan DJ. Frequency of Klebsiella pneumoniae carbapenemase (KPC)-producing and non-KPC-producing Klebsiella species contamination of healthcare workers and the environment. *Infect Control Hosp Epidemiol*. 2014;**35** (4):426–429.
47. Cohen CC, Cohen B, Shang J. Effectiveness of contact precautions against multidrug-resistant organism transmission in acute care: a systematic review of the literature. *J Hosp Infect*. 2015;**90**(4):275–284.
48. Kho AN, Dexter PR, Warvel JS, et al. An effective computerized reminder for contact isolation of patients colonized or infected with resistant organisms. *Int J Med Informatics*. 2008;**77** (3):194–198.
49. Palmore TN, Henderson DK. Managing transmission of carbapenem-resistant enterobacteriaceae in healthcare settings: a view from the trenches. *Clin Infect Dis*. 2013;**57**(11):1593–1599.
50. Schwaber MJ, Lev B, Israeli A, et al. Containment of a country-wide outbreak of carbapenem-resistant Klebsiella pneumoniae in Israeli hospitals via a nationally implemented intervention. *Clin Infect Dis*. 1 2011;**52** (7):848–855.
51. Lucet JC, Decre D, Fichelle A, et al. Control of a prolonged outbreak of extended-spectrum beta-lactamase-producing enterobacteriaceae in a university hospital. *Clin Infect Dis*. 1999;**29**(6):1411–1418.
52. Tamma PD, Savard P, Pal T, Sonnevend A, Perl TM, Milstone AM. An outbreak of extended-spectrum beta-lactamase-producing Klebsiella pneumoniae in a neonatal intensive care unit. *Infect Control Hosp Epidemiol*. 2012;**33**(6):631–634.
53. Munoz-Price LS, Hayden MK, Lolans K, et al. Successful control of an outbreak of Klebsiella pneumoniae carbapenemase-producing K. pneumoniae at a long-term acute care hospital. *Infect Control Hosp Epidemiol*. 2010;**31**(4):341–347.
54. Munoz-Price LS, Quinn JP. Deconstructing the infection control bundles for the containment of carbapenem-resistant Enterobacteriaceae. *Curr Op Infect Dis*. 2013;**26**(4):378–387.
55. Schwaber MJ, Carmeli Y. An ongoing national intervention to contain the spread of carbapenem-resistant enterobacteriaceae. *Clin Infect Dis*. Mar 2014;**58**(5):697–703.
56. Kramer A, Schwebke I, Kampf G. How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. *BMC Infect Dis*. 2006;**6**:130.
57. Denton M, Wilcox MH, Parnell P, et al. Role of environmental cleaning in controlling an outbreak of Acinetobacter baumannii on a neurosurgical intensive care unit. *Intensive Crit Care Nurs*. Ar 2005;**21** (2):94–98.
58. Carling PC, Parry MF, Bruno-Murtha LA, Dick B. Improving environmental hygiene in 27 intensive care units to decrease multidrug-resistant bacterial transmission. *Crit Care Med*. Apr 2010;**38**(4):1054–1059.
59. Hota B. Contamination, disinfection, and cross-colonization: are hospital surfaces reservoirs for nosocomial infection? *Clin Infect Dis*. Oct 2004;**39** (8):1182–1189.
60. Boyce JM. Environmental contamination makes an important contribution to hospital infection. *J Hosp Infect*. Jun 2007;**65**, Suppl 2:50–54.
61. Jawad A, Seifert H, Snelling AM, Heritage J, Hawkey PM. Survival of Acinetobacter baumannii on dry surfaces: comparison of outbreak and sporadic isolates. *J Clin Microbiol*. 1998;**36**(7):1938–1941.
62. Levin AS, Gobara S, Mendes CM, Cursino MR, Sinto S. Environmental contamination by multidrug-resistant Acinetobacter baumannii in an intensive care unit. *Infect Control Hosp Epidemiol*. Nov 2001;**22**(11):717–720.
63. Catalano M, Quelle LS, Jeric PE, Di Martino A, Maimone SM. Survival of Acinetobacter baumannii on bed rails during an outbreak and during sporadic cases. *J Hosp Infect*. 1999;**42** (1):27–35.
64. Das I, Lambert P, Hill D, Noy M, Bion J, Elliott T. Carbapenem-resistant Acinetobacter and role of curtains in an outbreak in intensive care units. *J Hosp Infect*. 2002;**50**(2):110–114.
65. Aygun G, Demirkiran O, Utku T, et al. Environmental contamination during a carbapenem-resistant Acinetobacter baumannii outbreak in an intensive care unit. *J Hosp Infect*. 2002;**52** (4):259–262.
66. Anaissie EJ, Penzak SR, Dignani MC. The hospital water supply as a source of nosocomial infections: a plea for action. *Arch Intern Med*. 2002;**162** (13):1483–1492.
67. Bonten MJ, Weinstein RA. Transmission pathways of Pseudomonas aeruginosa in intensive care units: don't go near the water. *Crit Care Med*. 2002;**30**(10):2384–2385.
68. Epstein L, Hunter JC, Arwady MA, et al. New Delhi metallo-beta-lactamase -producing carbapenem-resistant Escherichia coli associated with exposure to duodenoscopes. *JAMA*. 2014;**312**(14):1447–1455.
69. Ha J, Son BK. Current Issues in duodenoscope-associated infections:

now is the time to take action. *Clin Endoscopy.* 2015;**48**(5):361–363.

70. Muscarella LF. Risk of transmission of carbapenem-resistant Enterobacteriaceae and related "superbugs" during gastrointestinal endoscopy. *World J Gastrointest Endoscopy.* 2014;**6**(10):457–474.
71. Calfee D, Jenkins SG. Use of active surveillance cultures to detect asymptomatic colonization with carbapenem-resistant Klebsiella pneumoniae in intensive care unit patients. *Infect Control Hosp Epidemiol.* 2008;**29**(10):966–968.
72. Snitkin ES, Zelazny AM, Thomas PJ, et al. Tracking a hospital outbreak of carbapenem-resistant Klebsiella pneumoniae with whole-genome sequencing. *Sci Translational Med.* 2012;**4**(148):148ra116.
73. Akduman B, Akduman D, Tokgoz H, et al. Long-term fluoroquinolone use before prostate biopsy may increase the risk of sepsis caused by resistant microorganisms. *Urology.* 2011; **78**(2):250–255.
74. Boucher HW, Talbot GH, Bradley JS, et al. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. *Clin Infect Dis.* 2009; **48**(1):1–12.
75. Hsu AJ and Tamma PD. Treatment of multidrug-resistant Gram-negative infections in children. *Clin Infect Dis* May 2014; **58**(10):1439–1448.
76. Centers for Disease Control and Prevention (CDC). Centers for Disease Control (CDE). www.cdc.gov/drugresistance/pdf/ar-threats-2013–508.pdf. Accessed November 13, 2015.
77. Tamma PD and Cosgrove SE. Antimicrobial stewardship. *Infec Dis Clin North Am* 2011; **25**(1):245–260.
78. Marchaim D, Chopra T, Bhargava A, et al. Recent exposure to antimicrobials and carbapenem-resistant Enterobacteriaceae: the role of antimicrobial stewardship. *Infect Control Hosp Epidemiol.* 2012;**33**(8):817–830.
79. Carmeli Y, Lidji SK, Shabtai E, Navon-Venezia S, Schwaber MJ. The effects of group 1 versus group 2 carbapenems on imipenem-resistant Pseudomonas aeruginosa: an ecological study. *Diagn Microbiol Infect Dis.* 2011;**70**(3):367–372.
80. Dortch MJ, Fleming SB, Kauffmann RM, Dossett LA, Talbot TR, May AK. Infection reduction strategies including antibiotic stewardship protocols in surgical and trauma intensive care units are associated with reduced resistant gram-negative healthcare-associated infections. *Surg Infecti.* 2011;**12**(1):15–25.
81. Rahal JJ, Urban C, Horn C, et al. Class restriction of cephalosporin use to control total cephalosporin resistance in nosocomial Klebsiella. *JAMA.* 1998;**280**(14):1233–1237.
82. Ntagiopoulos PG, Paramythiotou E, Antoniadou A, et al. Impact of an antibiotic restriction policy on the antibiotic resistance patterns of Gram-negative microorganisms in an intensive care unit in Greece. *Int J Antimicrob Agents.* 2007; **30**:360–365.
83. Altunsoy A, Aypak C, Azap A, et al. The impact of a nationwide antibiotic restriction program on antibiotic usage and resistance against nosocomial pathogens in Turkey. *Int J Med Sci.* 2011;**4**:339–344.
84. Davey P, Brown E, Charani E, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Systematic Review Apr 20134: CD003543. doi:10.1002/14651858.CD003543.pub3.
85. Roquilly A, Marret E, Abraham E, Asehnoune K. Pneumonia prevention to decrease mortality in intensive care unit: a systematic review and meta-analysis. *Clin Infect Dis.* 2015;**60**(1):64–75.
86. Price R, MacLennan G, Glen J, Su DC. Selective digestive or oropharyngeal decontamination and topical oropharyngeal chlorhexidine for prevention of death in general intensive care: systematic review and network meta-analysis. *BMJ.* 2014;**348**:g2197.
87. de Smet AM, Kluytmans JA, Blok HE, et al. Selective digestive tract decontamination and selective oropharyngeal decontamination and antibiotic resistance in patients in intensive-care units: an open-label, clustered group-randomised, crossover study. *Lancet Infect Dis.* 2011;**11**(5):372–380.
88. Oostdijk EA, Kesecioglu J, Schultz MJ, et al. Effects of decontamination of the oropharynx and intestinal tract on antibiotic resistance in ICUs: a randomized clinical trial. *JAMA.* 2014;**312**(14):1429–1437.
89. Lin MY, Lolans K, Blom DW, et al. The effectiveness of routine daily chlorhexidine gluconate bathing in reducing Klebsiella pneumoniae carbapenemase-producing Enterobacteriaceae skin burden among long-term acute care hospital patients. *Infect Control Hosp Epidemiol.* 2014;**35**(4):440–442.
90. Septimus EJ, Hayden MK, Kleinman K, et al. Does chlorhexidine bathing in adult intensive care units reduce blood culture contamination? A pragmatic cluster-randomized trial. *Infect Control Hosp Epidemiol.* 2014; **35** Suppl 3: S17–S22.
91. Milstone AM, Elward A, Song X, et al. Daily chlorhexidine bathing to reduce bacteraemia in critically ill children: a multicentre, cluster-randomised, crossover trial. *Lancet.* 2013;**381**(9872):1099–1106.
92. Climo MW, Yokoe DS, Warren DK, et al. Effect of daily chlorhexidine bathing on hospital-acquired infection. *N Engl J Med.* Feb 7 2013;**368**(6):533–542.
93. Climo MW, Sepkowitz KA, Zuccotti G, et al. The effect of daily bathing with chlorhexidine on the acquisition of methicillin-resistant Staphylococcus aureus, vancomycin-resistant Enterococcus, and healthcare-associated bloodstream infections: results of a quasi-experimental multicenter trial. *Crit Care Med.* 2009;**37**(6):1858–1865.
94. Hayden MK, Lin MY, Lolans K, et al. Prevention of colonization and infection by Klebsiella pneumoniae carbapenemase-producing enterobacteriaceae in long-term acute-care hospitals. *Clin Infect Dis.* 2015;**60**(8):1153–1161.
95. Brooks SE, Walczak MA, Hameed R, et al. Chlorhexidine resistance in antibiotic-resistant bacteria isolated from the surfaces of dispensers of soap containing chlorhexidine. *Infect Control Hosp Epidemiol.* 2002; **23**(11):692–695.
96. Tattawasart U, Maillard JY, Furr JR, Russell AD. Outer membrane changes in Pseudomonas stutzeri resistant to chlorhexidine diacetate and cetylpyridinium chloride. *Int J Antimicrob Agents.* 2000;**16**(3):233–238.
97. Thomas L, Maillard JY, Lambert RJ, Russell AD. Development of resistance to chlorhexidine diacetate in Pseudomonas aeruginosa and the effect of a "residual" concentration. *J Hosp Infect.* 2000;**46**(4):297–303.
98. Higgins CS, Murtough SM, Williamson E, et al. Resistance to antibiotics and biocides among non-fermenting Gram-negative bacteria. *Clin Microbiol Infect.* 2001;**7**(6):308–315.

99. Hilty M, Betsch BY, Bogli-Stuber K, et al. Transmission dynamics of extended-spectrum beta-lactamase-producing Enterobacteriaceae in the tertiary care hospital and the household setting. *Clin Infect Dis.* 2012;**55**(7):967–975.
100. Madigan T, Johnson JR, Clabots C, et al. Extensive household outbreak of urinary tract infection and intestinal colonization due to extended-spectrum beta-lactamase-producing Escherichia coli sequence type 131. *Clin Infect Dis.* 2015;**61**(1):e5–12.
101. Doi Y, Park YS, Rivera JI, et al. Community-associated extended-spectrum beta-lactamase-producing Escherichia coli infection in the United States. *Clin Infect Dis.* 2013;**56**(5):641–648.
102. Gould CV, Rothenberg R, Steinberg JP. Antibiotic resistance in long-term acute care hospitals: the perfect storm. *Infect Control Hosp Epidemiol.* 2006;**27**(9): 920–925.
103. O'Fallon E, Pop-Vicas A, D'Agata E. The Emerging Threat of multidrug-resistant gram-negative organisms in long-term care facilities. *J Ger Ser A*. 2009; **64** (1):138–141.
104. Mills JP, Talati NJ, Alby K, Han JH. The epidemiology of carbapenem-resistant Klebsiella pneumoniae colonization and infection among long-term acute care hospital residents. *Infect Control Hosp Epidemiol.* **12** 2015:1–6.
105. Lin MY, Lyles-Banks RD, Lolans K, et al. The importance of long-term acute care hospitals in the regional epidemiology of Klebsiella pneumoniae carbapenemase-producing Enterobacteriaceae. *Clin Infect Dis*. 2013;**57**(9):1246–1252.
106. O'Fallon E, Gautam S, D' Agata EM. Colonization with multidrug-resistant gram-negative bacteria: prolonged duration and frequent colonization. *Clin Infect Dis.* 2009;**48** (10):1375–1381.
107. Siegel JD, Rhinehart E, Jackson M, Chiarello L, Healthcare Infection Control Practices Advisory C: management of multidrug-resistant organisms in health care settings, 2006. *Am J Infect Control*. 2007;**35**(10 Suppl 2):S165–S193.
108. Siegel JD, Rhinehart E, Jackson M, Chiarello L, Health Care Infection Control Practices Advisory C. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Health Care Settings. *Am J Infect Control*. 2007;**35**(10 Suppl 2): S65–S164.
109. Centers for Disease Control and Prevention (CDC). ww.cdc.gov/hai/organisms/cre/cre-toolkit/index.html. Accessed November 13th, 2015.
110. Feldman N, Adler A, Molshatzki N, et al. Gastrointestinal colonization by KPC-producing Klebsiella pneumoniae following hospital discharge: duration of carriage and risk factors for persistent carriage. *Clin Microbiol Infect.* 2013;**19**(4):E190–196.
111. Oren I, Sprecher H, Finkelstein R, et al. Eradication of carbapenem-resistant Enterobacteriaceae gastrointestinal colonization with nonabsorbable oral antibiotic treatment: a prospective controlled trial. *Am J Infecti Control.* 2013;**41**(12):1167–1172.

Chapter

18

Clostridium Difficile Infection

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Introduction

Clostridium difficile is a Gram-positive, spore-forming, anaerobic rod first described in 1935 by Hall and O'Toole while studying the acquisition of gut bacteria in neonates. The name "*difficile*" (originally "*difficilis*") was first given because it was difficult to grow in culture.[1,2] Based on their experiments in animals, they hypothesized *C. difficile* produced highly lethal toxins, but was not a human pathogen.

Soon after antimicrobials were introduced into clinical practice, pseudomembranous colitis was recognized as a not uncommon complication of antibiotic usage. In the late 1970s, *C. difficile* was identified as the causative agent of pseudomembranous colitis. Numerous studies were done in the 1980s that established *C. difficile* as a healthcare-associated pathogen and identified metronidazole and oral vancomycin as effective treatments for *C. difficile* infection (CDI), but general interest in *C. difficile* quickly tapered off.[1,2]

Interest in CDI remained low until the early 2000s, when notable increases in CDI incidence and severity associated with the emergence of the BI/NAP1/027 strain were identified.[1,2] In the present day, *C. difficile* is now the most common infectious cause of healthcare-associated diarrhea, and the most common healthcare-associated infection (HAI) in the US.[3] CDI is associated with significant morbidity and mortality.[4,5] Although the incidence of *C. difficile* remains highest among people with healthcare exposures, improved population-based surveillance has identified more community onset CDI than previously recognized.[6] In order to curtail transmission of *C. difficile* and prevent CDI, systematic and targeted infection prevention measures are necessary.

Epidemiology

C. difficile is a ubiquitous organism, and has been found in the environment, food, and in animals. In a large study in the United Kingdom, a total of 2,580 samples were taken from the environment, and 184 (7.1 percent) of isolates were positive for *C. difficile*.[7] In this study, the highest yield was from river (87.5 percent) and seawater (44 percent), and also from swimming pools (50 percent).[7] *C. difficile* has also been identified in retail foods worldwide, including ground meats, poultry and vegetables.[8–10] *C. difficile* has been found in animals such as chickens, elephants, dogs and horses, but its pathogenesis has been poorly understood.[11]

Although *C. difficile* is ubiquitous, infection due to *C. difficile* has traditionally been associated with the healthcare setting. This may be because the types of people who are most prone to CDI are more concentrated within the healthcare setting (see risk factors).

Since the early 2000s, the incidence and attributable burden of CDI has been increasing. Due to a lack of surveillance definitions historically, it is difficult to precisely quantify CDI incidence rates in acute care hospitals. But CDI incidence has likely increased approximately three-fold since the early 2000s.[12] In addition, the severity of CDI has also increased, with some outbreaks associated with dramatic increases in colectomies and deaths. A recent study by the Centers for Disease Control and Prevention (CDC) estimates there were 453,000 incident cases of CDI in the US in 2011, resulting in 29,300 deaths.[13] Further compounding the problem, 10 percent to 30 percent of people who have an initial episode of CDI will develop at least one recurrence,[4] and based on the number of incident cases found in 2011, there were likely anywhere from 45,300 to 135,900 people who developed recurrent CDI.[4,13] The costs attributable to treating CDI in the hospital is estimated to be $3,427 to $9,960 (in 2012 dollars), and the cost of treating patients with recurrent CDI is $11,631, for a total cost of over $2.1 to 6.1 billion per year in the US.[4,14] Additionally, hospital CDI incidence comparisons are now publically available on the Centers for Medicare & Medicaid Services hospital compare website and CDI will likely become a value-based purchasing measure, thereby further increasing the cost of CDI to hospitals.

The majority of data available on the epidemiology of CDI is focused in the healthcare setting, but population-based surveillance is identifying more CDI in the community than previously recognized. In a study conducted by the CDC of 15,461 cases of CDI in 10 geographic areas, 65.8 percent were healthcare-associated, but only 24.2 percent had onset during hospitalization.[13] In this same dataset, 46.2 percent were community-associated, and by definition had no documented inpatient exposure.[13] In another related study utilizing the same surveillance program, 82 percent of patients with community-associated CDI reported they had visited outpatient healthcare settings in the 12 weeks prior to stool collection.[15]

The presence of toxigenic *C. difficile* in stool alone does not equate the diagnosis of CDI, and asymptomatic *C. difficile* carriage is common. One study demonstrated 15 percent of patients admitted to the hospital without diarrhea had toxigenic *C. difficile* in their stool.[16] This is important because emerging data indicate at least 30 percent of new cases of hospital onset CDI are due to transmission from asymptomatic carriers, and current approaches to prevent CDI focus on preventing *C. difficile* transmission only from people with CDI.

Pathophysiology

C. difficile can exist in either a spore or vegetative form. As an obligate anaerobe, the vegetative form dies quickly after exposure to air, so it is the spore form that is ingested. The spore form is highly heat-stable, can survive harsh conditions such as the high acidity of the stomach and commercial disinfectants, and can survive in the hospital environment for prolonged periods of time.[17–19] Transmission occurs via the fecal-oral route, person to person, or via fomites. Once ingested, *C. difficile* spores can germinate, and the vegetative cells can then colonize the colon.[20,21] *C. difficile* then reproduces in intestinal crypts, releasing exotoxins A and B, leading to severe inflammation.[20,21] Toxin A (enterotoxin) attracts neutrophils and monocytes while toxin B (cytotoxin) degrades colonic epithelial cells.[21] These toxins disrupt cell membranes, causing shallow intestinal mucosal ulcerations, leading to the release of proteins, mucus, and inflammation.[20] This manifests as a pseudomembrane, hence the name pseudomembranous colitis.[20]

Exposure to *C. difficile* can result in no acquisition, asymptomatic colonization, or CDI. Host and external factors that alter the intestinal microbiota, most commonly due to exposure to antimicrobials, allow *C. difficile* to establish colonization.[22] Among hospitalized patients who acquire *C. difficile*, 10 percent to 50 percent will go on to develop CDI. There are few studies designed to determine the incubation period from *C. difficile* acquisition to CDI, but all of these studies have found the median incubation period to be <7 days.[23] Among the people who develop CDI, current evidence suggests these people fail to mount a protective antibody mediated immune response against *C. difficile* toxins.[24] Strain type likely also impacts development of CDI, as Loo et al. found ~50 percent of people who acquired the BI/NAP1/027 strain developed CDI versus ~30 percent for other strains. The probability of developing CDI after acquiring *C. difficile* in other settings is likely lower than in the hospital setting, considering the prevalence of asymptomatic carriage and the ubiquitous nature of *C. difficile* exposures.

Risk Factors

Knowledge of CDI risk factors is important to help develop methods for intervention and prevention of CDI. The primary independent risk factors for CDI include exposure to antimicrobials and high severity of underlying illness. The highest risk antimicrobials for CDI are aminopenicillins, clindamycin, cephalosporins, and fluoroquinolones. Traditionally, age has been included as a primary risk factor for CDI, as the incidence of CDI increases with each decade after the age of 50. However, recent work indicates that when assessing an individual's risk for CDI, physiological age is more important than chronological age.[25] Populations identified as high risk for CDI are those that have high concentrations of patients with frequent antimicrobial exposures and high severity of underlying illness, such as ICU, oncology and transplant, renal insufficiency, and hemodialysis.[26–28] Although many studies have identified gastric acid suppression as a risk factor for CDI, this may be a marker for severity of underlying illness and not part of the causal pathway to CDI.

The other key risk factor for CDI is new acquisition of *C. difficile*. As stated above, most studies have found CDI typically occurs within a week of a new *C. difficile* acquisition. Therefore preventing *C. difficile* transmission is paramount to any CDI prevention program. Of note, some recent studies have suggested those colonized with *C. difficile* on admission to the hospital may be at greater risk for CDI than those not colonized on admission.[29] Although there will be asymptomatically colonized patients who go on to develop CDI, how the relative risk was assessed in these analyses is biased toward an increased relative risk for asymptomatic carriers. First, it is not possible to develop CDI without acquiring *C. difficile*. As such, most of the people in the noncolonized comparison group will never have the "opportunity" to develop CDI. In addition, many of the more recent studies used PCR-based assays to diagnose CDI, which are much more likely to detect asymptomatic colonization than toxin assays (see discussion below). Many of the asymptomatic carriers diagnosed with CDI may actually still be asymptomatic carriers with diarrhea due to other reasons. Finally, even with the supposition that asymptomatic carriers are at higher risk for CDI than people not colonized on admission to the hospital, approximately two-thirds of CDI cases were among the people not colonized; again supporting the notion more CDI will be prevented by reducing transmission than preventing CDI among asymptomatic carriers.

Clinical Manifestations

As the detection of *C. difficile* alone does not indicate the presence of infection due to *C. difficile*, CDI is a clinical diagnosis supported by laboratory findings. Diarrhea is a key presenting symptom, being defined as the passage of three or more unformed stools in a 24-hour period. The only times when a patient with CDI does not have diarrhea are those rare instances where the patient presents with an ileus. Signs and symptoms of CDI include diarrhea, cramplike abdominal pain, abdominal tenderness, distension and alteration of bowel sounds.[30,31] In severe cases, signs of septic shock may develop. The white blood cell count (WBC) is often elevated, as high as 30,000 to 50,000 cells/microL, with the extent of leukocytosis often correlating with disease severity.[30,31] Plain abdominal radiographs may show distended loops of bowel, or in severe cases, toxic megacolon. Computed tomography images may include colonic wall thickening, stranding, dilation, edema and perforation. Endoscopy may reveal pseudomembranes.

Diagnosis

There are no currently available diagnostic assays for CDI. Currently available assays detect presence of *C. difficile*, presence of a toxigenic strain of *C. difficile*, or presence of *C. difficile* toxin in stool. The diagnosis of CDI is established by the presence of appropriate signs and symptoms consistent with CDI in combination with a positive test for *C. difficile* toxin / toxigenic *C. difficile*.[32] Because asymptomatic *C. difficile*

carriage is common, and asymptomatic carriage can be detected by all *C. difficile* assays, any laboratory testing should only be performed on unformed stools in patients with an appropriate clinical suspicion for CDI. Endoscopy can show the presence of pseudomembranes, which is virtually pathognomonic for CDI (although it can be seen with ischemic colitis and CMV colitis). Histopathology findings may confirm the diagnosis.

There is no true gold standard for CDI, however, toxigenic culture is the gold standard for detection of toxin-producing *C. difficile* in stool, and the cell culture cytotoxicity neutralization assay (CCNA) is the gold standard for detecting free toxin in stool.[33–35] Both of these procedures are labor intensive and can take several days for results, so they are rarely performed in clinical practice in the US. Other assays that are available include enzyme immunoassays (EIA) for toxin A and B, EIAs for glutamate dehydrogenase (GDH) and polymerase chain reaction (PCR)–based assays (note: although not all of these assays use PCR, assays that detect *C. difficile* nucleic acid will be referred to as PCR-based assays).

There are advantages and disadvantages to all assays, and performance characteristics can vary within an assay class (e.g., the sensitivity of membrane-based EIAs is typically 10 percent less than the sensitivity of microwell EIAs). Important features to keep in mind are that toxin assays are more specific for CDI and GDH EIAs and PCR-based assays are much more likely to detect asymptomatic colonization. Although there are no randomized controlled trials that demonstrate this, most observational data indicate outcomes of patients who are PCR positive / toxin assay negative are no different than those who are negative by both assays. Another important consideration is that GDH assays will detect both toxigenic and nontoxigenic strains of *C. difficile*, so they should never be used as a stand-alone test (Table 18.1).[33–35]

A two-stage testing / algorithm strategy has been implemented in some institutions, by combining a highly sensitive rapid screening test with a more specific confirmatory test. A GDH EIA is typically used as the initial screen as they are rapid and inexpensive. The preferred algorithm would follow a positive GDH with a test for toxin detection, such as CCNA or toxin EIA. A stool specimen positive for toxin would be considered supportive of a diagnosis of CDI. Some laboratories do a third test if the GDH is positive and toxin test is negative, most commonly PCR. In this setting, a positive PCR indicates toxigenic *C. difficile* is present, but does not differentiate between CDI and asymptomatic *C. difficile* carriage. Ideally, PCR would be performed only if there is a high index of suspicion for CDI, not automatically if GDH is positive and toxin is negative. Regardless of the test(s) used, it is always important to remember the presence of toxigenic *C. difficile* in stool alone does not confirm the diagnosis of CDI. The focus should be on treating the patient, not the test result.[36]

In general, a single specimen at the onset of illness is recommended, as there is little diagnostic gain of repeating testing either by PCR or EIA.[37] Automatic repeat testing should be strongly discouraged, and repeat testing should be done on the basis of the clinical index of suspicion and the pretest likelihood of CDI.

Treatment

Once the diagnosis of CDI is made, things to consider when selecting treatment include severity of CDI, previous history of CDI and ability to take medications by mouth. In most instances, it is safe to not initiate treatment until the diagnosis of CDI has been established. However, if there is a high clinical index of suspicion for CDI and the patient is at high risk for poor outcome due to CDI if treatment is withheld while waiting for confirmation, empirical therapy is reasonable. Also, all diagnostics are with limitations. High index of suspicion should outweigh a negative test result in the appropriate clinical context.

The first step in managing CDI is to discontinue any clinically unnecessary antimicrobials, unless there is a compelling clinical indication to continue. Continued exposure to non-CDI treatment antimicrobials are associated with a slower response to CDI treatment and increased risk for recurrence.[45] The Society of Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA) published CDI clinical guidelines in 2010, and are expected to release updated guidelines in 2016.[23] Based on observational studies and a single center randomized controlled trial, the 2010 SHEA/IDSA clinical guidelines recommended to treat a first or second episode of CDI based on severity. Evidence of mild to moderate CDI included a white blood count ≤15,000 cells/μL and a serum creatinine <1.5 times the premorbid level.[23] For patients meeting these criteria, metronidazole 500 mg orally three times per day for 10–14 days was recommended.[23] If there was evidence of severe CDI, defined as a white blood cell count > 15,000 cells/μL or a serum creatinine ≥1.5 times the premorbid level, then vancomycin 125 mg orally four times per days for 10–14 days was recommended.[23] For patients with hypotension, shock, ileus, or megacolon, it was recommended to give vancomycin 500 mg orally four times per day plus metronidazole 500 mg intravenously three times per day, and consider vancomycin enemas in the setting of an ileus.[23] Of note, there are no data to indicate a higher dose of vancomycin or combination therapy is any more efficacious than the lower dose of vancomycin recommended for severe CDI (and studies have actually found that combination/high dose vancomycin to not be associated with improved outcomes).[23] The rationale behind this regimen is to get active drug to the colon as quickly as possible.

There have been two important developments since the 2010 guidelines were published. First, fidaxomicin was approved for treatment of CDI. In its phase three trials, fidaxomicin was associated with ~40 percent decrease in risk of recurrence compared to oral vancomycin in patients experiencing a first CDI episode or first recurrence, which was statistically significant.[45] The lower risk for recurrence is believed to be because fidaxomicin is more selective for *C. difficile* than vancomycin, allowing "protective" microbiota to recover while on CDI treatment. Despite these promising results, use of

Table 18.1 *Clostridium difficile* diagnostic testing[2,20,38–44]

Diagnostic test	Comments	Advantages	Disadvantages
Endoscopy	Direct visualization of bowel walls	Direct diagnosis of pseudomembranous colitis; tissue can be obtained for histopathology	Low sensitivity macroscopically; Endoscopist dependent
Toxigenic culture	Gold standard for detection of toxin-producing *C. difficile*	Most sensitive test for detecting toxigenic *C. difficile*	Technically demanding; Time-consuming; low specificity for CDI
Cell culture cytotoxicity assay (CCNA)	Gold standard for detecting free toxin	Sensitive and specific for CDI	Technically demanding Time-consuming Lacks standardization
Toxin enzyme immunoassays (EIA)	Direct toxin detection (all currently available toxin EIAs detect both toxin A and B)	Direct toxin detection Specific for CDI Rapid Relatively inexpensive	Lowest sensitivity, especially for membrane-based EIAs
Glutamate dehydrogenase (GDH) common antigen	EIA for glutamate (GDH), which is produced by all *C. difficile* strains, as well as other organisms	Rapid Sensitive Inexpensive Potential use for screening	Does not differentiate between toxigenic and nontoxigenic strains Cannot be used alone Cross reacts with other anaerobes
PCR-based assays	Uses primers targeting specific genes encoding toxins	Rapid Sensitive	Does not test for active toxin production Lower specificity for CDI than toxin detection
Multi-step testing strategies	Combination of various tests, generally a highly sensitive test combined with a test with better specificity for CDI	Attempt to increase sensitivity and specificity	Discordant results may be difficult to interpret

fidaxomicin has been limited due to its cost. The other important development was publication of the tolevamer phase 3 trial data.[46] With clinical success of only 44.2 percent, tolevamer did not meet its noninferiority endpoint, but the blinded randomized controlled trial included both metronidazole and vancomycin arms. Vancomycin was an independent predictor of clinical success when controlling for CDI severity on multivariable analysis. These data indicate the threshold for vancomycin should perhaps be lower than the criteria stated in the 2010 clinical guidelines.

A challenge in the management of CDI is recurrence. Recurrence is defined as another CDI episode that occurs within 8 to 12 weeks of discontinuation of treatment for the initial episode, and occurs following resolution of approximately 15 percent to 30 percent of initial CDI episodes. Risk factors for recurrence include continuation of antimicrobials (other than CDI treatment agents), severe underlying diseases, longer hospitalization, and inadequate antitoxin antibody response.[47] Resistance to metronidazole or vancomycin is uncommon and does not explain recurrence. Rather, CDI treatment with metronidazole and vancomycin causes further disruption of the microbiota, providing additional opportunity for *C. difficile* to cause disease after treatment is stopped. The SHEA/IDSA clinical guidelines recommend treating a second recurrence (third episode) with a vancomycin taper or pulse.[23] Other approaches for patients with multiple CDI recurrences include a "chaser" with rifaximin or fidaxomicin, or a fidaxomicin taper.[48,49]

A promising therapy for prevention of recurrent CDI is fecal microbiota transplantation (FMT). The goal of FMT is to restore healthy colonic flora and colonization resistance. Stool from a healthy related or unrelated donor is infused via endoscopy, nasoduodenal tube, or enema to the patient. A review of 536 patients with recurrent CDI showed an 81–93 percent response rate regardless of method of instillation, and several recent prospective studies indicate the success of a single dose of FMT to be 70 percent to 80 percent, with success increasing to 90 percent with a second dose.[50–54] Frozen FMT has also been used. The donor and donor stool must be screened for infectious agents prior to FMT, and the FDA requires consent to be obtained prior to FMT explaining it is still investigational and a discussion of potential risks.[55]

Other agents to treat CDI have been studied, but there are few high-quality data to support the use of these medications.

These include probiotics, fusidic acid, teicoplanin, nitazoxanide and tigecycline. Probiotics are live microorganisms that are thought to restore gastrointestinal microflora. Most studies have employed the use of *Lactobacillus* species or *Saccharomyces boulardii* in an effort to prevent or treat CDI. A few small studies have shown a trend toward benefit; however, none were able to demonstrate adequate statistical power for efficacy.[56] Occasional cases of fungemia have been reported in immunocompromised patients and those with central venous catheters, therefore probiotics should be avoided in those patients.

A response to therapy should be monitored clinically. Decreasing stool frequency, a declining WBC count, and reversal of hemodynamic instability are objective measures of response.[57] For severe, progressive disease with toxic megacolon, a total colectomy can be considered as a last measure for patients who remain critically ill despite standard therapy. Some observational studies suggest intravenous immunogolobulin may be beneficial in these cases, and decrease the need for colectomy. Mortality rate for total colectomy can be high, ranging from 35 to 80 percent.[58–61] In one study of 42 patients, a diverting loop ileostomy and intraoperative colonic lavage with polyethylene glycol, followed by postoperative antegrade vancomycin flushes resulted in improved outcomes.[62] Currently, this surgical procedure is not standard of care. No "tests of cure" are indicated and are not valuable in monitoring disease, because tests can remain positive even after improvement.

Surveillance

Surveillance for CDI is important to be able to recognize outbreaks and to monitor the effectiveness of infection control practices (Table 18.2).[63] At a minimum, healthcare facilities should track the rate of healthcare facility–onset CDI (HO-CDI, reported as the number of CDI cases per 10,000 patient-days). Although the HO-CDI rate does not capture all cases of healthcare-associated CDI, it acts as a good surrogate marker and allows healthcare epidemiologists to effectively gauge responses to CDI control measures.[64,65] Currently, US hospitals accomplish this by reporting CDI incidence through the LabID Event module to the National Healthcare Safety Network (NHSN). LabID Event is based on date of admission and date of collection of stool that was positive for *C. difficile* and/or its toxins, where HO-CDI is defined as a positive stool collected >4 days after admission.

Table 18.2 *Clostridium difficile* Infection (CDI) Surveillance Definitions[63]

CDI Type	Definition
Healthcare facility–onset, healthcare facility–associated CDI	CDI symptom onset more than 3 days after admission to a healthcare facility, with day of admission being day 1
Community-onset, healthcare facility–associated CDI	CDI symptom onset in the community or less than or equal to 3 days from admission, provided symptom onset was less than 4 weeks after the last discharge from a healthcare facility
Community-associated CDI	CDI symptom onset in the community or less than or equal to 3 days after admission to a healthcare facility, provided that symptom onset was more than 12 weeks after the last discharge from a healthcare facility
Indeterminate onset CDI	CDI case patient who does not fit any of the above criteria for an exposure setting (e.g., onset in the community greater than 4 weeks but less than 12 weeks after the last discharge from a healthcare facility)
Unknown	Exposure setting cannot be determined because of lack of available data
Recurrent CDI	An episode of CDI that occurs less than or equal to 8 weeks after the onset of a previous episode, provided that CDI symptoms from the earlier episode resolved

Prevention

The morbidity, mortality, and cost of CDI highlight the importance of CDI prevention. Preventing CDI is a multidisciplinary effort involving physicians, nurses, infection preventionists, pharmacists, microbiology laboratories, housekeeping, and hospital leadership. Another challenge to preventing CDI, in contrast to other HAIs, is that the quality of data to support CDI prevention recommendations are relatively poor. For example, in the SHEA compendium to prevent HAIs, all components of the basic central line–associated bloodstream infection (CLABSI) prevention bundle have a moderate to high level of evidence from randomized, controlled clinical trials.[63,66] Additionally, the CLABSI bundle itself has been validated.[67,68] In contrast, there are no CDI prevention recommendations with a high quality of evidence, and most recommendations have low quality of evidence to support their use.[69] As a result of the lack of high quality data, there are misperceptions about what are the key areas to focus on to optimize CDI prevention in hospitals. Therefore, the focus of this section is to identify the most important areas of prevention, and discussion of common misperceptions.

CDI infection control measures should focus on preventing patient exposure to *C. difficile* and reducing the chance of CDI development after a patient is exposed to *C. difficile*.[38,69] Strategies to reduce the patient exposure to *C. difficile* include the use of barrier precautions, environmental cleaning and hand hygiene. Strategies to reduce the development of CDI after *C. difficile* exposure has occurred focus on antimicrobial stewardship.

Ever since emergence of the epidemic BI/NAP1/027 strain, many investigators have documented the utility of infection

control measures in preventing HO-CDI.[12,70] These "bundles" of infection control practices have emphasized expansion of existing measures, such as use of contact precautions for a longer duration (i.e., duration of the entire hospitalization) and daily enhanced cleaning of CDI patient rooms using sodium hypochlorite.[12,70] Although most acute care hospitals utilize infection control policies to prevent the spread of *C. difficile*, practices are variable and nonuniform. A study of hospitals in the Canadian Nosocomial Infection Surveillance Program found that there was some form of *C. difficile* infection control precautions used in all hospitals surveyed, but there was considerable variation in terms of testing strategies, cleaning protocols, cleaning products, and isolation practices.[71,72]

The practice recommendations regarding CDI in the "Strategies to Prevent *Clostridium difficile* Infections in Acute Care Hospitals: 2014 Update" offer a comprehensive approach to implementing *C. difficile* prevention programs.[63,69] To prevent patient exposure to CDI, interventions include 1) use of contact precautions for patients with CDI, including the use of gowns and gloves; 2) meticulous adherence to hand hygiene practices in compliance with the CDC or World Health Organization recommendations; and 3) proper cleaning and disinfection of equipment and environment.[63,69] Each of the strategies is discussed in further detail below.

Barrier Precautions and Hand Hygiene

Patients with CDI should be placed in contact precautions with dedicated disposable medical equipment (stethoscope, thermometer, etc.). In the acute care setting, whenever possible, patients with CDI should be placed into private rooms. This is because semiprivate rooms may be more difficult to clean and decontaminate, and compliance with hand hygiene may be negatively impacted in multiple-bed rooms.[73] If private rooms are not available, cohorting of patients may be considered, although it is important not to cohort patients discordant for infection or colonization with other epidemiologically important organisms (such as vancomycin-resistant *Enterococcus* or methicillin-resistant *Staphylococcus aureus*). Patients with CDI are most contagious before treatment is started, therefore it is important to promptly identify patients with CDI, initiate treatment, and place them on contact precautions. The key to prompt diagnosis is identifying patients with clinically significant diarrhea. Kundrapu et al. found the median time from diarrhea onset to CDI diagnosis at their healthcare facility was 3.2 days.[74] To further minimize the risk of *C. difficile* transmission to other patients, patients who are tested for *C. difficile* can be placed into contact precautions while the test result is pending.

Adherence to glove use is of utmost importance. A common opinion is that upon leaving a room of a patient with CDI, soap and water is preferable over alcohol-based hand rubs (ABHR) for hand hygiene. Although alcohol does not kill *C. difficile* spores, there have been no studies that have found increases in CDI with ABHR or decreases in CDI with soap and water.[69] In addition, several of these studies have found reductions in MRSA and/or VRE with ABHR compared to soap and water. There are several potential explanations for these findings. One is compliance with a 15- to 30-second soap and water hand wash is extremely low, typically in the 20 percent to 40 percent range.[75] This is too low to have much of an impact on overall *C. difficile* (or other organism) transmission.[75] Another contributing factor could be that the sink being used by healthcare workers (HCWs) to perform hand hygiene is the same sink that the patient with CDI used after his/her last bowel movement. Therefore in the process of using soap and water, the HCW may actually increase hand contamination. Likely the primary reason ABHR have not been associated with increase in CDI incidence is that glove use is a component of contact precautions, which should prevent hand contamination in the first place.

It is imperative that HCWs wear gloves every time they enter a room of a patient with CDI. Hand contamination is uncommon when gloves are donned and doffed properly. Landelle found gloves were not worn in only 30/386 (7.8 percent) of HCW encounters with a patient with CDI, but these encounters accounted for almost half (7/16) of HCWs who had *C. difficile* recovered from their hands.[76] It is also possible even hand hygiene with soap and water does not remove enough *C. difficile* spores. Edmonds et al. found hand washing with recommended methods and products resulted in a less than one log reduction in *C. difficile* spores, a reduction not thought to be sufficient to adequately prevent transmission of organisms.[77] Supporting the aforementioned studies, McFarland et al. found none of the HCWs exiting the room of a patient with CDI who wore gloves had *C. difficile* cultured from their hands. However, there was no difference in *C. difficile* recovery among those HCWs who did not wear gloves whether or not they washed hands (65 percent versus 44 percent, respectively).[19] These data indicate it is more important to stress compliance and proper donning and doffing of gloves compared to hand hygiene. Of note, McFarland also found there was no difference in recovery of *C. difficile* from hands whether or not the HCW actually touched the patient.[19]

When comparing glove use to environmental disinfectant use, glove use is more important than using sporicidal agents for environmental disinfection. *C. difficile* spores can persist in the environment for months and are resistant to standard hospital environmental disinfectants, and one study found that admission to an ICU room that just previously housed a patient with CDI to be risk factor for CDI (HR = 2.35, $p = 0.01$).[78] However, only 11 percent of new CDI cases actually had this exposure. Other studies have found that most new acquisitions of *C. difficile* are related to transmission of *C. difficile* from a colonized patient that is in a different room. A study modeling *C. difficile* transmission estimated approximately 10 percent of new CDI cases are related to preexisting environmental contamination, and environmental decontamination with sporicidal agents would be the least effective method to prevent CDI (compared to antimicrobial stewardship and adherence to contact precautions).[79]

Additionally, most studies that have evaluated sporicidal agents in nonoutbreak settings have failed to identify a reduction in CDI with that agent.[69]

Environmental Decontamination

C. difficile produces spores that are resistant to most standard hospital environmental disinfectants and can survive for months on environmental surfaces.[80] Patients colonized with *C. difficile* shed spores and contaminate their local environment, then these spores serve as a source of *C. difficile* transmission to other patients. *C. difficile* spores have been cultured from toilets, commodes, floors, bed rails, call buttons, sinks, and over bed tables.[81,82] Although some studies have found epidemic strains have increased capacity for sporulation, other studies have not.[83,84] The degree of contamination correlates with the colonization status of the patient. Environmental contamination is lowest in rooms of culture-negative patients (fewer than 8 percent of rooms), intermediate in rooms of patients with asymptomatic *C. difficile* colonization (8 percent to 30 percent of rooms), and highest in rooms of patients with CDI (9 percent to 50 percent of rooms).[19,80,82,85] Samore et al. found the degree of environmental contamination to correlate with the degree of HCW contamination.[82] Hand contamination was 0 percent, 8 percent, and 26 percent when environmental contamination was 0–25 percent, 26–50 percent, greater than 50 percent respectively. Notably, this study was conducted prior to the routine use of contact precautions for patients with CDI, so if implemented, regular use of gloves may have decreased the degree of hand contamination.

It is difficult to decipher the role of environmental agents with sporicidal activity, as available data indicate that most CDI cases are not related to *C. difficile* acquisition from the environment, different methods to apply the agents, and inconsistent impact of sporicidal agents on reducing CDI incidence in nonoutbreak settings. Several studies highlight this finding. Shaughnessy et al. found admission to an ICU room that previously housed a patient with CDI to be a risk factor for CDI, however, only 11 percent of patients who developed CDI had this risk factor.[78] In addition, studies using whole genome sequencing found only 2 percent to 7 percent of new CDI cases could be attributed to environmental contamination.[86,87] Studies that have found a reduction in CDI after implementation of a sporicidal agent have mostly occurred in outbreaks settings with the concurrent implementation of other CDI prevention interventions.[88–90] Conversely, sporicidal agents have often not been associated with reductions in CDI in nonoutbreak settings.[91,92] A further complication is that several products have been used, including various concentrations of sodium hypochlorite, phenol-based agents, peroxide-based agents, and ultraviolet irradiation, applied by people or by automated systems, and with daily cleaning alone, daily cleaning and terminal cleaning, terminal cleaning alone, and periodic "deep cleaning." Of these methods and products, "no touch" disinfection technologies have garnered the most interest. In general, these products use ultraviolet radiation or hydrogen peroxide vapor to disinfect the environment, and several studies have found these products are effective at reducing viable *C. difficile* spores from patient rooms.[93–95] No single methodology appears superior in regards to reductions in CDI incidence.[96]

What has been demonstrated is that the thoroughness of cleaning with a sporicidal agent has been associated with reductions in viable *C. difficile* spores in the environment. One hospital found over the course of several interventions to decrease *C. difficile* spore contamination including terminal infection with bleach, use of fluorescent markers to assess cleaning adequacy, use of an automated ultraviolet radiation device, to a dedicated team focused on daily cleaning of rooms housing patients with CDI, the latter intervention was clearly the most effective at removing viable *C. difficile* spores from the environment.[95] Several methods have been used to assess thoroughness of cleaning, including fluorescent markers and ATP bioluminescence.[97,98] These cleaning assessment measures are most effective when feedback is given in real time. Potential barriers to effective cleaning include insufficient time for cleaning, inadequate cleaning supplies, inadequate education, and poor communication.[69] For a successful environmental decontamination program, it is important to work collaboratively with, and to provide feedback to environmental services staff.[95]

Antimicrobial Stewardship

Currently the only way to prevent CDI if transmission occurs is antimicrobial stewardship. A successful antimicrobial stewardship program aims to limit inappropriate antimicrobial use while maximizing clinical utility by optimizing the choice of agent, dose, route, and duration of therapy.[99] Prior exposure to antimicrobials is a strong risk factor for the development of CDI, and, unfortunately, 20–50 percent of all antimicrobials prescribed in US acute care hospitals are either unnecessary or inappropriate.[100–102] By limiting exposure to unnecessary antimicrobials, the risk of development of CDI after *C. difficile* exposure will decrease.

Clindamycin has long been identified as a major culprit in the development of CDI, and fluoroquinolones have also been implicated after emergence of the fluoroquinolone-resistant epidemic strain BI/NAP1/027.[103] However, virtually all antimicrobials can increase the propensity for CDI development.[103] Given this, controlling the use of antimicrobials via stewardship is a cornerstone of CDI prevention and has been effective in reducing the rate of CDI in the inpatient setting.[104,105] Most antimicrobial stewardship programs have focused on restricting the use of high-risk antimicrobials (second-and third-generation cephalosporins, fluoroquinolones, and clindamycin). However, antimicrobial stewardship programs can also reduce use of these agents through nonrestrictive means, such as clinician education and provision of antimicrobial guidelines.[105] Antimicrobial stewardship is often difficult to evaluate as a single CDI prevention strategy, given that

it is often implemented as part of an infection control bundle that includes enhanced contact precautions and specialized cleaning methods.[12,70]

Other Preventative Strategies

There are insufficient data to recommend administration of probiotics for primary prevention of CDI. Several meta-analyses indicate probiotics may be effective at preventing CDI when given to patients on antimicrobials without a history of CDI.[106–108] The typical CDI incidence among hospitalized people >65 years of age on antimicrobials with a length of stay > 2 days is ≤ 3 percent, even during outbreaks of CDI.[109–111] The studies with the greatest influence on the results of the meta-analyses had a CDI incidence 7 to 20 times higher in the placebo arms than would otherwise be expected based on the patient population studied, potentially biasing the results to benefit of the probiotic.[112,113] In addition, there are other methodological differences between the studies, including differences in probiotic formulations, duration of administration, CDI definitions, duration of follow-up, and inclusion of patients not typically considered at high risk for CDI, making it difficult to make recommendations on when probiotics should be used and which probiotic. There is also the potential for the probiotic organisms to cause infections in hospitalized patients.[114–116]

Emerging data suggest asymptomatic *C. difficile* carriers play an important role in *C. difficile* transmission and HO-CDI.[86,117,118] However, the best test for colonization and methods to prevent transmission from asymptomatic carriers remains unknown, therefore screening for asymptomatic carriage is currently not recommended. Prophylactic use of vancomycin or metronidazole to prevent the CDI in patients receiving antimicrobials or in asymptomatic *C. difficile* carriers is also not recommended, as treatment may increase a patient's risk for developing an actual CDI.[69]

Proton-pump inhibitors are now one of the most prescribed groups of drugs in the US. Several studies have noted an association between receipt of acid-suppressive therapy and development of CDI.[83,119] However, it is not clear if this association represents causation, as people who receive acid-suppressive medications in general are more ill than those patients not on these medications, and a common side effect of these medications is diarrhea. Although there have been no studies to determine the impact of restricting of acid-suppressive medications on CDI incidence, several studies have demonstrated that a large proportion of people on these medications do not have an indication for them. Even in the absence of data to support restriction for CDI prevention, medications that are not indicated should be discontinued regardless.

Key Points

Since the early 2000s, *Clostridium difficile* infection (CDI) has become more frequent, more severe, and more difficult to manage. Below is a list of the most relevant aspects of recognizing, managing and preventing CDI from the IP perspective.

-CDI is a clinical diagnosis supported by laboratory findings.

-Treatment for CDI should only be initiated in the setting of a positive test and concordant clinical findings, unless the patient is at high risk for CDI and severely ill, in which case empirical therapy is justified.

-Rates of HO-CDI should be tracked for surveillance purposes.

-Whenever possible, patients with CDI should be placed in private rooms with barrier precautions and dedicated disposable medical equipment.

-Antimicrobial stewardship programs should focus on reducing unnecessary use antimicrobials.

-Testing asymptomatic patients for *C. difficile* carriage and repeating *C. difficile* testing at the end of treatment for CDI are not recommended.

Reference List

1. Bartlett JG. Clostridium difficile infection: historic review. *Anaerobe.* 2009;**15**(6):227–229.
2. Kelly CP, Pothoulakis C, LaMont JT. Clostridium difficile colitis. *N Engl J Med.* 1994;**330**(4):257–262.
3. Magill SS, Edwards JR, Bamberg W, et al. Multistate point-prevalence survey of health care-associated infections. *N Engl J Med.* 2014;**370**(13):1198–1208.
4. Kwon JH, Olsen MA, Dubberke ER. The morbidity, mortality, and costs associated with Clostridium difficile infection. *Infect Dis Clin North Am.* 2015;**29**(1):123–134.
5. Bartlett JG. Narrative review: the new epidemic of Clostridium difficile–associated enteric disease. *Ann Intern Med.* 2006;**145**(10):758–764.
6. Honda H, Dubberke ER. The changing epidemiology of Clostridium difficile infection. *Curr Opin Gastroenterol.* 2014;**30**(1):54–62.
7. al Saif N, Brazier JS. The distribution of Clostridium difficile in the environment of South Wales. *J Med Microbiol.* 1996;**45**(2):133–137.
8. Bakri MM, Brown DJ, Butcher JP, Sutherland AD. Clostridium difficile in ready-to-eat salads, Scotland. *Emerg Infect Dis.* 2009;**15**(5):817–818.
9. Gould LH, Limbago B. Clostridium difficile in food and domestic animals: a new foodborne pathogen? *Clin Infect Dis.* 2010;**51**(5):577–582.
10. Songer JG, Trinh HT, Killgore GE, Thompson AD, McDonald LC, Limbago BM. Clostridium difficile in retail meat products, USA, 2007. *Emerg Infect Dis.* 2009;**15**(5):819–21.
11. Rupnik M. Is Clostridium difficile-associated infection a potentially zoonotic and foodborne disease? *Clin Microbiol Infect.* 2007;**13**(5):457–459.
12. Muto CA, Blank MK, Marsh JW, et al. Control of an outbreak of infection with the hypervirulent Clostridium difficile BI strain in a university hospital using a comprehensive "bundle" approach. *Clin Infect Dis.* 2007;**45**(10):1266–1273.
13. Lessa FC, Mu Y, Bamberg WM, et al. Burden of Clostridium difficile

infection in the United States. *N Engl J Med*. 2015;**372**(9):825–834.

14. Dubberke ER, Schaefer E, Reske KA, Zilberberg M, Hollenbeak CS, Olsen MA. Attributable inpatient costs of recurrent Clostridium difficile infections. *Infect Control Hosp Epidemiol*. 2014;**35** (11):1400–1407.
15. Chitnis AS, Holzbauer SM, Belflower RM, et al. Epidemiology of community-associated Clostridium difficile infection, 2009 through 2011. *JAMA Intern Med.* 2013;**173** (14):1359–1367.
16. Alasmari F, Seiler SM, Hink T, Burnham CA, Dubberke ER. Prevalence and risk factors for asymptomatic Clostridium difficile carriage. *Clin Infect Dis.* 2014;**59** (2):216–222.
17. Fekety R, Kim KH, Brown D, Batts DH, Cudmore M, Silva J, Jr. Epidemiology of antibiotic-associated colitis: isolation of Clostridium difficile from the hospital environment. *Am J Med.* 1981;**70**(4):906–908.
18. Jump RL, Pultz MJ, Donskey CJ. Vegetative Clostridium difficile survives in room air on moist surfaces and in gastric contents with reduced acidity: a potential mechanism to explain the association between proton pump inhibitors and C. difficile-associated diarrhea? *Antimicrob Agents Chemother.* 2007;**51** (8):2883–2887.
19. McFarland LV, Mulligan ME, Kwok RY, Stamm WE. Nosocomial acquisition of Clostridium difficile infection. *N Engl J Med.* 1989;**320** (4):204–210.
20. Sunenshine RH, McDonald LC. Clostridium difficile–associated disease: new challenges from an established pathogen. *Cleve Clin J Med.* 2006;**73**(2):187–197.
21. Hurley BW, Nguyen CC. The spectrum of pseudomembranous enterocolitis and antibiotic-associated diarrhea. *Arch Intern Med.* 2002;**162** (19):2177–2184.
22. Donskey CJ. The role of the intestinal tract as a reservoir and source for transmission of nosocomial pathogens. *Clin Infect Dis*. 2004;**39** (2):219–226.
23. Cohen SH, Gerding DN, Johnson S, et al. Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the infectious diseases society of America (IDSA). *Infect Control Hosp Epidemiol.* 2010;**31** (5):431–455.
24. Loo VG, Bourgault AM, Poirier L, et al. Host and pathogen factors for Clostridium difficile infection and colonization. *N Engl J Med.* 2011;**365** (18):1693–1703.
25. Olsen MA, Stwalley D, Demont C, Mahe C, Dubberke ER. Minimal contribution of age to risk of Clostridium difficile infection in the elderly. *ID Week.* **2015**. 10-8-2015.

Ref Type: Abstract

26. Bignardi GE. Risk factors for Clostridium difficile infection. *J Hosp Infect.* 1998;**40**(1):1–15.
27. Dubberke ER, Reske KA, Seiler S, Hink T, Kwon JH, Burnham CA. Risk factors for acquisition and loss of C. difficile colonization in hospitalized patients. *Antimicrob Agents Chemother.* 2015;.
28. McFarland LV, Surawicz CM, Stamm WE. Risk factors for Clostridium difficile carriage and C. difficile-associated diarrhea in a cohort of hospitalized patients. *J Infect Dis.* 1990;**162**(3):678–684.
29. Zacharioudakis IM, Zervou FN, Pliakos EE, Ziakas PD, Mylonakis E. Colonization with toxinogenic C. difficile upon hospital admission, and risk of infection: a systematic review and meta-analysis. *Am J Gastroenterol.* 2015;**110**(3):381–390.
30. Bagdasarian N, Rao K, Malani PN. Diagnosis and treatment of Clostridium difficile in adults: a systematic review. *JAMA.* 2015;**313** (4):398–408.
31. Wanahita A, Goldsmith EA, Musher DM. Conditions associated with leukocytosis in a tertiary care hospital, with particular attention to the role of infection caused by Clostridium difficile. *Clin Infect Dis*. 2002;**34** (12):1585–1592.
32. Dubberke ER, Han Z, Bobo L, et al. Impact of clinical symptoms on interpretation of diagnostic assays for Clostridium difficile infections. *J Clin Microbiol*. 2011;**49**(8):2887–2893.
33. Bartlett JG, Gerding DN. Clinical recognition and diagnosis of Clostridium difficile infection. *Clin Infect Dis*. 2008;**46** Suppl 1:S12–S18.
34. Stamper PD, Alcabasa R, Aird D, et al. Comparison of a commercial real-time PCR assay for tcdB detection to a cell culture cytotoxicity assay and toxigenic culture for direct detection of toxin-producing Clostridium difficile in clinical samples. *J Clin Microbiol*. 2009;**47**(2):373–378.
35. Wilkins TD, Lyerly DM. Clostridium difficile testing: after 20 years, still challenging. *J Clin Microbiol*. 2003;**41** (2):531–534.
36. Dubberke ER, Burnham CD. Diagnosis of Clostridium difficile infection: treat the patient, not the test. *JAMA Intern Med*. 2015;1–2.
37. Aichinger E, Schleck CD, Harmsen WS, Nyre LM, Patel R. Nonutility of repeat laboratory testing for detection of Clostridium difficile by use of PCR or enzyme immunoassay. *J Clin Microbiol*. 2008;**46**(11):3795–3797.
38. Gerding DN, Johnson S, Peterson LR, Mulligan ME, Silva J, Jr. Clostridium difficile–associated diarrhea and colitis. *Infect Control Hosp Epidemiol*. 1995;**16** (8):459–477.
39. Ticehurst JR, Aird DZ, Dam LM, Borek AP, Hargrove JT, Carroll KC. Effective detection of toxigenic Clostridium difficile by a two-step algorithm including tests for antigen and cytotoxin. *J Clin Microbiol*. 2006;**44** (3):1145–1149.
40. Shanholtzer CJ, Willard KE, Holter JJ, Olson MM, Gerding DN, Peterson LR. Comparison of the VIDAS Clostridium difficile toxin A immunoassay with C. difficile culture and cytotoxin and latex tests. *J Clin Microbiol*. 1992;**30** (7):1837–1840.
41. Longtin Y, Trottier S, Brochu G, et al. Impact of the type of diagnostic assay on Clostridium difficile infection and complication rates in a mandatory reporting program. *Clin Infect Dis*. 2013;**56**(1):67–73.
42. van den Berg RJ, Bruijnesteijn van Coppenraet LS, Gerritsen HJ, Endtz HP, van der Vorm ER, Kuijper EJ. Prospective multicenter evaluation of a new immunoassay and real-time PCR for rapid diagnosis of Clostridium difficile–associated diarrhea in hospitalized patients. *J Clin Microbiol*. 2005;**43** (10):5338–5340.
43. Bartlett JG. Clinical practice: antibiotic-associated diarrhea. *N Engl J Med*. 2002;**346**(5):334–339.
44. Shannon-Lowe J, Matheson NJ, Cooke FJ, Aliyu SH. Prevention and medical management of Clostridium difficile infection. *BMJ*. 2010;**340**: c1296.
45. Louie TJ, Miller MA, Mullane KM, et al. Fidaxomicin versus vancomycin for

Clostridium difficile infection. *N Engl J Med*. 2011;**364**(5):422–431.

46. Johnson S, Louie TJ, Gerding DN, et al. Vancomycin, metronidazole, or tolevamer for Clostridium difficile infection: results from two multinational, randomized, controlled trials. *Clin Infect Dis*. 2014;**59**(3):345–354.
47. Johnson S. Recurrent Clostridium difficile infection: a review of risk factors, treatments, and outcomes. *J Infect*. 2009;**58**(6):403–410.
48. Garey KW, Ghantoji SS, Shah DN, et al. A randomized, double-blind, placebo-controlled pilot study to assess the ability of rifaximin to prevent recurrent diarrhoea in patients with Clostridium difficile infection. *J Antimicrob Chemother*. 2011;**66**(12):2850–2855.
49. Soriano MM, Danziger LH, Gerding DN, Johnson S. Novel fidaxomicin treatment regimens for patients with multiple clostridium difficile infection recurrences that are refractory to standard therapies. *Open Forum Infect Dis*. 2014;**1**(2):ofu069.
50. Cammarota G, Ianiro G, Gasbarrini A. Fecal microbiota transplantation for the treatment of Clostridium difficile infection: a systematic review. *J Clin Gastroenterol*. 2014 Jan 16.
51. Hirsch BE, Saraiya N, Poeth K, Schwartz RM, Epstein ME, Honig G. Effectiveness of fecal-derived microbiota transfer using orally administered capsules for recurrent Clostridium difficile infection. *BMC Infect Dis*. 2015;**15**:191.
52. Orenstein R, Dubberke E, Hardi R, et al. Safety and durability of RBX2660 (microbiota suspension) for recurrent Clostridium difficile infection: results of the PUNCH CD Study. *Clin Infect Dis*. 2015 Nov 12.
53. van Nood E, Vrieze A, Nieuwdorp M, et al. Duodenal infusion of donor feces for recurrent Clostridium difficile. *N Engl J Med*. 2013;**368**(5):407–415.
54. Youngster I, Russell GH, Pindar C, Ziv-Baran T, Sauk J, Hohmann EL. Oral, capsulized, frozen fecal microbiota transplantation for relapsing Clostridium difficile infection. *JAMA*. 2014;**312**(17):1772–1778.
55. Guidance for Industry: Enforcement Policy Regarding Investigational New Drug Requirements for Use of Fecal Microbiota for Transplantation to Treat Clostridium difficile Infection Not Responsive to Standard Therapies, Food and Drug Administration, (2013).
56. Allen SJ. The potential of probiotics to prevent Clostridium difficile infection. *Infect Dis Clin North Am*. 2015;**29**(1):135–144.
57. Gerding DN, Muto CA, Owens RC, Jr. Treatment of Clostridium difficile infection. *Clin Infect Dis*. 2008;**46** Suppl 1:S32–S42.
58. Byrn JC, Maun DC, Gingold DS, Baril DT, Ozao JJ, Divino CM. Predictors of mortality after colectomy for fulminant Clostridium difficile colitis. *Arch Surg*. 2008;**143**(2):150–154.
59. Lamontagne F, Labbe AC, Haeck O, et al. Impact of emergency colectomy on survival of patients with fulminant Clostridium difficile colitis during an epidemic caused by a hypervirulent strain. *Ann Surg*. 2007;**245**(2):267–272.
60. Pepin J, Vo TT, Boutros M, et al. Risk factors for mortality following emergency colectomy for fulminant Clostridium difficile infection. *Dis Colon Rectum*. 2009;**52**(3):400–405.
61. Sailhamer EA, Carson K, Chang Y, et al. Fulminant Clostridium difficile colitis: patterns of care and predictors of mortality. *Arch Surg*. 2009;**144**(5):433–439.
62. Neal MD, Alverdy JC, Hall DE, Simmons RL, Zuckerbraun BS. Diverting loop ileostomy and colonic lavage: an alternative to total abdominal colectomy for the treatment of severe, complicated Clostridium difficile associated disease. *Ann Surg*. 2011;**254**(3):423–427.
63. Yokoe DS, Anderson DJ, Berenholtz SM, et al. A compendium of strategies to prevent healthcare-associated infections in acute care hospitals: 2014 updates. *Infect Control Hosp Epidemiol*. 2014;**35**(8):967–977.
64. Dubberke ER, McMullen KM, Mayfield JL, et al. Hospital-associated Clostridium difficile infection: is it necessary to track community-onset disease? *Infect Control Hosp Epidemiol*. 2009;**30**(4):332–337.
65. Dubberke ER, Butler AM, Hota B, et al. Multicenter study of the impact of community-onset Clostridium difficile infection on surveillance for C. difficile infection. *Infect Control Hosp Epidemiol*. 2009;**30**(6):518–525.
66. Marschall J, Mermel LA, Fakih M, et al. Strategies to prevent central line–associated bloodstream infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol*. 2014;**35**(7):753–771.
67. Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med*. 2006;**355**(26):2725–2732.
68. Warren DK, Zack JE, Cox MJ, Cohen MM, Fraser VJ. An educational intervention to prevent catheter-associated bloodstream infections in a nonteaching, community medical center. *Crit Care Med*. 2003;**31**(7):1959–1963.
69. Dubberke ER, Carling P, Carrico R, et al. Strategies to prevent Clostridium difficile infections in acute care hospitals: 2014 Update. *Infect Control Hosp Epidemiol*. 2014;**35**(6):628–645.
70. Weiss K, Boisvert A, Chagnon M, et al. Multipronged intervention strategy to control an outbreak of Clostridium difficile infection (CDI) and its impact on the rates of CDI from 2002 to 2007. *Infect Control Hosp Epidemiol*. 2009;**30**(2):156–162.
71. Gravel D, Gardam M, Taylor G, et al. Infection control practices related to Clostridium difficile infection in acute care hospitals in Canada. *Am J Infect Control*. 2009;**37**(1):9–14.
72. Wilkinson K, Gravel D, Taylor G, et al. Infection prevention and control practices related to Clostridium difficile infection in Canadian acute and long-term care institutions. *Am J Infect Control*. 2011;**39**(3):177–182.
73. Detsky ME, Etchells E. Single-patient rooms for safe patient-centered hospitals. *JAMA*. 2008;**300**(8):954–956.
74. Kundrapu S, Jury LA, Sitzlar B, Sunkesula VC, Sethi AK, Donskey CJ. Easily modified factors contribute to delays in diagnosis of Clostridium difficile infection: a cohort study and intervention. *J Clin Microbiol*. 2013;**51**(7):2365–2370.
75. Boyce JM, Pittet D. Guideline for Hand Hygiene in Health-Care Settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. *MMWR Recomm Rep*. 2002;**51**(RR-16):1–45, quiz.
76. Landelle C, Verachten M, Legrand P, Girou E, Barbut F, Buisson CB. Contamination of healthcare workers' hands with Clostridium difficile spores after caring for patients with C. difficile

infection. *Infect Control Hosp Epidemiol*. 2014;**35**(1):10–15.

77. Edmonds SL, Zapka C, Kasper D, et al. Effectiveness of hand hygiene for removal of Clostridium difficile spores from hands. *Infect Control Hosp Epidemiol*. 2013;**34**(3):302–305.
78. Shaughnessy MK, Micielli RL, Depestel DD, et al. Evaluation of hospital room assignment and acquisition of Clostridium difficile infection. *Infect Control Hosp Epidemiol*. 2011;**32**(3):201–206.
79. Starr JM, Campbell A, Renshaw E, Poxton IR, Gibson GJ. Spatio-temporal stochastic modelling of Clostridium difficile. *J Hosp Infect*. 2009;**71**(1):49–56.
80. Kim KH, Fekety R, Batts DH, et al. Isolation of Clostridium difficile from the environment and contacts of patients with antibiotic-associated colitis. *J Infect Dis*. 1981;**143**(1):42–50.
81. Dumford DM, III, Nerandzic MM, Eckstein BC, Donskey CJ. What is on that keyboard? Detecting hidden environmental reservoirs of Clostridium difficile during an outbreak associated with North American pulsed-field gel electrophoresis type 1 strains. *Am J Infect Control*. 2009;**37**(1):15–19.
82. Samore MH, Venkataraman L, DeGirolami PC, Arbeit RD, Karchmer AW. Clinical and molecular epidemiology of sporadic and clustered cases of nosocomial Clostridium difficile diarrhea. *Am J Med*. 1996;**100**(1):32–40.
83. Cunningham R, Dale B, Undy B, Gaunt N. Proton pump inhibitors as a risk factor for Clostridium difficile diarrhoea. *J Hosp Infect*. 2003;**54**(3):243–245.
84. Merrigan M, Venugopal A, Mallozzi M, et al. Human hypervirulent Clostridium difficile strains exhibit increased sporulation as well as robust toxin production. *J Bacteriol*. 2010;**192**(19):4904–4911.
85. Dubberke ER, Reske KA, Noble-Wang J, et al. Prevalence of Clostridium difficile environmental contamination and strain variability in multiple health care facilities. *Am J Infect Control*. 2007;**35**(5):315–318.
86. Curry SR, Muto CA, Schlackman JL, et al. Use of multilocus variable number of tandem repeats analysis genotyping to determine the role of asymptomatic carriers in Clostridium difficile transmission. *Clin Infect Dis*. 2013;**57**(8):1094–1102.
87. Eyre DW, Griffiths D, Vaughan A, et al. Asymptomatic Clostridium difficile colonisation and onward transmission. *PLoS One*. 2013;**8**(11):e78445.
88. Kaatz GW, Gitlin SD, Schaberg DR, et al. Acquisition of Clostridium difficile from the hospital environment. *Am J Epidemiol*. 1988;**127**(6):1289–1294.
89. McMullen KM, Zack J, Coopersmith CM, Kollef M, Dubberke E, Warren DK. Use of hypochlorite solution to decrease rates of Clostridium difficile–associated diarrhea. *Infect Control Hosp Epidemiol*. 2007;**28**(2):205–207.
90. Orenstein R, Aronhalt KC, McManus JE, Jr., Fedraw LA. A targeted strategy to wipe out Clostridium difficile. *Infect Control Hosp Epidemiol*. 2011;**32**(11):1137–119.
91. Mayfield JL, Leet T, Miller J, Mundy LM. Environmental control to reduce transmission of Clostridium difficile. *Clin Infect Dis*. 2000;**31**(4):995–1000.
92. Wilcox MH, Fawley WN, Wigglesworth N, Parnell P, Verity P, Freeman J. Comparison of the effect of detergent versus hypochlorite cleaning on environmental contamination and incidence of Clostridium difficile infection. *J Hosp Infect*. 2003;**54**(2):109–114.
93. Barbut F, Menuet D, Verachten M, Girou E. Comparison of the efficacy of a hydrogen peroxide dry-mist disinfection system and sodium hypochlorite solution for eradication of Clostridium difficile spores. *Infect Control Hosp Epidemiol*. 2009;**30**(6):507–514.
94. Boyce JM, Havill NL, Otter JA, et al. Impact of hydrogen peroxide vapor room decontamination on Clostridium difficile environmental contamination and transmission in a healthcare setting. *Infect Control Hosp Epidemiol*. 2008;**29**(8):723–729.
95. Sitzlar B, Deshpande A, Fertelli D, Kundrapu S, Sethi AK, Donskey CJ. An environmental disinfection odyssey: evaluation of sequential interventions to improve disinfection of Clostridium difficile isolation rooms. *Infect Control Hosp Epidemiol*. 2013;**34**(5):459–465.
96. Anderson D, Chen LF, Weber DJ, et al. The benefits of enhanced terminal room (betr) disinfection study: a cluster randomized, multicenter crossover study with 2x2 factorial design to evaluate the impact of enhanced terminal room disinfection on acquisition and infection caused by multidrug-resistant organisms (MDRO). ID Week. 2015. 10-9-2015.

Ref Type: Abstract

97. Boyce JM, Havill NL, Dumigan DG, Golebiewski M, Balogun O, Rizvani R. Monitoring the effectiveness of hospital cleaning practices by use of an adenosine triphosphate bioluminescence assay. *Infect Control Hosp Epidemiol*. 2009;**30**(7):678–684.
98. Carling PC, Parry MF, Von Beheren SM. Identifying opportunities to enhance environmental cleaning in 23 acute care hospitals. *Infect Control Hosp Epidemiol*. 2008;**29**(1):1–7.
99. Dellit TH, Owens RC, McGowan JE, Jr., et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis*. 2007;**44**(2):159–177.
100. Fridkin S, Baggs J, Fagan R, et al. Vital signs: improving antibiotic use among hospitalized patients. *MMWR Morb Mortal Wkly Rep*. 2014;**63**(9):194–200.
101. Levin PD, Idrees S, Sprung CL, et al. Antimicrobial use in the ICU: indications and accuracy–an observational trial. *J Hosp Med*. 2012;**7**(9):672–678.
102. Camins BC, King MD, Wells JB, et al. Impact of an antimicrobial utilization program on antimicrobial use at a large teaching hospital: a randomized controlled trial. *Infect Control Hosp Epidemiol*. 2009;**30**(10):931–938.
103. Owens RC, Jr., Donskey CJ, Gaynes RP, Loo VG, Muto CA. Antimicrobial-associated risk factors for Clostridium difficile infection. *Clin Infect Dis*. 2008 ;**46** Suppl 1:S19–S31.
104. Nuila F, Cadle RM, Logan N, Musher DM. Antibiotic stewardship and Clostridium difficile–associated disease. *Infect Control Hosp Epidemiol*. 2008;**29**(11):1096–1097.
105. Valiquette L, Cossette B, Garant MP, Diab H, Pepin J. Impact of a reduction in the use of high-risk antibiotics on the course of an epidemic of Clostridium difficile–associated disease caused by the hypervirulent NAP1/027 strain. *Clin Infect Dis*. 2007;**45** Suppl 2:S112–S121.
106. Goldenberg JZ, Ma SS, Saxton JD, et al. Probiotics for the prevention of

Clostridium difficile–associated diarrhea in adults and children. *Cochrane Database Syst Rev*. 2013;**5**: CD006095.

107. Pattani R, Palda VA, Hwang SW, Shah PS. Probiotics for the prevention of antibiotic-associated diarrhea and Clostridium difficile infection among hospitalized patients: systematic review and meta-analysis. *Open Med*. 2013;**7**(2):e56–e67.
108. Johnson S, Maziade PJ, McFarland LV, et al. Is primary prevention of Clostridium difficile infection possible with specific probiotics? *Int J Infect Dis*. 2012;**16** (11):e786–e792.
109. Dubberke ER, Reske KA, Yan Y, Olsen MA, McDonald LC, Fraser VJ. Clostridium difficile–associated disease in a setting of endemicity: identification of novel risk factors. *Clin Infect Dis*. 2007;**45** (12):1543–1549.
110. Dubberke ER, Butler AM, Yokoe DS, et al. Multicenter study of Clostridium difficile infection rates from 2000 to 2006. *Infect Control Hosp Epidemiol*. 2010;**31**(10):1030–1037.
111. Loo VG, Poirier L, Miller MA, et al. A predominantly clonal multi-institutional outbreak of Clostridium difficile-associated diarrhea with high morbidity and mortality. *N Engl J Med*. 2005;**353** (23):2442–2449.
112. Gao XW, Mubasher M, Fang CY, Reifer C, Miller LE. Dose-response efficacy of a proprietary probiotic formula of Lactobacillus acidophilus CL1285 and Lactobacillus casei LBC80 R for antibiotic-associated diarrhea and Clostridium difficile-associated diarrhea prophylaxis in adult patients. *Am J Gastroenterol*. 2010;**105** (7):1636–1641.
113. Kotowska M, Albrecht P, Szajewska H. Saccharomyces boulardii in the prevention of antibiotic-associated diarrhoea in children: a randomized double-blind placebo-controlled trial. *Aliment Pharmacol Ther*. 2005;**21** (5):583–590.
114. Hennequin C, Kauffmann-Lacroix C, Jobert A, et al. Possible role of catheters in Saccharomyces boulardii fungemia. *Eur J Clin Microbiol Infect Dis*. 2000;**19**(1):16–20.
115. Enache-Angoulvant A, Hennequin C. Invasive Saccharomyces infection: a comprehensive review. *Clin Infect Dis*. 2005;**41**(11): 1559–1568.
116. Gouriet F, Million M, Henri M, Fournier PE, Raoult D. Lactobacillus rhamnosus bacteremia: an emerging clinical entity. *Eur J Clin Microbiol Infect Dis*. 2012;**31** (9):2469–2480.
117. Eyre DW, Cule ML, Wilson DJ, et al. Diverse sources of C. difficile infection identified on whole-genome sequencing. *N Engl J Med*. 2013;**369** (13):1195–1205.
118. Lanzas C, Dubberke ER, Lu Z, Reske KA, Grohn YT. Epidemiological model for Clostridium difficile transmission in healthcare settings. *Infect Control Hosp Epidemiol*. 2011;**32** (6):553–561.
119. McDonald EG, Milligan J, Frenette C, Lee TC. Continuous proton pump inhibitor therapy and the associated risk of recurrent Clostridium difficile infection. *JAMA Intern Med*. 2015;**175** (5):784–791.

Chapter 19

Antimicrobial Stewardship

Sharon Tsay, MD, and Keith Hamilton, MD

1 Introduction

When discovered in the early twentieth century, penicillin was described as a "magic bullet," providing cure for infections that had previously killed the healthiest, most productive members of society.[1] This dramatic shift in the practice of medicine has cast a long shadow, undoubtedly contributing to patterns of inappropriate use observed today. During an average hospital stay in the United States (US), over half of patients receive an antibiotic for at least one day.[2] However, these prescriptions are often given in the absence of appropriate confirmatory testing, for inappropriate indications, or for excessive durations of therapy. These practices also frequently occur in the ambulatory setting, where antibiotics are most often prescribed for upper respiratory tract infections, despite these being predominantly viral in etiology.[2] Even when antibiotics are given for appropriate indications, (e.g., severe sepsis or septic shock), the correct timing and coverage of prescribed antibiotics are of utmost importance.[3]

Although antibiotics are essential for the treatment of bacterial infections, they are not benign. Like other medications, patients may experience adverse drug reactions, which can range from mild gastrointestinal symptoms to life-threatening anaphylaxis and organ failure. For example, vancomycin, one of the most commonly prescribed antibiotics in the hospital setting, has been associated with the development of nephrotoxicity in 7–28 percent of patients.[4] The use of another broad-spectrum antibiotic, linezolid, is limited by drug-associated thrombocytopenia; in a recent study, up to 42 percent (range 15–50 percent) developed thrombocytopenia.[5] In addition to these adverse drug effects, antibiotic use leads to dysbiosis of the fecal microbiota, increasing the risk for the development of *Clostridium difficile* colitis.[2] The incidence of *C. difficile* infection has increased over the past decade in the US, both in hospitalized patients and in the community, and has been associated with mortality rates of 15–20 percent.[6]

In addition, antimicrobial resistance is increasing at an alarming rate. Data suggest that "antibiotic use – whether appropriate or inappropriate – is associated with selective pressures for the emergence of resistant bacteria."[7] Resistant organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) have been of significant public health concern in the past decade, but more recently, the emergence of carbapenem-resistant *Enterobacteriaceae* (CRE) has challenged the existing arsenal of antibiotic therapy.[8] In September 2014, the US Department of Health and Human Services' Presidential Advisory Council released a report "National Strategy for Combating Antibiotic-Resistant Bacteria" that comments that "this brewing problem has become a crisis. The evolution of antibiotic resistance is now occurring at an alarming rate and is outpacing the development of new countermeasures."[9] According to the Centers for Disease Control and Prevention (CDC), each year, "at least two million illnesses and 23,000 deaths are caused by antibiotic-resistant bacteria in the United States alone."[10] And while resistance is increasing, antibiotic development and production has declined. Succinctly labeling the problem "*Bad bugs, No drugs*," a recent review highlights the drop-off in antibiotic development over the past three decades, further highlighting the urgency of stewardship efforts.[11]

Despite these daunting problems, "a growing body of evidence demonstrates that programs dedicated to improving antibiotic use, known as 'antibiotic stewardship' programs (ASP), can help slow the emergence of resistance while optimizing treatment and minimizing costs."[9] These programs seek to improve judicious use of antibiotics by promoting "the use of the right antibiotics, at the right dose, route, and duration, for the right bacterial infection at the right time."[12] Systematic efforts of ASPs aim not only to reduce inappropriate antibiotic use, but also to improve antibiotic prescribing when use is appropriate.[13] Collaboration among varied disciplines is necessary for ASPs to be effective.[14] The goal of this chapter is to provide healthcare epidemiologists in a variety of clinical settings with practical information on how to structure a program, design interventions, and measure outcomes in their respective facilities in order to "[improve] patient outcomes, [ensure] cost-effective therapy, and [reduce] the adverse health and ecological effects of antimicrobial use, including drug resistance."[15]

2 Organization of an Antimicrobial Stewardship Program

Designing a successful ASP is a multidisciplinary, multistep process.[16] Support of hospital administration should be garnered early in the process. In addition, maintaining effective communication throughout the process is essential to success. Baseline information, including institutional antimicrobial use, antimicrobial cost, hospital-acquired infection rates, and antimicrobial resistance can be used to justify the program to administration. Issues identified during baseline data gathering can also help to frame specific management strategies for the institution (e.g., overuse of a particular class of antibiotics)

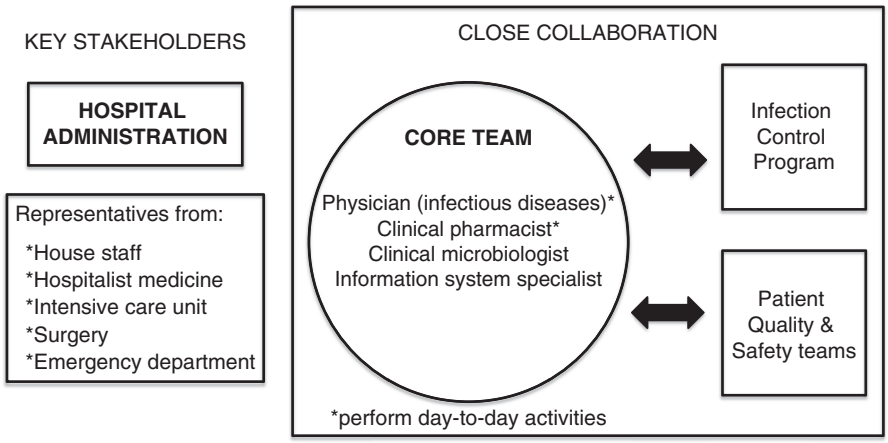

Figure 19.1 Structure of an antimicrobial stewardship program

and can also help identify important members of the stewardship team. In general, experts suggest the inclusion of a physician (infectious diseases or hospital epidemiologist), clinical pharmacist, clinical microbiologist, and information system specialist in addition to close collaboration with infection control professionals and quality and patient safety officers.[16–19] Inclusion of representatives from groups that are key stakeholders in antimicrobial prescribing including house staff, hospitalist medicine staff, intensive care unit staff, emergency department staff, and surgery staff can augment the effectiveness of stewardship interventions by improving acceptance of recommendations, providing feedback, and identifying stewardship issues from front-line providers (Figure 19.1).

However, the daily working group, or core ASP team, is typically comprised of stewardship physicians and pharmacists who perform the daily functions of the ASP. Other members of the ASP provide input and guidance as a part of a larger stewardship committee. The core ASP team should have protected time to perform daily stewardship activities. The larger committee can be organized as a freestanding stewardship committee or as an antibiotic subcommittee of an institution's pharmacy and therapeutics (P&T) committee. A benefit of the latter organizational structure is that association with an institution's P&T committee provides an official link to maintenance of the healthcare facility antibiotic formulary and to approval of antibiotic guidelines. Regardless of the structure, the stewardship committee is essential for providing expert guidance, strategic planning, and overall vision for the ASP.

In a joint policy statement, the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Infectious Diseases Society (PIDS) recommend developing a program that is "physician-directed or supervised. At a minimum, one or more members of the team should have training in antimicrobial stewardship."[19] This infectious diseases–trained physician should be able to dedicate a significant portion of his or her time to designing, implementing, and evaluating the program.[17] Having a physician in this role also "may increase acceptance and compliance of the program by other physicians."[17] In addition, the physician can provide clinical guidance and can help establish institutional guidelines on antimicrobial recommendations. If no infectious diseases–trained physician is available, a hospitalist or hospital epidemiologist with interest and less formal training in antimicrobial stewardship may also be a successful leader.[14]

A clinical pharmacist (ideally with infectious diseases training) can perform most of the day-to-day activities of the program. Pharmacists with expertise in appropriate antimicrobial use are well trained to provide approval for restricted antimicrobials and recommendations for antimicrobial prescribing. Other activities, including education, prescription review, and guideline development, can also be completed with clinician support.[17] The pharmacist's role can be tailored based on the structure of the program. In larger hospitals, a team may be comprised of multiple pharmacists with more specific roles.[17]

Clinical microbiologists are key components of any successful ASP, providing timely identification and surveillance of pathogens.[20] Not only does the laboratory help ensure quality standards in specimen collection and work-up of positive cultures, but implementation of new technologies can also aid stewardship efforts by allowing for more rapid streamlining of antibiotic therapy.[17] Technologies such as matrix-assisted laser desorption/ionization time of flight (MALDI-TOF) mass spectrometry decrease the time to identification of organisms. Other rapid molecular diagnostics such as polymerase chain reaction (PCR) of *mec*-A in MRSA isolates can decrease the time to identification of resistance genotypes, facilitating earlier targeted antimicrobial therapy when these genes are confirmed to be present or absent.[21–23] Healthcare facilities that have linked ASPs to MALDI-TOF and other rapid diagnostics have demonstrated improved time to effective antibiotic therapy, improved time to targeted antibiotics, decreased hospital length of stay, and decreased hospital costs.[22,24] In addition, the clinical microbiology lab is essential in the surveillance of resistant organisms and communication of susceptibility trends via tables of antimicrobial susceptibility known as "antibiograms." This information can help to dictate formulary, institutional antimicrobial guidelines, and prescribing decisions.[20,25]

In addition to these core members, direct collaboration with the hospital's infection control program is important.

Inclusion of an infection preventionist and/or healthcare epidemiologist dedicated to infection prevention in the ASP facilitates communication and collaboration to ensure goals of both programs are aligned. For example, the identification of a cluster of particular infections in a medical unit or operating room can help inform both antimicrobial guidelines in that unit and the opportunity to provide prescribing education to the providers. Collaboration with quality and safety teams provides additional support for implementation and identification of specific stewardship interventions and often brings substantial administrative resources and innovation. Inclusion of a data analyst, if available, can help generate reports for the program as discussed later in this chapter in the section "Measuring Outcomes" and can help implement computer-based interventions.[14,16,17]

Although a multidisciplinary team is important to the success of ASPs, programs will differ in their composition depending on the needs and resources of the individual institution. Even if a hospital does not have all the recommended resources for an ASP, the hospital should apply its available resources to perform antimicrobial stewardship. Some of the most innovative interventions have come from ASPs with limited resources. In a recent review article, authors reinforce: "Every hospital should work within its resources to create an effective team given its budget and personnel constraints. The stewardship team does not have to fit a particular mold, and it would be a mistake to delay implementation of a stewardship program because of a lack of availability of one or more of the typical team participants."[14]

3 Implementation and Interventions

Just as there are many potential members of an ASP, "a wide variety of interventions has been shown to be successful in changing antibiotic prescribing to hospital inpatients" and can be tailored to address particular issues.[26] These interventions can target all aspects of the antimicrobial prescription process, beginning very early in the process and continuing throughout (Figure 19.2).

When planning any strategy or intervention, there are some basic issues that should be considered, including available institutional resources, resources required to implement the intervention, and potential return on investment. Strategies and interventions with the strongest potential are those most likely to improve patient care, decrease inappropriate antimicrobial prescribing, reduce medication errors, and cut costs. They ideally should have a high likelihood of success and physician acceptance. In addition, with finite resources, healthcare facilities should focus efforts on the conditions that represent a majority of the antimicrobial prescriptions and, ideally, that represent a majority of the *inappropriate* antimicrobial prescriptions. Identifying units, services, groups of providers, and even individual providers that represent significant proportions of inappropriate antimicrobial use is helpful when identifying targets. The process of identifying candidate interventions and strategies can vary based on available resources, but preferably includes discussion with infectious diseases consultants, audits of specific units or practices, and aggregate data collection and analysis of antimicrobial use and associated costs by service line, unit, or provider. However, the approach can be simplified based on the situation as well as available time and resources. It may simply involve collecting qualitative data from relevant medical personnel and focusing on common, often inappropriately treated infections such as community-acquired pneumonia, urinary tract infections, and skin and soft tissue infections.

Institutional guidelines and formulary restrictions are two early interventions that are essential for a robust ASP. These interventions shape the prescribing of antibiotics by providing an overall framework for antibiotic prescribing activities.

Institutional Guidelines: The creation and dissemination of comprehensive management recommendations for common infection syndromes are critical to the success of ASPs.[18,19] These guidelines should be evidence-based and adapted from professional society guidelines and results from randomized-controlled trials. Adaptation of professional society guidelines should be based on considerations such as antimicrobial susceptibility guidelines, drug cost, and antimicrobial formulary status. Often, these guidelines should be simplified and adapted to the specific healthcare context, while aligning them with stewardship goals and priorities. Not only can institutional guidelines offer antimicrobial recommendations, but they can also guide work-up, diagnostics, and other aspects

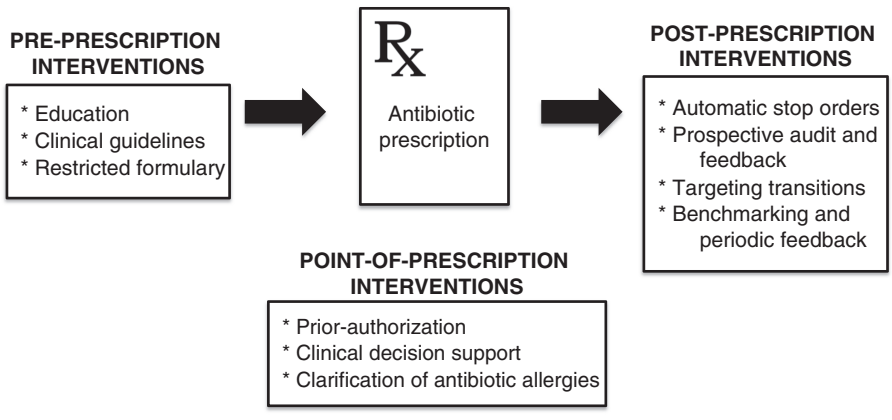

Figure 19.2 Targets of antimicrobial stewardship interventions

of management that inform judicious antibiotic prescribing.[27] In collaboration with the institution's surgeons, standard surgical antimicrobial prophylaxis guidelines should also be created. Such guidelines promote a standardized, algorithmic approach to choice and duration of antimicrobials and can be a strong opportunity for education in addition to unifying an institution's priorities for antimicrobial use. From a practical perspective, surgical prophylaxis also serves as a point-of-care reference for prescribers. Financial incentives related to adherence to national surgical prophylaxis guidelines and to rates of surgical site infections provide motivation for institutions to support development of evidence-based guidelines by ASPs. If a healthcare facility provides care for significant numbers of patients representing special populations, such as recipients of organ transplant and patients with hematologic malignancies, guidelines for prophylaxis and treatment should be developed for these populations as well.

Formulary Restrictions: It is nearly impossible, not to mention costly, to allow for an unrestricted number of different antimicrobials in an institution's formulary. Restricting the formulary to a selected group of antimicrobials is not only important for practical reasons, but also helpful in furthering the goals of antimicrobial stewardship. These goals can be achieved by curating "a formulary limited to nonduplicative antibiotics with demonstrated clinical need."[19] Institution-specific needs should be taken into account when selecting antimicrobials to place on formulary including pharmacy acquisition cost, presence of duplicative agents already on formulary, and local resistance patterns. For example, if an institution has no CRE, the institution may want to avoid adding to formulary expensive antibiotics that are effective against these organisms. Adding such agents in this situation may lead to inappropriate use of these antimicrobials as well as unnecessary pharmacy waste if these agents were to go unused. Formulary decisions are often facilitated by a P&T committee and should be reassessed over time.

Development of both institutional guidelines and formulary restrictions require substantial efforts at the outset, but once implemented provide ongoing support to ASP goals. These interventions require periodic reassessment and updating, but do not necessitate significant ongoing staff support or resources. Devising a calendar to make sure guidelines and restrictions are reassessed and updated on a regular basis can be useful. Although integral to the success of ASPs, institutional guidelines and formulary restrictions provide only a reference framework for antimicrobial prescribing. In order to have a comprehensive and sustained effect on daily antimicrobial prescribing practices, proactive, targeted interventions must be implemented. These fit into three major categories: prior authorization, prospective audit, and prescriber-level interventions.

Prior Authorization or Approval: A core antimicrobial stewardship strategy requires the approval of prespecified agents prior to use by a member of the ASP team such as a pharmacist or physician trained in infectious diseases.[16,28–31] Arguably, prior authorization offers the most immediate, dramatic effect on antimicrobial prescribing compared to other stewardship strategies.[28] However, almost no healthcare facility has the resources to require prior authorization for every antimicrobial agent. Conceptually not unlike the prior-authorization an insurance company might require for the use of a novel or expensive therapy, antibiotics may be expensive, overused, or on shortage. Implementation of this strategy has been shown to be successful in many studies demonstrating improved patient outcomes, reduced cost, and decreased antimicrobial resistance.[7,32] In addition, this approach offers the ability to influence prescribing at the point of prescription, often early in the patient's course of infection; appropriate agents can be suggested prior to the patient receiving less optimal ones as well as recommendations for appropriate initial evaluation and testing.

Although prior authorization is very effective, the process requires full-time staffing by a specialty-trained pharmacist or physician who can grant approval and provide clinical support. Prior authorization does place a barrier for timely antimicrobial prescribing, as antimicrobial administration may be delayed while awaiting approval. This delay may be appropriate for some antimicrobial agents, but not for agents that are commonly used to treat severe conditions such as severe sepsis or septic shock. Also, because approval decisions are based on phone interactions with the prescriber, critical information may be overlooked if not provided by the prescriber.[33] If prior authorization is the only proactive strategy used by the ASP team, it will miss opportunities to streamline therapy and provide feedback after the antimicrobial is approved.

A variation on prior authorization has been described in which providers may use restricted antibiotics initially without approval for a prespecified period of time (e.g., single-dose, 24 hours, 48 hours, 72 hours), after which the prescriber must obtain approval for continued use. This approach mitigates some of the concerns over the potential barriers to prompt antibiotic administration and increases the amount of information such as culture results that may be available at the time of approval request. Automatic stop orders, which are discussed separately in this chapter, can facilitate this process, especially for longer gaps of time. A disadvantage of a gap in approval from initial prescription is that the ASP team is less able to affect empiric antimicrobial prescribing practices. Therefore, consideration toward selection of restricted antimicrobials and the timing of approval should be adjusted based on institutional characteristics and resources. Coupling prior authorization with prospective audit and feedback supplements this strategy by allowing the ASP team to streamline antimicrobial agents and provide feedback as the clinical course and diagnostic work-up unfolds.

Prospective Audit and Feedback, or Post-Prescription Review: In this strategy, individual patients' antibiotic prescriptions are reviewed prospectively in order to optimize use through constructive feedback.[27,34–36] The reviewer, typically the ASP team's clinical pharmacist and/or physician, interacts directly with the prescriber and recommends appropriate changes based on available data.[37] It is often impractical to review every antimicrobial prescription in a healthcare facility.

In most cases, prospective audit and feedback interventions need to be targeted.

Targets for prospective audit and feedback can be antimicrobial-, diagnosis-, or practice-based. There are a number of ways to institute and focus such a strategy. For antimicrobial-based interventions, an ASP team may select cases for review based on the antimicrobial agent. Selecting cases for audit based on a drug is relatively straightforward: a list can be created via an electronic health record (EHR) or pharmacy dispensing. Antimicrobials can be selected for review using a variety of criteria including cost of acquisition, spectrum of activity, and frequency of inappropriate use. Diagnosis-based targets can be selected based on frequency of inappropriate antimicrobial prescribing and presence of guidelines or regulations. Some commonly targeted diagnoses with high rates of inappropriate prescribing include viral respiratory infections, urinary tract infections, asymptomatic bacteriuria, skin and soft tissue infections, and pneumonia.[38–43] Diagnosis-based targets can be more challenging to identify because diagnoses or antimicrobial indications can be difficult to identify prospectively, although the EHR can be leveraged to retrieve some data. Practice-based targets can also be identified for prospective audit and feedback. Streamlining redundant therapy such as double anaerobic coverage and de-escalating therapy to an agent with a narrower spectrum of activity based on susceptibility results are potential targets.[18] In some cases, prescribers may neglect to treat a pathogen or may choose an inappropriately narrow-spectrum antimicrobial agent for a given clinical situation. These *bug-drug mismatches* can also be targeted, especially for severe infections such as bacteremia and central nervous system infections. The ASP team may also suggest dosing and route of administration changes, including transitioning from parental to oral therapy whenever possible.[32,44] Arguably, the most important practice-based focuses for prospective audit and feedback are limiting unnecessary antimicrobial use for durations of therapy longer than necessary, for noninfectious or nonbacterial syndromes, and for treatment of organisms representing colonization or contamination and not true infections, as these practices represent most inappropriate antimicrobial prescribing.[45] In addition, limiting these practices decreases *overall* antimicrobial use instead of shifting it to use of other agents.[42,43] Some diagnoses in particular have recommended durations that have been more clearly defined, as detailed in Table 19.1.[38]

Table 19.1 Diagnoses with clearly defined durations of therapy

Condition	Duration
Pneumonia	
Community-acquired (CAP)	
– Normal lungs, typical organisms	3–5 days
– Underlying lung disease, mild-moderate immunosuppression, slow response to therapy	7 days
– Special pathogens*, severe pneumonia, severe immunosuppression	14 days
Healthcare- or ventilator-associated (HCAP or VAP)	
– Typical organisms	7–8 days
– Special pathogens* or very severe pneumonia	14 days
Urinary Tract Infection (Uncomplicated Cystitis)	
– TMP-SMX or Fluoroquinolone	3 days
– Nitrofurantoin	5 days
– Other	7 days
Pyelonephritis (Complicated Cystitis)	
– Fluoroquinolone	5–7 days
– Other	14 days
Skin and Soft Tissue Infections	7–10 days
Bloodstream Infection (no endocarditis)	
– Staphylococcus aureus	4–6 days
– Others	7–14 days

* Special pathogens: S. aureus, P. aeruginosa (and other non-lactose fermenters), Legionella

With regard to providing feedback, receiving a call or electronic message from a clinical pharmacist to prescribers is most common; however, another proposed approach is to conduct ward rounds for select patients.[13] In this strategy, the clinical pharmacist can identify particular cases to discuss with the infectious diseases physician, and the two round on the associated the hospital ward, review patient charts, and talk with the clinical care teams.[13] Although more time-intensive, this approach offers the opportunity to provide education and real-time feedback and should be considered.

Acquiring baseline data on antimicrobial prescribing practices can help focus attention on particular problem units or conditions within one's institution.[14,16,17] For example, a particular patient care unit may be identified as disproportionately prescribing one antibiotic more frequently than other units, and thereby could be targeted for closer scrutiny. Prospective audit and feedback interventions should be scaled to the resources of the ASP and targeted based on available data. As discussed above, interventions can be scaled by provider, patient care unit, antimicrobial, indication, practice, or various combinations of these criteria.

Additionally, if the program is able to interface with computerized records, data from the EHR, either via periodic review or electronic alert, provide an efficient way to identify potential interventions. Targeted conditions can be identified through the identification of diagnoses or orders in the EHR. For example, if the ASP is targeting treatment of urinary tract infection or asymptomatic bacteriuria, ASP personnel may identify potential interventions based on specific urine culture or urinalysis results or more simply based on the presence of an order for one of these tests. Electronic alerts are particularly helpful if they include laboratory and microbiology results. Some programs have created comprehensive series of alerts based on de-escalation, bug-drug mismatch, unlikely bacterial infection, inappropriate double anaerobic coverage,

intravenous-to-oral transition, and drug dosing.[46] For instance, an electronic alert may identify a case in which a patient is prescribed vancomycin but has cultures with methicillin-susceptible *Staphylococcus aureus* (MSSA), which represents an opportunity for de-escalation. Electronic alerts offer an efficient, potentially high yield approach to identifying cases for further audit and feedback.

Prescriber-Level Interventions: ASPs can also design interventions that disseminate guidelines and aid individual providers in making appropriate antimicrobial prescribing decisions. Some provider-level interventions that have demonstrated effectiveness for antimicrobial stewardship include education, clinical decision support, rounding tools, and periodic feedback and academic detailing.

Focusing efforts on education of providers at all levels of training in order to bridge gaps in knowledge, provide a systematic approach to antimicrobial prescribing, and highlight adverse outcomes associated with antimicrobial prescribing can be effective.[47–50] At baseline, many trainees demonstrate low scores on their knowledge base of antimicrobials and report low confidence in antimicrobial prescribing.[51–53] The most effective formats to educate students, graduate trainees, and practitioners have not clearly been defined and may differ depending on level of experience and area of practice. Lectures, small group sessions, and distribution of informative material such as pocket guides may be effective.[48] Some programs, such as Wake Forest University and the University of Pennsylvania, have developed stewardship curricula for trainees that are available for download.[54,55] While baseline education is important for trainees and practitioners, its effect often wanes without reinforcement.[56] Reinforcing education with clinical decision support, rounding tools, or benchmarking and academic detailing is likely necessary to achieve a sustained effect.

Clinical decision support via paper or computer-generated prompts at the time of antimicrobial prescription may provide more sustainable effects.[48] Computer-assisted decision support systems (CDSS) can help integrate institutional guidelines with active decision making and "can improve antimicrobial decisions through the incorporation of data on patient-specific microbiology cultures and susceptibilities, hepatic and renal function, drug-drug interactions, allergies, and cost."[18] In one such example, researchers created a five-step algorithm in which the user was first asked to assess whether infection was likely, next identify the infection suspected, create a differential diagnosis, and identify any diagnostic procedures that would aid in definitive diagnosis. After all of these steps, suggestions were offered for empiric antimicrobial therapy.[57] Many EHRs have flexibility in designing institution-specific CDSS. For healthcare facilities without EHRs, paper antimicrobial order forms may achieve a similar effect.[58] Antimicrobial order forms can incorporate formalized criteria for use of antimicrobial agents, suggest dosing regimens, and define the duration of therapy. Clinical decision support approaches can provide provider-level, scenario-specific guidance and have been shown to have durable effect.[57,59]

Table 19.2 Core principles of antimicrobial prescribing

- Prescribe correct antimicrobial promptly at correct dose for correct duration based on guidelines
- Order appropriate microbiologic and other diagnostic testing
- Document the dose, duration, and indication for all antimicrobial prescriptions
- Conduct periodic review, or antimicrobial "time out" (e.g. at or after 48 hours) of antimicrobial prescription(s) and diagnostic studies with goal of streamlining to most appropriate choice and transitioning any intravenous antimicrobials to oral as able
- Remain aware of local antimicrobial resistance patterns

Adapted from Centers for Disease Control and Prevention. CDC. Core Elements of Hospital Antibiotic Stewardship Programs. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. available at http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html.

Some institutions have implemented rounding tools in the form of flow sheets or checklists that reinforce judicious antimicrobial prescribing practices.[36,50] The CDC has defined several core principles of antimicrobial prescribing that all clinicians should follow, listed in Table 19.2. Checklists or flow sheets offer one way to implement these principles systematically. These tools have been shown to be effective, although time intensive and potentially less practical in certain patient care settings. Potentially, a more efficient way to implement these practices into prescriber workflow is by embedding them into the EHR. Some healthcare facilities have created EHR systems that provide "closed loop" antimicrobial prescribing. In one Chinese healthcare system, an EHR was created that includes CDSS for physician order entry as well as several key principles of antimicrobial prescribing.[60] For example, the EHR requires that prescribers have culture and sensitivity data to support use of restricted antimicrobial agents within 48 hours of the prescription order, essentially hard-coding an antibiotic "time-out." Many other EHR software vendors have also taken steps to encode core antimicrobial prescribing practices within electronic order entry.[61]

Another strategy to continually reinforce education and judicious antimicrobial prescribing is through periodic feedback and academic detailing. Using these strategies, individualized feedback on aggregate prescribing practices is provided to clinicians. Through periodic feedback, prescribers are given reports of antimicrobial use. In these reports, individual antimicrobial use can also be benchmarked against that of peers. This approach can supplement other stewardship strategies and can offer an alternative solution for healthcare facilities or healthcare settings in which daily audit and feedback is impractical. One such setting is the ambulatory setting where real-time feedback is impractical. Periodic feedback has been demonstrated to be an effective intervention in decreasing inappropriate antimicrobial prescribing in the ambulatory setting.[62] Through academic detailing, the ASP team can identify individual providers who could benefit from one-on-one discussion about overall prescribing practices. This practice is labor-intensive and not

practical to perform for every prescriber, but could be "an effective way to approach extreme prescribing outliers."[48]

Antimicrobial Cycling: The practice of antimicrobial cycling typically involves the scheduled removal and substitution of different broad-spectrum antimicrobials as recommended empiric agents of choice. Antimicrobials commonly cycled include beta-lactam/beta-lactamase inhibitor combinations, fluoroquinolones, carbapenems, and cephalosporins. *Cycles* typically rotate every several months. Pilot studies initially demonstrated reduced emergence of antimicrobial resistance compared with historical controls.[63,64] However, these studies were confounded by other concurrent interventions. Antimicrobial cycling may transiently decrease selection pressure and reduce resistance; however, there are insufficient data to routinely recommend this practice due to lack of well-designed studies demonstrating improvement in outcomes.[14,18] Antimicrobial cycling may also be impractical in certain institutions with limited formularies or needs for particular antibiotics or classes.

Clarifying Antibiotic Allergies: The issue of antibiotic allergies is an "often neglected but imperative consideration in antimicrobial stewardship."[13] Patients with reported antimicrobial allergies often receive broader-spectrum therapy, suboptimal therapy, and more toxic therapy when compared to those patients without a reported allergy. Allergy to penicillin is the most commonly reported allergy of any drug, reported in 16.7 percent of patients.[65–68] Penicillin allergy has been associated with increased antimicrobial resistance, cost, length of hospital stay, and mortality.[65,66] It is estimated that of patients reporting penicillin allergy, only 10 to 15 percent actually have a positive skin-test to penicillin.[66] Furthermore, up to 68 percent of allergies in medical records lack documentation of the nature and severity of the reaction, and 22 percent have major discrepancies from the verbal history given by the patient.[65,69,70] Once present in the medical record, documentation of an allergy changes antimicrobial prescribing decisions in approximately one-third of cases. Clarification of antimicrobial allergies by history coupled with penicillin skin testing is an important strategy for a comprehensive stewardship program. Performing a careful history with or without penicillin skin testing can clarify many antimicrobial allergies (see Figure 19.3 for additional details). Studies have suggested that using penicillin skin testing to clarify allergies and facilitate antibiotic selection is both safe and cost-effective in a variety of situations including the emergency department, preoperative, inpatient, and intensive care unit.[13,66,71–76] Skin testing could be considered as an adjunctive approach to stewardship. Any skin testing program should be developed in collaboration with experts in allergy and immunology. Because skin testing cannot be performed on every patient with a penicillin allergy, the ASP should define specific infectious conditions or patient populations that may garner the most significant benefit.

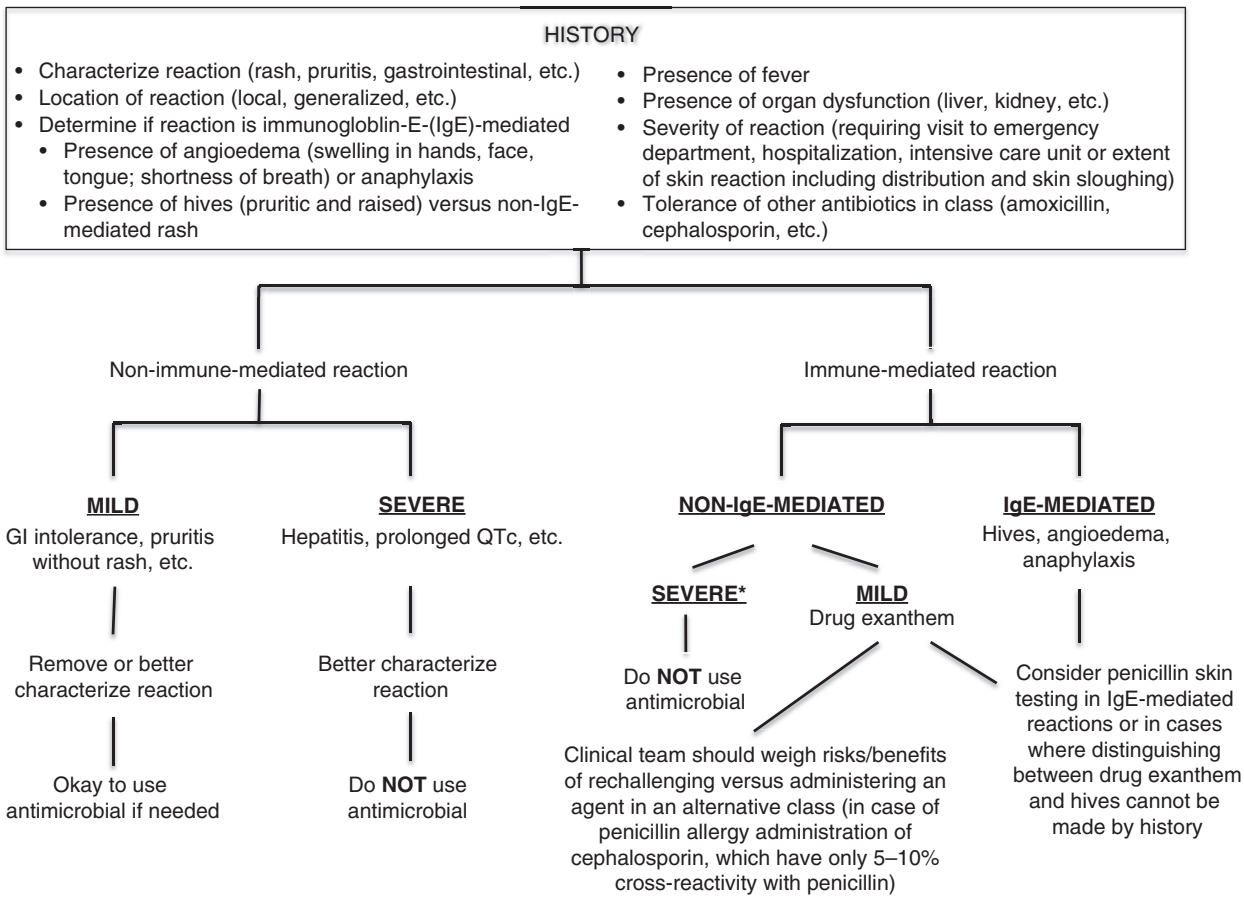

Figure 19.3 Clarifying antimicrobial allergies

For those institutions in which skin testing is not a practical stewardship intervention, clarification of antimicrobial allergies by history alone may be an effective alternative, especially in cases where mild, nonimmunologic side effects such as gastrointestinal symptoms are recorded as allergies.

Targeting Transitions of Care: In addition to monitoring initiation and continuation of antibiotic therapy as previously described, targeting optimization at discharge or other transitions of care can supplement antimicrobial stewardship efforts. For example, detailed medication reconciliation efforts, especially at discharge from hospital, can ensure appropriate duration of therapy.[13] In addition, some centers have instituted mandatory infectious disease consultation for all patients with plans to be discharged on parenteral antimicrobial therapy in order to optimize antibiotic choice, dose, and duration. Early reports of experiences in these centers have shown decreases in overall use and cost without increases in complications or cure rate.[77–79] Although this approach may not be feasible for all institutions, other strategies for monitoring antibiotic use at transitions of care should be considered to augment ongoing efforts.

Using Technology Creatively: Over the past decade, the types and availability of technology have increased dramatically. Smartphones, tablets, and other portable electronic devices are now ubiquitous and offer a unique opportunity for ongoing education, prescribing advice, and communication between the ASP team and prescribers. A variety of software, applications, websites, and even entire reference books can be downloaded to these devices and literally kept in one's pocket, making their use during real-time patient care convenient.[80]

4 Measuring Outcomes

"It is widely believed that you cannot manage what you cannot measure. It is also true that you cannot measure what you cannot define."[81] As discussed previously, the goal of creating and maintaining an ASP is to decrease antibiotic use, cost, and resistance while improving patient outcomes. In a joint policy statement, infectious diseases professional societies state that at the minimum, programs should have "processes to measure and monitor antimicrobial use at the institutional level for internal benchmarking [and] periodic distribution of a facility-specific antibiogram indicating the rates of relevant antibiotic susceptibilities to key pathogens."[19] There are several reasons to measure outcomes of an ASP, including identifying areas for intervention, assessing response to interventions, providing feedback to prescribers, justifying stewardship resources to administration, and reporting to national agencies.

It is through ongoing monitoring and measurement that the program can identify areas of intervention, determine how successful interventions have been, and target future efforts. Measuring outcomes helps to justify ongoing support for programs from hospital administration. In addition, the implementation of quality measures in hospitals is rapidly becoming a mandated activity for reimbursement: "Antimicrobial stewardship programs can be pivotal in the rollout, implementation, and maintenance of government-sponsored mandatory and voluntary quality improvement programs, as well as locally motivated, hospital-specific initiatives" and in the monitoring of these programs.[25]

In measuring the effects of ASPs, it is important to define two distinct types of measures: process and outcome.[82] *Process measures* assess the performance of stewardship activities. Examples of process measures include rates of interventions made by the ASP team, rates of acceptance of ASP interventions, rates of adherence to guidelines, and rates of antimicrobial use. However, these measures are only proxies of the goals of ASPs of decreasing antimicrobial resistance and other collateral consequences of antimicrobial use. *Outcome measures* examine the actual effects of interventions, including reduction or prevention in antimicrobial resistance and clinical outcome measures such as mortality, clinical cure rates, readmission rates, and rates of *Clostridium difficile*.[18] For example, if a stewardship intervention were aimed at decreasing broad-spectrum antimicrobial use in order to decrease rates of multidrug-resistant pathogens, rates of broad-spectrum antimicrobial use would be considered a process measure and rates of multidrug-resistant pathogens the outcome measure. Both types of metrics offer important information, and both should be measured to ensure that the goals of interventions are achieved and that clinical objectives are met.[83]

***Process Measures*:** An essential process measure to guide ASP interventions is antimicrobial use, which can be assessed in a variety of ways. A simple way of measuring antimicrobial use is through pharmacy purchasing information or total antibiotic consumption; however, neither of these measures truly captures antibiotic use.[84] Instead, "aggregate antimicrobial use is usually expressed as a rate at which the use metric (numerator) is normalized for hospital census (denominator)."[83] The three most common numerator metrics are: daily defined dose (DDD), days of therapy (DOT), and length of therapy (LOT). DDD is the total amount of an antimicrobial used by pharmacy divided by a typical daily dose for an adult that has been defined by the World Health Organization (WHO).[85] Of the three numerator metrics, it is the easiest to calculate because it requires having only aggregate pharmacy antimicrobial use data. However, DDD does not capture antimicrobial use at the prescription level and can be discordant with prescription-level antimicrobial use, making inference of prescribing practices challenging.[86] Because WHO standards use adult dosing, it also is not appropriate for pediatric populations.

DOT and LOT assess individual prescription-level data. One DOT represents the administration of a single antimicrobial agent on a given day. If three antibiotics were given on a particular day, there would be three DOT despite the fact that they were given on only one day. With LOT, each day counts as one day regardless of the number of antibiotics given on that day (Figure 19.4). Both DOT and LOT require patient-level data and are more time-intensive to calculate; however, they offer a more accurate picture of antibiotic use than purchasing data and DDD. Once calculated, DOT and/or LOT should be divided by some measure of healthcare facility occupancy in order to arrive at a standardized rate. This denominator could be patient-

Patient 1 day:	1	2	3	4	5		
Antimicrobials:							
vancomycin	X	X	X	X	X		
levofloxacin	X	X	X	X	X		
metronidazole	X	X	X	X	X		
days of therapy (DOT):	3	3	3	3	3	=	15 DOT
length of therapy (LOT):	1	1	1	1	1	=	5 LOT

Patient 2 day:	1	2	3	4	5		
Antimicrobials:							
vancomycin	X	X	X				
nafcillin			X	X	X		
days of therapy (DOT)	1	1	2	1	1	=	6 DOT
length of therapy (LOT)	1	1	1	1	1	=	5 LOT

Figure 19.4 Example calculations: days of therapy (DOT) and length of therapy (LOT). An "X" denotes receipt of antibiotic on given day

days (PD), days present, or hospital admissions. Facility occupancy metrics are fairly readily assessed because they are often calculated for other reasons by facility administration. PD is the product of the number of patients admitted and the mean length of stay. Days present is the total number of days that any patient received care in a specific patient care unit.[87] If a patient was transferred from one unit to another on a given day, it would count as a day present for each location. If days present were calculated for an entire healthcare facility, it would equal PD. Rates of antimicrobial use can be calculated for the healthcare facility or specific units.

Other aggregate metrics that may help evaluate antimicrobial use are DOT/LOT and DOT/unique patients. Dividing DOT by LOT provides an estimate of the mean number of antimicrobials a patient receives per day. If DOT for a given antimicrobial agent is divided by the total number of unique patients or medical record numbers, it provides a crude estimate of average duration. Stewardship interventions may be different if use of a given agent is high because of long durations of treatment versus frequent use of agents for 48 hours of empiric therapy. If the former is true, the ASP may focus on prospective audit and feedback, specifically on the inappropriately long durations of treatment. If the latter is true, the ASP may focus on provider education and interventions at the point of prescription. If antimicrobial use for a particular agent, for a given condition, or within a specific unit is high, more detailed investigation may be warranted. This investigation usually takes the form of a drug use evaluation (DUE).[83] DUE is a method of evaluating the appropriate use of drugs, in this case antimicrobial agents, that aim to identify areas of improvement. Depending on the number of antimicrobial prescriptions, an ASP may choose to review a random or convenient sample of all prescriptions. This review confirms the rate of inappropriate use as well as identifing targets for future intervention.

Other process measures such as rate of stewardship interventions and rate of acceptance of stewardship interventions can be utilized to refine and improve the process of ASP interventions. Because antibiotic use as well as other process metrics represent only surrogate metrics, "reduction in use in itself does not equal desirable outcome . . . Moreover, reduction in use may not result in the inferred benefit."[88]

Outcome Measures: In order to determine the direct benefits of ASP interventions, outcome metrics must be assessed. These measures may include cost savings, length of stay, all-cause mortality, infection-related mortality, clinical cure, adverse events, antimicrobial resistance, and *Clostridium difficile* infections. These outcomes can be calculated for the entire healthcare facility or for specific patient populations in order to evaluate the impact of a specific intervention. What is measured can be adjusted based on interventions and ASP targets; for example, in one study, the researchers augmented existing stewardship guidelines with regard to broad spectrum agents and followed rates of *Clostridium difficile* infection.[89] Antibiotic resistance patterns require measurement of longer periods of time to be helpful as an outcome metric. Interpreted together with antibiotic-use data, they can show the effects of changing antimicrobial prescribing patterns. The clinical microbiology lab is instrumental in helping display this information in antibiograms.[20]

Ultimately, the success of the program depends on monitoring and measurement. Future interventions must be informed by the results of current ones. Although many types of data are described here, it is important to determine what data are available at one's institution and how to use them most effectively to further the goals of the program.

5 Non-Traditional settings

Most of the data published on antimicrobial stewardship are derived from acute care hospitals.[19] However, the number and type of facilities at which patients obtain healthcare are rapidly expanding, and in effect, increasing the diversity of settings in which antimicrobials are prescribed. Examples of these settings

include ambulatory practices, dialysis units, ambulatory surgery centers, long-term acute care hospitals (LTACH), and long-term care facilities (LTCF). "Inasmuch as these settings account for a significant portion of the antimicrobial use in the United States and there is ample evidence that antimicrobial resistance is emerging as a problem in the community, effective and efficient antimicrobial stewardship initiatives must be developed for these settings."[19] Professional society guidelines recommend specialized personnel for antimicrobial stewardship, many of which these healthcare facilities lack. However, lacking every recommended component of an ASP should not preclude performing antimicrobial stewardship. In addition, traditional stewardship interventions may not be appropriate for nontraditional settings. These healthcare facilities should start interventions on a more focused or smaller scale, targeting a select group of antimicrobials, conditions, or practices and taking advantage of currently available resources.

Ambulatory practices are unique opportunities for antimicrobial stewardship. They account for a majority of all antimicrobials administered to patients, and overuse of antimicrobials is pervasive with viral infections representing a majority of encountered conditions. About 80 percent of adults are prescribed an antibiotic for rhinosinusitis. Similarly, antibiotics are prescribed in 21 percent of acute pediatric ambulatory visits, more than 70 percent of which are for upper respiratory tract infections.[90–93] In addition, core antimicrobial stewardship interventions such as prior authorization and prospective audit and feedback are not feasible in this setting. Periodic feedback to prescribers appears to be an effective intervention in this setting in several studies.[62,94–97] Other feasible strategies include prescriber education and CDSS.[62,98–102]

LTCFs are another opportunity for stewardship given that residents are "vulnerable, elderly, and crowded ... and in frequent contact with acute care hospitals," and antibiotics are among the most common medications prescribed.[103] In addition, inappropriate antimicrobial use has been estimated to be as high as 72 percent.[104] There are over 15,000 LTCFs in the United States with 1.7 million licensed beds.[105] Experts have suggested the implementation of antimicrobial stewardship teams in these settings if feasible, or at a minimum, regular reviews of antimicrobial use.[103] However, LTCFs have unique challenges, as prescribers are infrequently located on site and must make decisions based on remote data and reports from nursing home staff. Urinary tract infections (UTIs) are the most common infections reported in LTCFs, but high rates of asymptomatic bacteriuria and atypical manifestations of UTI make the appropriate diagnosis of infection in the elderly population challenging.[106] The focus and organization of ASPs may be significantly different from acute care hospitals because there are few physicians and pharmacists in LTCFs, so stewardship may benefit from engaging clinical nurses or by performing stewardship using remote consultants. LTCFs that have focused on high-impact conditions such as UTI and asymptomatic bacteriuria have demonstrated benefit.[107]

LTACHs also have very unique challenges. Due to their mission as specialty acute care hospitals, they admit complicated patients with complex needs including mechanical ventilation and intravenous antimicrobials. These healthcare facilities deal with many infections seen in acute care hospitals but usually without many of the central resources of a typical ASP. Because these patients often have had extended stays in healthcare facilities, are critically ill, and have received prior antimicrobials, they have high rates of healthcare-associated infections and multidrug-resistant organisms.[108] Some LTACHs have demonstrated decreased antimicrobial use and inappropriate test utilization using periodic feedback to prescribers.[109,110]

6 Behavior Change and Antimicrobial Stewardship

The immediate goal of antimicrobial stewardship is to change poor prescribing behavior and to reinforce good prescribing behavior through a variety of interventions including education, prior approval, and audit and feedback. In order to do so, ASPs need to understand not only the problems with antimicrobial prescribing in their institutions, but also the socio-behavioral context in which they occur. Antimicrobial prescribing is a complex, multifaceted process that depends on the system in which the prescriber operates as well as the prescriber's education, experience, and priorities. Many factors motivate prescribing behavior, including knowledge of antimicrobials and their side effects, guidelines, personal experience, level of training, patient preferences, administrative pressures, and medical hierarchy.[47,111,112] Understanding the facilitators and barriers to appropriate antimicrobial prescribing is important to design effective interventions as well as to shape prescribing behavior.[113] Understanding which prescribers make antimicrobial decisions and why these decisions are made can optimize the success of stewardship interventions by selecting the most effective approach and engaging the most appropriate stakeholders. Ultimately, antimicrobial prescribing is a highly socio-behavioral process.

Two of the most powerful motivators of antimicrobial prescribing experience are personal experience and medical hierarchy.[47,111,112] Many providers are aware that often more influential than formal education is what providers learn through the daily practice of medicine and from their mentors and colleagues, the so-called hidden curriculum. This phenomenon can be amplified by the deference prescribers demonstrate to each other: junior physicians defer to more senior colleagues, and clinicians are often unwilling to alter prescribing decisions made by their colleagues, behaviors collectively referred to as *prescribing etiquette*.[111] If antimicrobial prescribing culture is favorable, ASPs and their interventions are more likely to be successful; however, if it is not, the hidden curriculum and prescribing etiquette can undermine formal education, guidelines, and potential success of stewardship interventions. These attitudes and practices can vary by specialty so understanding the intricacies of socio-behavioral interactions in each relevant specialty group is crucial.[114] Effective methods to improve prescribing culture have not been well delineated.

However, since prescribing culture is complex, effective candidate approaches are likely multifaceted and may include prescriber education, guideline dissemination, and audit and feedback. In addition, engaging key, influential stakeholders of antimicrobial prescribing in the ASP and relevant committees is important. Academic detailing may also be a strategy to address influential providers that adversely affect prescribing behaviors of others.

ASPs should also not underestimate the influence of patients on antimicrobial prescribing. Prescribers cite similar sentiments to the power of these therapeutic relationships: "My relationship with my patient is much stronger than my relationship with the hospital inpatient population and the microbial ether that we live in. You've got an emotional bond with that patient."[115] Even if prescribers understand the adverse consequences of antimicrobial prescribing, they may place more weight on patient-specific factors, which can be appropriate or inappropriate based on the situation. Many prescribers perceive that the risk of undertreating a patient is higher than the risk associated with receiving potentially inappropriate antimicrobial therapy.[116,117] Patients themselves may also request or demand antimicrobials, a concern most prevalent in ambulatory settings. Physicians mention patient demand as a key motivator for inappropriate antimicrobial prescribing.[112,118] International efforts are underway to educate patients on appropriate indications for antimicrobials as well as consequences of inappropriate prescribing.[119] Patients have in recent years become more cautious regarding antimicrobials.[120] In fact, prescribers often overestimate patient demand for antimicrobials and so may be prescribing based on perceived rather than actual patient expectations.[121,122] Therefore, ASPs may need to educate prescribers on how to discuss antimicrobial use with their patients as well as to better align perceived versus actual patient expectations.

Because clinicians prescribe in complicated environments of shifting priorities, expectations, and demands, they may view stewardship interventions with skepticism depending on how they are presented.[118] The way that interventions and feedback are presented may determine the way that they are perceived by prescribers as well as their likelihood of being followed. Better understanding the barriers and facilitators of antimicrobial prescribing and how these factors influence whether a clinician is likely to follow guidelines or recommendations may be useful in designing more successful approaches to stewardship as well as to addressing prescriber and patient concerns. Otherwise, if the ASP ignores prescriber input and concerns, prescribers will find ways to circumvent these interventions.[33,118]

7 Conclusions

The inappropriate use of antimicrobials is common worldwide, and ASPs are essential for decreasing unnecessary antimicrobial use and the emergence of antimicrobial resistance. However, they are also crucial for the safety of patients in order to decrease adverse events and to improve clinical outcomes. Antimicrobial stewardship should not be viewed as the restriction of antimicrobials, but as a comprehensive set of interventions to promote appropriate use of antimicrobial agents and to optimize the delivery of these agents to patients that need them. Selection and organization of the appropriate team members is important for the success of an ASP. Strategically positioning the ASP in the realm of patient safety and with support from administration will also help to assure that the program has resources allocated to ensure success. Selecting and designing appropriate strategies and interventions should be made based on a careful analysis of antimicrobial use patterns and prescriber behavior. When these interventions are created and implemented, they should engage key stakeholders in the prescribing process. ASPs should also measure both process and outcome measures to track the success of interventions and to guide future objectives.

References

1. Bentley R. The development of penicillin: genesis of a famous antibiotic. *Perspect Biol Med*. 2005;**48:**444–452.
2. CDC VitalSigns – Making Health Care Safer. *Centers for Disease Control and Prevention*. Available at: www.cdc.gov/vitalsigns/antibiotic-prescribing-practices/index.html.
3. Gaieski DF, Mikkelsen ME, Band RA, et al. Impact of time to antibiotics on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department. *Crit Care Med.* 2010;**38**:1045–1053.
4. Wong-Beringer A, Joo J, Tse E, Beringer P. Vancomycin-associated nephrotoxicity: a critical appraisal of risk with high-dose therapy. *Int J Antimicrob Agents* (2011);**37:**95–101.
5. Natsumoto B, Yokota K, Omata F, Furukawa K. Risk factors for linezolid-associated thrombocytopenia in adult patients. *Infection.* 2014;**42:**1007–1012.
6. Leffler DA, Lamont JT. Clostridium difficile Infection. *N Engl J Med*. 2015;**372**:1539–1548
7. Fishman N. Antimicrobial stewardship. *Am. J Infect. Control.* 2006;**34**:S55–63; discussion S64–73.
8. Bartlett JG. A call to arms: the imperative for antimicrobial stewardship. *Clin Infect Dis.* 2011;**53,** Suppl 1:S4–S7.
9. Executive Order: Combating Antibiotic-Resistant Bacteria. Available at: www.whitehouse.gov/the-press-office/2014/09/18/executive-order-combating-antibiotic-resistant-bacteria.
10. Slayton RB, Toth D, Lee BY, et al. Vital signs: estimated effects of a coordinated approach for action to reduce antibiotic-resistant infections in health care facilities – United States. *MMWR Morb. Mortal. Wkly. Rep*. 2015;**64**:826–831.
11. Boucher HW, Talbot GH, Bradley JS, et al. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. *Clin. Infect. Dis.* 2009; **48**:1–12
12. Dryden MS, Cooke J, Davey P. Antibiotic stewardship: more education and regulation not more availability? *J Antimicrob Chemother*. 2009;**64**:885–888.
13. Hamilton KW, Fishman NO. Antimicrobial stewardship interventions: thinking inside and

outside the box. *Infect Dis Clin North Am*. 2014;**28**:301–313.

14. Doron S, Davidson LE. Antimicrobial stewardship. *Mayo Clin Proc*. (2011);**86**:1113–1123.
15. Allerberger F, Gareis R, Jindrák V, Struelens MJ Antibiotic stewardship implementation in the EU: the way forward. *Expert Rev Anti Infect Ther*. 2009;**7**:1175–1183.
16. Drew R H. Antimicrobial stewardship programs: how to start and steer a successful program. *J Manag Care Pharm. MCP*. 2009;**15**:S18–23.
17. Tamma PD, Cosgrove SE. Antimicrobial stewardship. *Infect Dis Clin North Am*. 2011;**25**:245–260.
18. Dellit TH, Owens RC, McGowan JE Jr, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis.* 2007;**44**:159–177.
19. Society for Healthcare Epidemiology of America, Infectious Diseases Society of America & Pediatric Infectious Diseases Society: policy statement on antimicrobial stewardship by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Infectious Diseases Society (PIDS); *Infect Control Hosp Epidemiol*. 2012;**33**:322–327.
20. Avdic E, Carroll KC. The role of the microbiology laboratory in antimicrobial stewardship programs. *Infect Dis Clin North Am*. 2014;**28**:215–235.
21. Wieser A, Schneider L, Jung J, Schubert S. MALDI-TOF MS in microbiological diagnostics-identification of microorganisms and beyond (mini review); *Appl Microbiol Biotechnol*. 2012;**93**:965–974.
22. Huang AM Newton D, Kunapuli A et al. Impact of rapid organism identification via matrix-assisted laser desorption/ionization time-of-flight combined with antimicrobial stewardship team intervention in adult patients with bacteremia and candidemia. *Clin Infect Dis.* 2013;**57**:1237–1245.
23. Croxatto A, Prod'hom G, Greub G. Applications of MALDI-TOF mass spectrometry in clinical diagnostic microbiology. *FEMS Microbiol Rev.* 2012;**36**:380–407.
24. Perez KK Olsen RJ, Musick WL, et al. Integrating rapid pathogen identification and antimicrobial stewardship significantly decreases hospital costs. *Arch Pathol Lab Med*. 2013;**137**:1247–1254.
25. File TM, Solomkin JS, Cosgrove SE. Strategies for improving antimicrobial use and the role of antimicrobial stewardship programs. *Clin Infect Dis.* 2011;**53**, Suppl 1:S15–22.
26. Davey P, Brown E, Fenelon L, et al. in *Cochrane Database of Systematic Reviews.* Hoboken, NJ: John Wiley & Sons, Ltd, 2013. Available at: http://onlinelibrary.wiley.com/doi/10.1002/14651858.cd003543.pub3/abstrac.t.
27. Cheng VCC, To KK, Li IW, et al. Antimicrobial stewardship program directed at broad-spectrum intravenous antibiotics prescription in a tertiary hospital. *Eur J Clin Microbiol Infect Dis.* 2009;**28**: 1447–1456.
28. Mehta JM, Haynes K, Willeyto EP, et al. Comparison of prior authorization and prospective audit with feedback for antimicrobial stewardship. *Infect Control Hosp Epidemiol*. 2014;**35**:1092–1099.
29. Chan Y-Y Lin TY, Huang CT, et al. Implementation and outcomes of a hospital-wide computerised antimicrobial stewardship programme in a large medical centre in Taiwan. *Int J* 2011;*Antimicrob Agents* **38**:486–492.
30. Connor DM Binkley S, Fishman NO, et al. Impact of automatic orders to discontinue vancomycin therapy on vancomycin use in an antimicrobial stewardship program. *Infect Control Hosp Epidemiol*. 2007;**28**:1408–1410.
31. Hayashi Y, Davis L, Paterson DL. Why can't I prescribe that antibiotic? The role of antimicrobial stewardship programmes in modern medicine. *Intern Med J.* 2009;**39**:636–638.
32. Goff DA Bauer KA, Reed EE, et al. Is the "low-hanging fruit" worth picking for antimicrobial stewardship programs? *Clin Infect Dis.* 2012; **55**:587–592.
33. Linkin D R Fishman NO, Landis JR, et al. Effect of communication errors during calls to an antimicrobial stewardship program. *Infect Control Hosp Epidemiol*. 2007;**28**:1374–1381.
34. Patel S J Saiman L, Duchon JM, et al. Development of an antimicrobial stewardship intervention using a model of actionable feedback. *Interdiscip Perspect Infect Dis*. 2012;**12**;150367
35. Cosgrove SE, Seo SK, Bolon MK, et al. Evaluation of postprescription review and feedback as a method of promoting rational antimicrobial use: a multicenter intervention. *Infect Control Hosp Epidemiol*. 2012;**33**:374–380.
36. Senn L, Burnand B, Francioli P, Zanetti G. Improving appropriateness of antibiotic therapy: randomized trial of an intervention to foster reassessment of prescription after 3 days. *J Antimicrob Chemother*. 2004;**53**:1062–1067.
37. DiazGranados CA. Prospective audit for antimicrobial stewardship in intensive care: impact on resistance and clinical outcomes. *Am J Infect Control.* (2012);**40**:526–529.
38. Hayashi Y Paterson DL. Strategies for reduction in duration of antibiotic use in hospitalized patients. *Clin Infect Dis.* 2011;**52**:1232–1240.
39. Lin K, Fajardo K, U.S. Preventive Services Task Force. Screening for asymptomatic bacteriuria in adults: evidence for the U.S. Preventive Services Task Force reaffirmation recommendation statement. *Ann Intern Med.* (2008);**149**:W20–W24.
40. Jenkins TC, et al. Skin and soft-tissue infections requiring hospitalization at an academic medical center: opportunities for antimicrobial stewardship. *Clin Infect Dis.* 2010;**51**:895–903.
41. Boyce JM, et al. A trial of discontinuation of empiric vancomycin therapy in patients with suspected methicillin-resistant Staphylococcus aureus health care–associated pneumonia. *Antimicrob Agents Chemother*. 2013;**57**:1163–1168.
42. Micek ST, Ward S, Fraser VJ, Kollef MH. A randomized controlled trial of an antibiotic discontinuation policy for clinically suspected ventilator-associated pneumonia. *Chest.* 2004;**125**:1791–1799.
43. Avdic E Cushinotto LA, Hughes AH, et al. Impact of an antimicrobial stewardship intervention on shortening the duration of therapy for community-acquired pneumonia. *Clin Infect Dis.* 2012;**54**:1581–1587.
44. Jones M Huttner B, Madaras-Kelly K, et al. Parenteral to oral conversion of fluoroquinolones: low-hanging fruit for antimicrobial stewardship programs? *Infect Control Hosp Epidemiol*. 2012;**33**:362–367.
45. Hecker MT, Aron DC, Patel NP, Lehmann, MK, Donskey, CJ. Unnecessary use of antimicrobials in hospitalized patients: current patterns of misuse with an emphasis on the antianaerobic spectrum of activity. *Arch Intern Med.* 2003;**163**:972–978.

46. Hamilton K. Use of electronic de-escalation alerts to facilitate prospective audit and feedback for antimicrobial stewardship. In: (Idsa, 2014). Available at: https://idsa.confex.com/idsa/2014/webprogram/paper47325.html.
47. Charani E, Edwards R, Sevdalis N, et al. Behavior change strategies to influence antimicrobial prescribing in acute care: a systematic review. *Clin Infect Dis.* 2011;**53**:651–662.
48. Ohl CA, Luther VP. Health care provider education as a tool to enhance antibiotic stewardship practices. *Infect Dis Clin North Am*. 2014;**28**:177–193.
49. Lesprit P, Duong T, Girou E, Hemery F, Brun-Buisson C. Impact of a computer-generated alert system prompting review of antibiotic use in hospitals. *J Antimicrob Chemother*. 2009;**63**:1058–1063.
50. Hamilton KW Gerber JS, Moehring R, et al. Point-of-prescription interventions to improve antimicrobial stewardship. *Clin Infect Dis.* 2015;**60**:1252–1258.
51. Abbo LM Cosgrove SE, Pottinger PS, et al. Medical students' perceptions and knowledge about antimicrobial stewardship: how are we educating our future prescribers? *Clin Infect Dis*. 2013;**57**:631–638.
52. Davenport LAP, Davey PG, Ker JS, BSAC Undergraduate Education Working Party. An outcome-based approach for teaching prudent antimicrobial prescribing to undergraduate medical students: report of a Working Party of the British Society for Antimicrobial Chemotherapy. *J Antimicrob Chemother*. 2005;**56**:196–203
53. Dyar OJ, Pulcini C, Howard P, Nathwani D. ESGAP (ESCMID Study Group for Antibiotic Policies); European medical students: a first multicentre study of knowledge, attitudes and perceptions of antibiotic prescribing and antibiotic resistance. *J Antimicrob Chemother*. 2014;**69**:842–846.
54. Wake Forest School of Medicine. Antibiotic Stewardship Curriculum. Available at:www.wakehealth.edu/as-curriculum/.
55. Penn Medicine. Antimicrobial Stewardship. Available at: www.uphs.upenn.edu/antibiotics/.
56. Gerber JS Prasad PA, Fiks AG, et al. Durability of benefits of an outpatient antimicrobial stewardship intervention after discontinuation of audit and feedback. *JAMA.* 2014;**312**:2569–2570.
57. Nachtigall I. Tafelski S, Deja M, et al. Long-term effect of computer-assisted decision support for antibiotic treatment in critically ill patients: a prospective "before/after" cohort study. *BMJ Open.* 2014;**4**:e005370.
58. Lesar TS, Briceland LL. Survey of antibiotic control policies in university-affiliated teaching institutions. *Ann Pharmacother*. 1996;**30**:31–34.
59. Buising KL, Thursky KA, Robertson MB, et al. Electronic antibiotic stewardship: reduced consumption of broad-spectrum antibiotics using a computerized antimicrobial approval system in a hospital setting. *J Antimicrob Chemother*. 2008;**62**:608–616.
60. Li J-S, Zhang XG, Wang HQ, et al. The meaningful use of EMR in Chinese hospitals: a case study on curbing antibiotic abuse. 2013; *J Med Syst*. **37**:9937.
61. Kullar R, Goff DA, Schulz LT, Fox BC, Rose WE. The EPIC challenge of optimizing antimicrobial stewardship: the role of electronic medical records and technology. *Clin Infect Dis*. 2013;**57**(7):1005–1013.
62. Gerber JS. Prasad PA, Fisk AG, et al. Effect of an outpatient antimicrobial stewardship intervention on broad-spectrum antibiotic prescribing by primary care pediatricians: a randomized trial. *JAMA.* 2013; **309**:2345–2352.
63. Kollef MH Vlasnik J, Sharpless L, et al. Scheduled change of antibiotic classes: a strategy to decrease the incidence of ventilator-associated pneumonia. *Am J Respir Crit Care Med.* 1997;**156**:1040–1048.
64. Gruson . Hilbert G, Vargas F, et al. Rotation and restricted use of antibiotics in a medical intensive care unit: impact on the incidence of ventilator-associated pneumonia caused by antibiotic-resistant gram-negative bacteria. *Am J Respir Crit Care Med.* 2000;**162**:837–843.
65. Lee CE Zembower TR, Fotis MA, et al. The incidence of antimicrobial allergies in hospitalized patients: implications regarding prescribing patterns and emerging bacterial resistance. *Arch Intern Med.* 2000; **160**:2819–2822.
66. Unger NR, Gauthier TP, Cheung LW. Penicillin skin testing: potential implications for antimicrobial stewardship. *Pharmacotherapy.* 2013;**33**:856–867.
67. Charneski L, Deshpande G, Smith SW. Impact of an antimicrobial allergy label in the medical record on clinical outcomes in hospitalized patients. *Pharmacotherapy.* 2011;**31**:742–747.
68. Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: a cohort study. *J Allergy Clin Immunol.* 2014;**133**:790–796.
69. Weingart S. N. Toth M, Sands DZ, et al. Physicians' decisions to override computerized drug alerts in primary care. *Arch Intern Med.* 2003;**163**:2625–2631.
70. Lutomski DM, Lafollette JA, Biaglow MA, Haglund LA. Antibiotic allergies in the medical record: effect on drug selection and assessment of validity. *Pharmacotherapy.* 2008;**28**:1348–1353.
71. del Real GA Rose ME, Ramirez-Atamaros MT, et al. Penicillin skin testing in patients with a history of beta-lactam allergy. *Ann Allergy Asthma Immunol.* 2007;**98**:355–359.
72. Forrest DM Schellenberg RR, Thien VV, et al. Introduction of a practice guideline for penicillin skin testing improves the appropriateness of antibiotic therapy. *Clin Infect Dis*. 2001;**32**:1685–1690.
73. Arroliga ME Radojicic C, Gordon SM, et al. A prospective observational study of the effect of penicillin skin testing on antibiotic use in the intensive care unit. *Infect Control Hosp Epidemiol*. 2003;**24**:347–350.
74. Raja AS, Lindsell CJ, Bernstein, JA, Codispoti CD, Moellman JJ. The use of penicillin skin testing to assess the prevalence of penicillin allergy in an emergency department setting. *Ann Emerg Med*. 2009;**54**:72–77.
75. Logan HA, Bayliff CD. Analysis of therapeutic options in patients reporting a penicillin or cephalosporin allergy. *Can J Hosp Pharm*. 1997;**50**:201–207.
76. Park M, Markus P, Matesic D, Li JTC. Safety and effectiveness of a preoperative allergy clinic in decreasing vancomycin use in patients with a history of penicillin allergy. *Ann Allergy Asthma Immunol.* 2006;**97**:681–687.
77. Shrestha NK Bhaskaran A, Scalera NM, et al. Antimicrobial stewardship at transition of care from hospital to community. *Infect Control Hosp Epidemiol*. 2012;**33**:401–404.

78. Conant MM, Erdman SM, Osterholzer D. Mandatory infectious diseases approval of outpatient parenteral antimicrobial therapy (OPAT): clinical and economic outcomes of averted cases. *J Antimicrob Chemother.* 2014; **69**(6):1695–1700.
79. Shrestha NK, et al. Contribution of infectious disease consultation toward the care of inpatients being considered for community-based parenteral anti-infective therapy. *J Hosp Med.* 2012;**7**:365–369.
80. Kullar R, Goff DA. Transformation of antimicrobial stewardship programs through technology and informatics. *Infect Dis Clin North Am.* 2014;**28**:291–300.
81. Platt R. Toward better benchmarking. *Infect Control Hosp Epidemiol.* 2005;**26**:433–434.
82. Khadem TM, Dodds Ashley E, Wrobel MJ, Brown J. Antimicrobial stewardship: a matter of process or outcome? *Pharmacotherapy* 2012;**32**:688–706.
83. Ibrahim OM, Polk RE. Antimicrobial use metrics and benchmarking to improve stewardship outcomes: methodology, opportunities, and challenges. *Infect Dis Clin. North Am.* 2014;**28**:195–214.
84. Berrington A. Antimicrobial prescribing in hospitals: be careful what you measure. *J Antimicrob Chemother.* 2010;**65**:163–168.
85. WHO Collaborating Centre for Drug Statistics Methology. 2015. Available at: www.whocc.no/atc_ddd_index/.
86. Polk RE, Fox C, Mahoney A, Letcavage J, MacDougall C. Measurement of adult antibacterial drug use in 130 US hospitals: comparison of defined daily dose and days of therapy. *Clin Infect Dis.* 2007;**44**:664–670.
87. Fridkin SK, Srinivasan A. Implementing a strategy for monitoring inpatient antimicrobial use among hospitals in the United States. *Clin Infect Dis.* 2014;**58**:401–406.
88. McGowan JE. Antimicrobial stewardship–the state of the art in 2011: focus on outcome and methods. *Infect Control Hosp Epidemiol.* 2012;**33**:331–337.
89. Talpaert MJ, Gopal Rao G, Cooper BS, Wade P. Impact of guidelines and enhanced antibiotic stewardship on reducing broad-spectrum antibiotic usage and its effect on incidence of Clostridium difficile infection. *J Antimicrob Chemother.* 2011;**66**:2168–2174.
90. Fairlie T, Shapiro DJ, Hersh AL, Hicks LA. National trends in visit rates and antibiotic prescribing for adults with acute sinusitis. *Arch Intern Med.* 2012;**172**:1513–1514.
91. Smith SS, Kern RC, Chandra RK, Tan BK, Evans CT. Variations in antibiotic prescribing of acute rhinosinusitis in United States ambulatory settings. *Otolaryngol.* 2013;**148**:852–859.
92. Cooper RJ, Hoffman JR, Bartlett JG, et al. Principles of appropriate antibiotic use for acute pharyngitis in adults: background. *Ann Intern Med* 2001;**134**:509–517.
93. Hersh AL, Shapiro DJ, Pavia AT, Shah SS. Antibiotic prescribing in ambulatory pediatrics in the United States. *Pediatrics.* 2011;**128**:1053–1061.
94. Vinnard C Linkin DR, Localio AR, et al. Effectiveness of interventions in reducing antibiotic use for upper respiratory infections in ambulatory care practices. *Popul Health Manag.* 2013;**16**:22–27.
95. Gjelstad S. Høye S, Straand J, et al. Improving antibiotic prescribing in acute respiratory tract infections: cluster randomised trial from Norwegian general practice (prescription peer academic detailing (Rx-PAD) study). *BMJ.* 2013;**347**:f4403.
96. Madridejos-Mora R, Amado-Guirado E, Pérez-Rodríguez MT. Effectiveness of the combination of feedback and educational recommendations for improving drug prescription in general practice. *Med Care.* (2004);**42**:643–648.
97. Butler C. C. Simpson SA, Dunstan F, et al. Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: practice based randomised controlled trial. *BMJ.* 2012;**344**.
98. Finkelstein JA. Huang SS, Kleinman K, et al. Impact of a 16-community trial to promote judicious antibiotic use in Massachusetts. *Pediatrics.* 2008;**121**: e15–e23.
99. Gonzales R Anderer T, McCulloch CE, et al. A cluster randomized trial of decision support strategies for reducing antibiotic use in acute bronchitis. *JAMA Intern Med.* 2013;**173**:267–273.
100. Jenkins TC Irwin A, Coombs L, et al. Effects of clinical pathways for common outpatient infections on antibiotic prescribing. *Am J Med.* 2013;**126**:327–335.
101. McGinn, TG, McCullagh L, Kannry J, et al. Efficacy of an evidence-based clinical decision support in primary care practices: a randomized clinical trial. *JAMA Intern Med.* 2013; **173**:1584–1591.
102. Rattinger GB Mullins CD, Zuckerman IH, et al. A sustainable strategy to prevent misuse of antibiotics for acute respiratory infections. *PLoS ONE.* 2012; **7**:e51147.
103. Daneman N Gruneir A, Newman A, et al. Antibiotic use in long-term care facilities. *J Antimicrob Chemother.* 2011;**66**:2856–2863.
104. Rotjanapan P, Dosa D, Thomas KS. Potentially inappropriate treatment of urinary tract infections in two Rhode Island nursing homes. *Arch Intern Med.* 2011;**171**:438–443.
105. Centers for Disease Control and Prevention. FastStats: Nursing Home Care. Available at: www.cdc.gov/nchs /fastats/nursing-home-care.htm.
106. Rhee SM, Stone ND. Antimicrobial stewardship in long-term care facilities. *Infect Dis Clin North Am.* 2014;**28**:237–246.
107. Loeb M Brazil K, Lohfeld L, et al. Effect of a multifaceted intervention on number of antimicrobial prescriptions for suspected urinary tract infections in residents of nursing homes: cluster randomised controlled trial. *BMJ.* 2005;**331**:669.
108. Trivedi KK, Kuper K. Hospital antimicrobial stewardship in the nonuniversity setting. *Infect Dis Clin North Am.* 2014;**28**:281–289.
109. Rolek K Talati N, Binkley S, et al. Implementation of a provider-based antimicrobial stewardship strategy at a long term acute care hospital (LTACH) and inpatient physical medicine and rehabilitation (PMR) facility. In: (Idsa, 2014). Available at: https://idsa.confex.com/idsa/2014/webprogram/paper47305.html.
110. Pate PG, Storey DF, Baum DL. Implementation of an antimicrobial stewardship program at a 60-bed long-term acute care hospital. *Infect Control Hosp Epidemiol.* 2012;**33**:405–408.
111. Charani E Castro-Sanchez E, Sevdalis N, et al. Understanding the determinants of antimicrobial prescribing within hospitals: the role of "prescribing etiquette." *Clin Infect Dis.* 2013;**57**:188–196.
112. Brookes-Howell L Hood K, Cooper L, et al. Clinical influences on antibiotic prescribing decisions for lower

respiratory tract infection: a nine country qualitative study of variation in care. *BMJ Open.* 2012;**2**:1–8.

113. Charani E, Castro-Sánchez E, Holmes A. The role, of behavior change in antimicrobial stewardship. *Infect Dis Clin North Am*. 2014;**28**:169–175.
114. Cortoos P-J, De Witte K, Peetermans WE, Simoens S, Laekeman G. Opposing expectations and suboptimal use of a local antibiotic hospital guideline: a qualitative study. *J Antimicrob Chemother*. 2008;**62**:189–195.
115. Broom A, Broom J, Kirby E. Cultures of resistance? A Bourdieusian analysis of doctors' antibiotic prescribing. *Soc Sci Med. 1982.* 2014;**110**:81–88.
116. May L Gudger G, Armstrong P, et al. Multisite exploration of clinical decision making for antibiotic use by emergency medicine providers using quantitative and qualitative methods. *Infect Control Hosp Epidemiol*. 2014;**35**:1114–1125.
117. Björkman I, Berg J, Röing M, Erntell M, Lundborg C S. Perceptions among Swedish hospital physicians on prescribing of antibiotics and antibiotic resistance. *Qual Saf Health Care.* 2010;**19**:e8.
118. Szymczak JE, Feemster KA, Zaoutis TE, Gerber JS. Pediatrician perceptions of an outpatient antimicrobial stewardship intervention. *Infect Control Hosp Epidemiol*. 2014;**35**, Suppl 3, S69–S78.
119. Centers for Disease Control and Prevention. Get Smart: Know When Antibiotics Work. *Get Smart: Know When Antibiotics Work*. Available at: www.cdc.gov/getsmart/community/materials-references/index.html.
120. Finkelstein JA, Dutta-Linn M, Meyer R, Goldman R. Childhood infections, antibiotics, and resistance: what are parents saying now? *Clin Pediatr (Phila.).* 2014;**53**:145–150.
121. Mangione-Smith R, McGlynn EA, Elliott MN, Krogstad P, Brook RH. The relationship between perceived parental expectations and pediatrician antimicrobial prescribing behavior. *Pediatrics.* 1999;**103**:711–718.
122. Stivers T, Mangione-Smith R, Elliott MN, McDonald L, Heritage J. Why do physicians think parents expect antibiotics? What parents report vs what physicians believe. *J Fam Pract*. 2003;**52**: 140–148.

Chapter 20

Infection Control in Long-Term Care Facilities

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Background

The number of adults in the United States (US) older than 65 years of age is projected to more than double from 2000 to 2050.[1] Given the rapidly increasing aging population, long-term care facilities (LTCFs) represent an increasingly important setting for healthcare delivery in the US. Currently, there are approximately 15,600 LTCFs in the US, caring for an estimated 1.5 million residents each day.[2] By 2030, an estimated 5.3 million people in the US will require nursing home care.[3]

LTCFs, including nursing homes (NHs) and skilled nursing facilities (SNFs), are facilities that provide a spectrum of institutional healthcare programs and services outside the acute care hospital setting. While general patient characteristics and nursing requirements differ among these LTCF categories, collectively, these healthcare facilities care for a predominantly older, vulnerable population, with up to 75 percent of residents requiring assistance with at least four activities of daily living (ADLs).[1] The majority of NHs in the US provide a combination of long-term nursing care and skilled nursing services.

Infections in LTCF residents are common. An estimated 1.6 million to 3.8 million infections occur each year in LTCFs across the US and result in approximately 388,000 deaths.[4] However, reported incidence rates of infection in LTCFs have significantly varied across studies, ranging from 1.1 to 5.2 infections per 1,000 resident-days.[5–7] These variations in rates are likely due to differences in definitions used for infection, patient populations surveyed, and facility types.

Infections in the LTCF setting result in frequent acute care hospitalizations, and account for 27 percent to 63 percent of all resident transfers to acute care settings.[4,8] The morbidity attributable to infections among LTCF residents is substantial, including resident discomfort, cognitive and functional decline, and extended hospital stays. The cost of infections in LTCFs, including requirement for acute care hospitalization, represents a significant economic burden, ranging from $673 million to $2 billion annually.[9]

Urinary tract, lower respiratory tract, and skin and soft tissue infections are the most common infections in the LTCF setting. Skin and soft tissue infections include cellulitis, soft tissue abscesses, and infected pressure or vascular ulcers. The most frequent lower respiratory tract infection is pneumonia. In contrast, most commonly reported outbreaks of infection include viral gastrointestinal tract and respiratory tract infections such as influenza. Etiologic agents that have been frequently reported as causes of outbreaks in the long-term care setting are listed in Table 20.1.

Table 20.1 Etiologic agents identified as causes of outbreaks of infection in long-term care facilities

Respiratory tract infections
Rhinovirus
Influenza virus
Respiratory syncytial virus
Metapneumovirus
Streptococcus pneumoniae
Haemophilus influenzae
Mycobacterium tuberculosis
Legionella species
Gastrointestinal tract infections
Norovirus
Rotavirus
Clostridium difficile
Escherichia coli O157:H7
Shigella species
Staphylococcus aureus
Skin and soft tissue infections
Group A *Streptococcus*
Scabies

Risk Factors for Infections in LTCF Residents

Residents of LTCFs are at an increased risk for infection for a number of reasons. LTCFs provide care for a predominantly frail and older adult population. The Centers for Medicare and Medicaid Services (CMS) reported that in 2011, 85 percent of residents in CMS-certified NHs/SNFs were 65 years or older, and 42.9 percent were 85 years or older.[10] Aging-associated immune senescence, high rates of chronic comorbidities, and functional impairment all contribute to the frequency and severity of infections in older adults.[4] Chronic comorbidities that may predispose toward infection and are prevalent

among geriatric adults include diabetes mellitus, chronic obstructive lung disease, pressure ulcers, and conditions that diminish cardiac reserve (e.g., congestive heart failure). In its most recent survey, CMS also reported that 62 percent of LTCF residents have at least 4–5 ADL impairments, and 26 percent and 38 percent have moderate and severe cognitive impairment, respectively.

LTCF residents face additional risks for infection due to the use of indwelling devices. Despite this, there are limited data on the prevalence of specific indwelling device use in the LTCF setting. Studies report rates of urinary catheter use from 5–14 percent in NH residents.[10,11] Urinary catheters have been demonstrated to increase the risk of urinary tract infections, bacteremia, and septicemia in this population.[4] Similarly, approximately 3–7 percent of residents will have a feeding tube in place, although this can approach 40 percent in cognitively impaired residents.[12,13] The presence of a feeding tube increases the risk of aspiration pneumonia, as well as mortality due to pneumonia, compared to oral feeding.[14,15] Finally, while few studies report central venous catheter use in LTCFs, a survey performed in Veterans Affairs facilities reported a 5 percent rate.[11] Presence of central venous catheters contributes to device-associated bloodstream infections, and their use is likely increasing as the medical complexity and acuity of the LTCF population grows.

Finally, residents of LTCFs are at increased risk of infection due to close proximity and interactions with other residents and healthcare personnel. The LTCF creates a residential environment to promote socialization through group activities, including dining, recreational activities, and physical and occupational therapy. However, the unrestricted movement of infected or colonized residents within this closed institutional environment favors constant exposure to organisms from frequent contact with other residents, personnel, and the environment. The risk factors present in this population along with the environment of care increase the opportunities for transmission of organisms and subsequent infection.

Special Considerations for Infection Prevention and Control Programs in LTCFs

Understanding the key differences between acute care hospitals (ACHs) and LTCFs is fundamental to establishing an infection prevention and control program in the long-term care setting. While ACHs focus on identifying and stabilizing immediate, urgent changes in a person's health status, the goal in LTCFs is to increase or maintain the overall quality of life for an individual by fostering independence, socialization, and psychological well-being. Unlike acute care, LTCFs primarily operate as residential settings for individuals requiring long-term care support that can range from minimal support of ADLs to requirements for full-time skilled nursing care. Despite the increasing medical complexity of their population, NHs in particular continue to function in this residential care model. In addition, compared to ACHs, LTCFs are significantly lacking in resources despite the increasing care requirements of their residents.

Resources

LTCFs are required to maintain infection prevention and control (IPC) programs to comply with the federal regulations for governing licensing and certification.[16] However, compared to ACHs, LTCFs may lack adequately trained and dedicated infection control personnel and resources. These IPC personnel may be employed only part-time and may have multiple responsibilities in the facility that limit the time available specifically for infection control duties. For example, a study performed in Maryland showed that there was a fourfold lower number of infection preventionists (IPs) in NHs compared to ACHs of similar bed size.[17] In addition, some LTCFs may have limited access to personnel with the necessary expertise in infectious diseases, microbiology, and healthcare epidemiology required for maintaining an ICP program. Along these lines, a survey of 488 LTCFs in Canada reported that only one-fifth had physicians providing services to the IPC program. LTCFs often lack resources needed to implement higher levels of transmission-based precautions (e.g., negative pressure rooms for airborne precautions). Other barriers to implementing an effective IPC program in LTCFs include a frequent lack of on-site radiographic, laboratory, and microbiology services. Lastly, despite significant differences between LTCFs and ACHs, the most studies evaluating effective infection control interventions have been performed in the acute care setting and may not be applicable to the long-term care setting.

Resident-Related Considerations

Diagnosing infection in the older, LTCF population can be difficult. Residents often have multiple comorbidities and functional disabilities that complicate differentiating bacterial infection requiring antibiotics from a viral infection or noninfectious etiology. In addition, residents may be cognitively impaired, therefore making it difficult to ascertain symptoms. Typical symptoms and signs of infection are frequently absent or blunted in LTCF residents.[18] For example, older adults may not present with a fever or localizing symptoms despite having serious bacterial infections.[19,20]

Although the diagnosis of infection in the long-term care setting is challenging, the following guidelines have been formulated to aid in evaluating infections in older LTCF residents.

The McGeer criteria[21] are the most widely used and recognized surveillance definitions of infection in LTCF residents. These definitions are intended to serve as a national standard for infection surveillance in LTCFs and were updated in 2012 following evidence-based structured review and consensus opinion of experts in the field. Significant updates included changes to definitions for respiratory tract and urinary tract infections, as well as addition of *Clostridium difficile* and norovirus gastroenteritis.

A clinical practice guideline for evaluation of fever and infection in older LTCF residents is available from the Infectious Diseases Society of America (IDSA).[19] This

guideline provides recommendations for initial evaluation of suspected infections, including laboratory testing, in the context of resources that are available in LTCFs. This guideline also includes a general outline of how a suspected outbreak should be investigated in this setting.

The Loeb minimum criteria were developed through consensus conference of individuals with expertise in this area[22] and are proposed minimum criteria for initiation of antibiotics in the long-term care setting. These criteria were developed to target inappropriate use of antibiotics in LTCFs, recognizing that infection diagnosis can be difficult in the long-term care patient population.

Frequent Care Transitions

In comparison to patients in ACHs, LTCF residents are likely to experience more frequent transitions of care. These transitions result in movement from the LTCF to various locations, including ACHs, rehabilitation facilities, home care, ambulatory surgical centers, dialysis units, and outpatient clinics. Information communicated during these transitions can be incomplete or absent, especially pertaining to infection control care issues such as history of colonization and/or infection with an antibiotic-resistant organism, recent antibiotic use, and requirements for specific transmission-based precautions. These frequent transfers, as well as the fragmented communication, can increase the risk for transmission of antibiotic-resistant organisms. Established protocols for communication with transferring facilities are critical. The Centers for Disease Control and Prevention (CDC) has examples of interfacility transfer forms that can be adapted by an LTCF to facilitate communication of infection control information.[23]

Developing an Infection Prevention and Control and Prevention (IPC) Program

The core elements of an IPC are summarized in Table 20.2.

Table 20.2 LTCF IPC program elements

- Infection control oversight committee
  - -Designated responsibility and/or authority
  - -Report to the medical director, facility administrator, and other relevant LTCF personnel
- Surveillance
  - -Utilize appropriate surveillance definitions
  - -Systematic collection of surveillance data
  - -Analysis and reporting of surveillance data
- Standard & transmission-based precautions
  - -Hand hygiene
  - -Define and implement personal protective equipment for antibiotic-resistant organisms and transmissible diseases
  - -Injection safety
  - -Bloodborne pathogens issues
  - -Preparedness planning
- Resident health
  - -Surveillance for vaccination
  - -Surveillance for exposures
  - -Safety and adverse events
- Employee health
  - -Surveillance for vaccination
  - -Surveillance for exposures
- Antibiotic stewardship
- Facility management
  - -Environmental cleaning
  - -Linens management
  - -Food handling
  - -Waste management

Regulations

The IPC program must be in compliance with all national, state, and local regulations. These generally include activities related to handling of waste and disinfection practices, as well as specific disease reporting requirements and resident care policies such as vaccination.

However, IPs in LTCFs typically have less specialized training in infection prevention and control compared to their counterparts in ACHs. In a large national study of NHs, nearly 37 percent of NHs received an IPC-related deficiency citation.[24] NHs in states with mandatory or voluntary healthcare-associated infection reporting and those that provided some type of IPC training were less likely to receive an IPC-related citation.

Recently proposed CMS "Reform Requirements for Long-Term Care Facilities" take into account the increasing advances in resident care, quality practices, and medical complexity of the population. A key proposed requirement is the maintenance of a comprehensive, data-driven quality assurance and performance improvement (QAPI) program, which would include the IPC program. Proposed infection prevention and control regulation includes the requirement that facilities have a designated IPC officer for whom overseeing the IPC program is his or her major responsibility and who serves as a member of the facility's quality assessment and assurance committee. Notably, the IPC officer should have training specifically in infection prevention and control, in addition to his or her background clinical training (e.g., nursing). Along these lines, and given the increasing focus on care across the healthcare continuum, it is anticipated that changes to current IPC programs in LTCFs will be adopted in the near future.

Administration

IPs play a critical role in preventing and managing healthcare-associated infections in LTCFs. The size of the institution and complexity of the resident population should be used to determine the number of individuals required to support the IPC program. Specific time commitment to, and duties required for, the IPC program should be clearly outlined for each individual. Personnel with responsibility for infection control must have training on the basic principles of infection prevention practices and program management. Opportunities for continued education in data collection and methodology, including knowledge of updated surveillance metrics, are critical. In addition, if not available on site, outside individuals with expertise in areas such as infection control and outbreak investigation should be identified and consulted as needed.

An effective reporting and communications structure should also be established. This includes close collaboration by the IPC program staff with the medical director, facility administrator, nursing supervisor, and environmental services personnel of the LTCF. In addition, continuing review and oversight is typically provided within the context of the QAPI committee. These elements are all critical for establishment of an IPC program that allows for prompt and effective management of infections in individual residents, as well as for outbreak control.

Surveillance for Infections

Systematic surveillance for infections is a critical element of an IPC program. Infection control personnel should be well-versed in application of standard surveillance definitions for identification of infections, including the McGeer criteria and the CDC's National Healthcare Safety Network (NHSN) surveillance definitions for healthcare-associated infections. NHSN provides LTCFs with a customized system to track infections in a streamlined and systematic manner.[25] Case-finding methods include laboratory or floor-generated reports, nursing assessments, or clinical surveillance software. Infection control personnel should analyze data and report results to the administration, infection control committee, and other appropriate oversight committees on a regular basis. The data should be reviewed frequently to identify trends, including those that may signal a potential outbreak or increasing rates of antibiotic-resistant organisms. Most important, the data should be used in planning infection control interventions, including educational efforts and policy updates as needed.

Policies and Practices

Policies addressing facility-specific infection control issues should be established. Relevant guidelines are available through multiple authoritative bodies, including the CDC's website on infection control for LTCFs.[23] This resource includes guidance documents on infection control issues such as control of antibiotic-resistant organisms, influenza, emergency preparedness, and general guidelines on infection prevention in the long-term care setting. In addition, the Society for Healthcare Epidemiology of America (SHEA) and the Association for Professionals in Infection Control and Epidemiology (APIC) have drafted guidelines for infection prevention and control specifically in LTCFs.[9] In September 2015, the CDC also released guidance on antibiotic stewardship in NHs, including the recommendation that all NHs take steps to improve antibiotic prescribing practices and reduce inappropriate use.[26] This resource outlines the core elements of antibiotic stewardship, adapted for the long-term care setting.

Some specific issues to be addressed include the following:

- Standard and transmission-based precautions
- Hand hygiene
- Safe injection practices and point of care testing
- Management of patients with infections, including those requiring implementation of transmission-based precautions
- Preadmission and periodic screening of residents for transmissible infections (e.g., tuberculosis)
- Screening of employees for infections (e.g., tuberculosis) and work restriction policies for those with potentially transmissible infections
- Vaccination policies for residents and healthcare personnel
- Use of indwelling devices, such as urinary catheters and central venous catheters
- Outbreak identification, investigation, and control
- Antibiotic stewardship efforts, including standardized antibiotic prescribing algorithms and implementation of educational efforts for prescribers and staff
- Environmental cleaning, including disinfection of hard surfaces and common areas, management of linens, and waste disposal

Common Infections in LTCFs

Urinary Tract Infections

Urinary tract infections (UTIs) are the most commonly reported infection in the LTCF setting and can lead to significant morbidity and mortality. A study of older adult LTCF residents admitted with nursing home–acquired bacteremia demonstrated that a urinary source was identified in approximately 55 percent of cases.[27] UTIs are one of the leading causes for requirement for transfer to an acute care hospital, accounting for nearly 30 percent of hospital readmissions from LTCFs within 30 days.[28]

Genitourinary tract dysfunction in older individuals can increase the risk for UTIs, including urinary retention leading to incomplete emptying of the bladder. In postmenopausal women, declining estrogen can contribute to vaginal prolapse and urinary incontinence, increasing the risk for ascending migration of bacteria. The presence of a urinary catheter also significantly predisposes individuals toward the development of a UTI. Approximately 5 percent of LTCF residents with an indwelling urinary catheter will develop bacteriuria for each day that the catheter remains in place.[29]

Nearly 100 percent of residents with long-term indwelling urinary catheters will have bacterial colonization of the urinary tract without local signs or symptoms of infection, or asymptomatic bacteriuria (ASB). Difficulty in differentiation of ASB from symptomatic UTI represents a major challenge in the LTCF setting. The symptoms and signs necessary to meet minimum criteria to support antibiotic initiation for UTIs are frequently absent in NH residents with advanced dementia.[18] Inappropriate treatment of ASB leads to substantial overuse of antibiotics in this population and increases the risk for antibiotic-associated adverse events and development of antibiotic resistance. Therefore, interventions and educational initiatives to promote appropriate diagnosis and treatment of symptomatic UTI should be a high-level priority in the LTCF setting.

Infection prevention guidelines to prevent catheter-associated UTIs include limiting the use of urinary catheters, minimizing the duration of urinary catheter use, strict hand hygiene before and after catheter manipulation, aseptic technique for urinary catheter insertion, keeping the urinary drainage bag below the level of the bladder, and maintaining a closed drainage system.[30,31]

Respiratory Tract Infections

Pneumonia: Pneumonia and lower respiratory tract infections are a leading cause of mortality and acute care hospital transfers in LTCF residents. One study determined that 33 of 1,000 LTCF residents per year required acute care hospitalization for treatment of pneumonia versus 1.14 of 1,000 elderly community-dwelling adults.[32] Several factors, including impaired gag reflex, dysphagia, and poor oral hygiene in LTCF residents, particularly in individuals with neurologic conditions (e.g., stroke), increase the risk for development of pneumonia. In addition, the presence of a feeding tube compared to oral feeding increases the risk for aspiration pneumonia.[33]

Notably, older and frail or cognitively impaired residents may have an atypical presentation of pneumonia, making appropriate diagnosis a challenge in the LTCF setting. For example, fever or cough may be minimal or absent in older adults with pneumonia compared to nonspecific signs and symptoms such as general malaise, weakness, and altered mental status.[34] Limited access to radiologic testing (e.g., chest radiograph) in some LTCFs may further complicate the diagnosis of pneumonia in this population.

Influenza: LTCF residents are also at risk for influenza infection due to a number of reasons, including frequent contact with healthcare personnel and visitors, as well as close proximity to other residents. Increased age among residents drives risk for serious complications from influenza, with approximately 70 percent of influenza-attributable deaths occurring in individuals 75 years and older.[35] The high prevalence of comorbid respiratory and cardiovascular conditions in the LTCF population also increases morbidity and mortality from influenza. Therefore, vaccination of residents and healthcare personnel is a critical component of infection prevention in the long-term care setting. Widespread vaccination has been shown to reduce influenza incidence and associated mortality in LTCF residents.[36,37] However, since the 2011–2012 influenza season, healthcare personnel in LTCF settings have continued to have the lowest reported influenza vaccination rates among all healthcare personnel surveyed.[38] For these reasons, increasing influenza vaccination coverage for both residents and healthcare personnel in LTCFs are priority areas outlined in the National Action Plan to Prevent Health Care–Associated Infections developed by the US Department of Health and Human Services.[39]

Tuberculosis: The most important strategy for preventing the spread of tuberculosis is early identification and treatment of infected individuals.[40] LTCFs need to monitor for skin-test conversion among residents and staff, identify and promptly evaluate residents with pulmonary symptoms or radiologic findings consistent with tuberculosis, isolate patients with possible or proven pulmonary tuberculosis, and trace exposed patients and staff. Because many LTCFs are not equipped to manage residents with tuberculosis, individuals with suspected active tuberculosis will require transfer to an alternative setting such as an acute care hospital for appropriate isolation and evaluation. Diagnosing and treating tuberculosis also presents significant challenges in the long-term care setting. For example, there is limited data on the performance of interferon gamma release assays (IGRAs) compared to tuberculin skin testing (TST) in older adults.[41] Furthermore, obtaining chest radiographs and/or sputum samples may be difficult in LTCFs.

Gastrointestinal Tract Infections

Gastroenteritis: Viral gastroenteritis is the leading causes of diarrheal outbreaks in LTCFs. While gastroenteritis is usually mild and self-limited in healthy individuals, older adults experience more morbidity and mortality due in part to increased vulnerability to dehydration.[42] Norovirus is one of the main causes of gastroenteritis outbreaks worldwide, with LTCFs disproportionately affected. Of norovirus outbreaks reported to the CDC from 2009 to 2012, 69 percent occurred as a result of person-to-person transmission; of these, 80 percent occurred in LTCFs.[43] Outbreaks in LTCF settings can be prolonged, sometimes lasting months.[44] Norovirus is extremely infectious, with transmission primarily occurring person to person via the fecal-oral route, although airborne and fomite transmission may occur during outbreaks. Therefore, strict infection control measures are required during an outbreak, including isolation precautions, furloughing ill healthcare personnel, epidemiologic investigation and case-finding, hand hygiene, appropriate environmental disinfection, and staff education to limit transmission.

Clostridium difficile: *Clostridium difficile* infection (CDI) is also of increasing concern in the LTCF setting. Several surveillance studies evaluating the burden of CDI in US acute care hospitals demonstrate rapidly increasing rates of disease, likely due in part to a hypervirulent strain known as B1/NAP1/027.[45–48] For example, an analysis of National Inpatient Survey (NIS) data found that the rate of CDI more than doubled between 1999 and 2005,[45] from 37.6 episodes per 10,000 discharges to 76.9 episodes

per 10,000 discharges. The burden of CDI is also significantly increasing in LTCFs.[49–53] A recent analysis of acute care hospital discharges in the US determined that the number of patients transferred to an LTCF with a discharge diagnosis of CDI doubled between 2000 and 2003.[48] A national surveillance study on the burden of CDI in 2011 demonstrated that NH-onset CDI accounted for 104,400 cases.[54]

C. difficile poses a substantial infection control challenge in LTCFs due to its persistence in the environment as spores and potential for widespread contamination and transmission. This problem is compounded by increased socialization and interaction with other residents and healthcare workers typical of an LTCF. In addition, CDI-associated hospitalizations and mortality disproportionately affect individuals 65 years and older.[45–48] Appropriate hand hygiene with soap and water, early detection and containment of CDI through implementation of gown and glove use during resident care, staff education, environmental disinfection, and careful antibiotic use are critical components of CDI prevention efforts.

Skin and Soft-Tissue Infections

Pressure Ulcers: Skin changes associated with aging include epidermal thinning, decreased elasticity and vascularity, decline in subcutaneous fat, and poor wound healing. These changes predispose toward skin tears, pressure ulcer formation, and subsequent bacterial infection. Cellulitis and infected pressure ulcers are two of the most common types of skin and soft-tissue infections in the LTCF population.[19] Approximately 5.4 percent of residents in CMS-certified NHs/SNFs had a pressure ulcer that was stage II or higher.[10] Urinary or fecal incontinence, which was present in 35 percent of surveyed residents, increases the risk for subsequent infection of a pressure ulcer.[10] However, diagnosing infection of a pressure ulcer poses a significant challenge given chronic colonization of the ulcer with bacteria, including skin flora. Collection of wound cultures without clinical suspicion of infection, along with suboptimal collection techniques, contributes to unnecessary prescription of antibiotics for pressure ulcers. Education about antibiotic prescribing among residents with skin breakdown and pressure ulcers must emphasize that antibiotic therapy is not appropriate for positive surface swab cultures without signs or symptoms of infection.

Scabies: Scabies is a common skin infestation seen in the LTCF population.[55] Confirming the diagnosis of scabies is usually necessary, as it has significant infection control implications to LTCF staff and residents and can result in large, difficult to control outbreaks when initial cases are not recognized. The most common method for diagnosis is via skin scraping underneath the fingernails or at the terminal end of a burrow, followed by direct microscopic visualization. A systematic approach to identifying and treating affected residents and staff is critical, including patient isolation, cleaning of fomites, strict hand hygiene and glove use, appropriate handling of contaminated bedding and clothing, and treatment of all healthcare personnel and family members who have been in contact with the patient.[55]

Antibiotic Resistance in LTCFs

Rates of antibiotic use are extensive in LTCFs, with 60–70 percent of residents receiving at least one antibiotic prescription over the course of a year, most commonly for urinary tract infections, pneumonia, and skin and soft-tissue infections.[56–58] Even more concerning is that 25–75 percent of antibiotics prescribed to LTCF residents are inappropriate.[56,59–61] For example, utilizing chart review, investigators at a 160-bed Veterans Affairs skilled nursing facility determined that 42 percent of antibiotic regimens were entirely unnecessary, with the most common reason for inappropriate administration being ASB and treatment of noninfectious or nonbacterial syndromes.[60] A recent study evaluating approximately 67,000 residents from 630 LTCFs in Ontario demonstrated that 78 percent of residents received at least one new antibiotic treatment course and that 45 percent of these exceeded recommended short-course durations (i.e., ≤7 days) for common syndromes.[59] Inappropriate or excessive antibiotic use in this frail and older adult population can result in significant adverse drug events, drug-drug interactions, CDI, and development of antibiotic resistance.

The prevalence of antibiotic-resistant organisms is increasing in LTCFs. Methicillin-resistant *Staphylococcus aureus* (MRSA) has been the most well-characterized with colonization prevalence rates estimated at approximately 10 percent to 60 percent depending on the population studied.[62–65] The colonization prevalence in one study was reported at 75 percent among residents with indwelling devices.[64] The burden of MRSA in LTCFs is highly dependent on local prevalence and importation pressure. Identified risk factors have included transfer from an acute care hospital, pressure ulcers, prior antibiotic therapy, older age, poor functional status, and low nursing-to-bed ratios.[62–65]

Rates of multidrug resistant gram-negative bacilli (MDR-GNB) have also been increasing in the long-term care setting. For example, a study evaluating antibiotic resistance among gram-negative organisms recovered from urine cultures from a network of 63 LTCFs reported a fluoroquinolone resistance rate of 51 percent among *Escherichia coli*.[66] Similarly, a longitudinal study in three LTCFs demonstrated acquisition of new colonization with fluoroquinolone-resistant *E. coli* (FQREC) in nearly 50 percent of residents.[67] A survey of 16 nursing homes in Ireland demonstrated that 40 percent of residents were colonized with MDR-GNB, including FQREC and extended-spectrum beta-lactamase-producing Enterobacteriaceae.[68] Reported risk factors for MDR-GNB in the long-term care setting have included presence of wounds, urinary catheters, urinary incontinence, dementia, and antibiotic use.

Strategies to prevent the acquisition and transmission of antibiotic-resistant organisms in the long-term care setting are critical and include implementation of antibiotic stewardship programs, education of healthcare workers, and strict hand hygiene. Effective and feasible antibiotic stewardship programs may include facility-wide antibiotic utilization review by an infection control or QAPI committee, prospective audit and feedback at the prescribing level, implementation of

standardized antibiotic prescription guidelines, and ongoing education of healthcare workers on appropriate antibiotic use. Key infection prevention interventions for the control of antibiotic-resistant organisms include improving hand hygiene, implementation of contact precautions, and effective environmental cleaning and disinfection.

Long-Term Acute Care Hospitals

Long-term acute care hospitals (LTACHs) are increasingly important sites of clinical care.[69,70] In the past decade, the number of LTACHs has dramatically increased in the US.[71,72] LTACHs are defined by CMS as acute care hospitals with a mean length of stay of ≥25 days that provide care for medically complex patients with acute medical needs including mechanical ventilation, wound care, and intravenous antibiotics.[71] In addition, LTACHs are characterized by high rates of device utilization with studies reporting rates of up to ~75 percent for central venous catheter use.[73] The LTACH setting is also associated with high rates of administration of empiric antibiotics.[74] In a study of 45 LTACHs from 2002 to 2003,[74] carbapenem and vancomycin use were both higher than the fiftieth percentile intensive care unit (ICU) use reported by the National Nosocomial Infections Surveillance (NNIS) System. In the same study, fluoroquinolone use was comparable to the ninetieth percentile of ICU utilization.[74] LTACHs have been described as the "perfect storm"[74] for antibiotic-resistant organisms due to a patient population characterized by multiple comorbidities, prolonged length of stay, significant rates of antimicrobial and device use, and high rates of colonization with multidrug-resistant organisms.[73,75] However, there are significantly limited data on effective infection prevention strategies in the LTACH setting. Given all of the above, ongoing efforts are needed to define best practices for infection control in this increasingly important setting.

Conclusion

LTCFs provide a spectrum of healthcare services for a predominantly elderly population. Residents of LTCFs are at increased risk for infections for several reasons, including the presence of multiple chronic comorbidities, immune senescence associated with aging, and increased opportunities for person-to-person transmission of pathogens given the residential environment with promotion of socialization. Rates of antibiotic-resistant organisms are also increasing in long-term care settings. Development of an infection prevention and control program needs to take into consideration the key differences between LTCFs and acute care hospitals, including the residential setting of the LTCF, as well as more limited resources available for diagnosis and surveillance. Ultimately, given the rapidly growing aging population, as well as the increasing medical complexity of LTCF residents, effective infection prevention interventions targeted toward the long-term care setting are critical.

References

1. Jones AL, Dwyer LL, Bercovitz AR, Strahan GW. The National Nursing Home Survey: 2004 overview. *Vital Health Stat 13*. 2009(167):1–155.
2. American Healthcare Association. Quality report, 2014. Available at: www.ahcancal.org/qualityreport/Documents/AHCA_2014 percent20Quality percent20Report percent20FINAL.pdf. Accessed October 22, 2015.
3. Knickman JR, Snell EK. The 2030 problem: caring for aging baby boomers. *Health Serv Res*. 2002;**37**(4):849–884.
4. Strausbaugh LJ, Joseph CL. The burden of infection in long-term care. *Infect Control Hosp Epidemiol*. 2000;**21**(10):674–679.
5. Stevenson KB, Moore J, Colwell H, Sleeper B. Standardized infection surveillance in long-term care: interfacility comparisons from a regional cohort of facilities. *Infect Control Hosp Epidemiol*. 2005;**26**(3):231–238.
6. Koch AM, Eriksen HM, Elstrom P, Aavitsland P, Harthug S. Severe consequences of healthcare-associated infections among residents of nursing homes: a cohort study. *J Hosp Infect*. 2009;**71**(3):269–274.
7. Pennsylvania Patient Safety Authority. 2013 Annual Report. Available at: http://patientsafetyauthority.org/Documents?annual_report_2013.pdf. Accessed September 9, 2015.
8. Richards C. Infections in residents of long-term care facilities: an agenda for research: report of an expert panel. *J Am Geriatr Soc*. 2002;**50**(3):570–576.
9. Smith PW, Bennett G, Bradley S, et al SHEA/APIC guideline: infection prevention and control in the long-term care facility, July 2008. *Infect Control Hosp Epidemiol*. 2008;**29**(9):785–814.
10. CMS Nursing Home Data Compendium. Available at: www.cms.gov/Medicare/Provider-Enrollment-and-Certification/CertificationandComplianc/downloads/nursinghomedatacompendium_508.pdf. Accessed September 10, 2015.
11. Tsan L, Langberg R, Davis C, et al. Nursing home-associated infections in Department of Veterans Affairs community living centers. *Am J Infect Control*. 2010;**38**(6):461–466.
12. Ahronheim JC, Mulvihill M, Sieger C, Park P, Fries BE. State practice variations in the use of tube feeding for nursing home residents with severe cognitive impairment. *J Am Geriatr Soc*. 2001;**49**(2):148–152.
13. Mitchell SL, Kiely DK, Gillick MR. Nursing home characteristics associated with tube feeding in advanced cognitive impairment. *J Am Geriatr Soc*. 2003;**51**(1):75–79.
14. Finucane TE, Christmas C, Travis K. Tube feeding in patients with advanced dementia: a review of the evidence. *JAMA*. 1999;**282**(14):1365–1370.
15. Cogen R, Weinryb J. Aspiration pneumonia in nursing home patients fed via gastrostomy tubes. *Am J Gastroenterol*. 1989;**84**(12):1509–1512.
16. CMS State Operations manual. Available at: www.cms.gov/Regulations-and-Guidance/Guidance/Transmittals/downloads/r55soma.pdf. Accessed September 10, 2015.
17. Roup BJ, Roche JC, Pass M. Infection control program disparities between acute and long-term care facilities in Maryland. *Am J Infect Control*. 2006;**34**(3):122–127.
18. D'Agata E, Loeb MB, Mitchell SL. Challenges in assessing nursing home residents with advanced dementia for suspected urinary tract infections. *J Am Geriatr Soc*. 2013;**61**(1):62–66.

19. High KP, Bradley SF, Gravenstein S, et al. Clinical practice guideline for the evaluation of fever and infection in older adult residents of long-term care facilities: 2008 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;**48**(2):149–171.
20. Woodford HJ, Graham C, Meda M, Miciuleviciene J. Bacteremic urinary tract infection in hospitalized older patients: Are any currently available diagnostic criteria sensitive enough? *J Am Geriatr Soc*. 2011;**59**(3):567–568.
21. Stone ND, Ashraf MS, Calder J, et al. Surveillance definitions of infections in long-term care facilities: revisiting the McGeer criteria. *Infect Control Hosp Epidemiol*. 2012;**33**(10):965–977.
22. Loeb M, Bentley DW, Bradley S, et al. Development of minimum criteria for the initiation of antibiotics in residents of long-term-care facilities: results of a consensus conference. *Infect Control Hosp Epidemiol*. 2001;**22**(2):120–124.
23. Centers for Disease Control and Prevention (CDC). Nursing homes and assisted living (long-term care facilities [LTCFs]). Available at: www.cdc.gov/longtermcare/prevention/index.html. Accessed September 14, 2015.
24. Cohen CC, Engberg J, Herzig CT, Dick AW, Stone PW. Nursing homes in states with infection control training or infection reporting have reduced infection control deficiency citations. *Infect Control Hosp Epidemiol*. 2015:1–2.
25. Centers for Disease Control and Prevention (CDC). National Healthcare Safety Network (NHSN) tracking infections in long-term care facilities. Availabe at: www.cdc.gov/nhsn/LTC/. Accessed September 1, 2015.
26. Centers for Disease Control and Prevention (CDC). The core elements of antibiotic stewardship for nursing homes. Available at: www.cdc.gov/longtermcare/prevention/antibiotic-stewardship.html. Accessed September 17, 2015.
27. Mylotte JM, Tayara A, Goodnough S. Epidemiology of bloodstream infection in nursing home residents: evaluation in a large cohort from multiple homes. *Clin Infect Dis*. 2002;**35**(12):1484–1490.
28. Ouslander JG, Diaz S, Hain D, Tappen R. Frequency and diagnoses associated with 7- and 30-day readmission of skilled nursing facility patients to a nonteaching community hospital. *J Am Med Dir Assoc*. 2011;**12**(3):195–203.
29. Warren JW, Tenney JH, Hoopes JM, Muncie HL, Anthony WC. A prospective microbiologic study of bacteriuria in patients with chronic indwelling urethral catheters. *J Infect Dis*. 1982;**146**(6):719–723.
30. Nicolle LE, Long-Term-Care-Committee S. Urinary tract infections in long-term-care facilities. *Infect Control Hosp Epidemiol*. 2001;**22**(3):167–175.
31. Gould CV, Umscheid CA, Agarwal RK, Kuntz G, Pegues DA, Healthcare Infection Control Practices Advisory C. Guideline for prevention of catheter-associated urinary tract infections 2009. *Infect Control Hosp Epidemiol*. 2010;**31**(4):319–326.
32. Marrie TJ. Pneumonia in the long-term-care facility. *Infect Control Hosp Epidemiol*. 2002;**23**(3):159–164.
33. Wang L, Lansing B, Symons K, et al. Infection rate and colonization with antibiotic-resistant organisms in skilled nursing facility residents with indwelling devices. *Eur J Clin Microbiol Infect Dis*. 2012;**31**(8):1797–1804.
34. Mehr DR, Binder EF, Kruse RL, Zweig SC, Madsen RW, D'Agostino RB. Clinical findings associated with radiographic pneumonia in nursing home residents. *J Fam Pract*. 2001;**50**(11):931–937.
35. Matias G, Taylor R, Haguinet F, Schuck-Paim C, Lustig R, Shinde V. Estimates of mortality attributable to influenza and RSV in the United States during 1997–2009 by influenza type or subtype, age, cause of death, and risk status. *Influenza Other Respir Viruses*. 2014;**8**(5):507–515.
36. Potter J, Stott DJ, Roberts MA, et al. Influenza vaccination of health care workers in long-term-care hospitals reduces the mortality of elderly patients. *J Infect Dis*. 1997;**175**(1):1–6.
37. Carman WF, Elder AG, Wallace LA, et al. Effects of influenza vaccination of health-care workers on mortality of elderly people in long-term care: a randomised controlled trial. *Lancet*. 2000;**355**(9198):93–97.
38. Black CL YX, Ball SW, Donahue SM, et al. Centers for Disease Control and Prevention (CDC). Influenza vaccination coverage among health care personnel–United States, 2013–14 influenza season. *MMWR Morb Mortal Wkly Rep*. 2014;**63**(37):805–811.
39. National Action Plan to Prevent Health Care-Associated Infections: Road Map to Elimination. April 2013. Available at: http://health.gov/hcq/pdfs/hai-action-plan-ltcf.pdf. Accessed September 8, 2015.
40. Thrupp L, Bradley S, Smith P, et al. Committee SL-T-C. Tuberculosis prevention and control in long-term-care facilities for older adults. *Infect Control Hosp Epidemiol*. 2004;**25**(12):1097–1108.
41. Menzies D, Pai M, Comstock G. Meta-analysis: new tests for the diagnosis of latent tuberculosis infection: areas of uncertainty and recommendations for research. *Ann Intern Med*. 2007;**146**(5):340–354.
42. Frenzen PD. Mortality due to gastroenteritis of unknown etiology in the United States. *J Infect Dis*. 2003;**187**(3):441–452.
43. Hall AJ, Wikswo ME, Pringle K, Gould LH, Parashar UD, Centers for Disease Control and Prevention (CDC). Vital signs: foodborne norovirus outbreaks – United States, 2009–2012. *MMWR Morb Mortal Wkly Rep*. 2014;**63**(22):491–495.
44. Cieslak PR, Lee LE, Papafragkou E, An N, Centers for Disease Control and Prevention (CDC). Recurring norovirus outbreaks in a long-term residential treatment facility–Oregon, 2007. *MMWR Morb Mortal Wkly Rep*. 2009;**58**:694–698.
45. Lucado J, Gould C, Elixhauser A. Clostridium difficile infections (CDI) in hospital stays, 2009: Statistical Brief #124. 2006.
46. Archibald LK, Banerjee SN, Jarvis WR. Secular trends in hospital-acquired Clostridium difficile disease in the United States, 1987–2001. *J Infect Dis*. 2004;**189**(9):1585–1589.
47. Jarvis WR, Schlosser J, Jarvis AA, Chinn RY. National point prevalence of Clostridium difficile in US health care facility inpatients, 2008. *Am J Infect Control*. 2009;**37**(4):263–270.
48. McDonald LC, Owings M, Jernigan DB. Clostridium difficile infection in patients discharged from US short-stay hospitals, 1996–2003. *Emerg Infect Dis*. 2006;**12**(3):409–415.
49. Kim JH, Toy D, Muder RR. Clostridium difficile infection in a long-term care facility: hospital-associated illness compared with long-term care-associated illness. *Infect Control Hosp Epidemiol*. 2011;**32**(7):656–660.
50. Guerrero DM, Nerandzic MM, Jury LA, Chang S, Jump RL, Donskey CJ. Clostridium difficile infection in a Department of Veterans Affairs long-term care facility. *Infect Control Hosp Epidemiol*. 2011;**32**(5):513–515.
51. Mylotte JM, Russell S, Sackett B, Vallone M, Antalek M. Surveillance for

Clostridium difficile infection in nursing homes. *J Am Geriatr Soc*. 2013;**61**(1):122–125.

52. Pawar D, Tsay R, Nelson DS, et al. Burden of Clostridium difficile infection in long-term care facilities in Monroe County, New York. *Infect Control Hosp Epidemiol*. 2012;**33** (11):1107–1112.
53. Mylotte JM. Surveillance for Clostridium difficile-associated diarrhea in long-term care facilities: what you get is not what you see. *Infect Control Hosp Epidemiol*. 2008;**29** (8):760–763.
54. Lessa FC, Mu Y, Bamberg WM, et al. Burden of Clostridium difficile infection in the United States. *N Engl J Med*. 2015;**372**(9):825–834.
55. Tjioe M, Vissers WH. Scabies outbreaks in nursing homes for the elderly: recognition, treatment options and control of reinfestation. *Drugs Aging*. 2008;**25**(4):299–306.
56. Nicolle LE, Bentley DW, Garibaldi R, Neuhaus EG, Smith PW. Antimicrobial use in long-term-care facilities. SHEA Long-Term-Care Committee. *Infect Control Hosp Epidemiol*. 2000;**21** (8):537–545.
57. D'Agata E, Mitchell SL. Patterns of antimicrobial use among nursing home residents with advanced dementia. *Arch Intern Med*. 2008;**168**(4):357–362.
58. van Buul LW, van der Steen JT, Veenhuizen RB et al. Antibiotic use and resistance in long term care facilities. *J Am Med Dir Assoc*. 2013;**13**(6):568 e561-e513.
59. Daneman N, Gruneir A, Bronskill SE, et al. Prolonged antibiotic treatment in long-term care: role of the prescriber. *JAMA Intern Med*. 2013;**173**(8):673–682.
60. Peron EP, Hirsch AA, Jury LA, Jump RL, Donskey CJ. Another setting for stewardship: high rate of unnecessary antimicrobial use in a veterans affairs long-term care facility. *J Am Geriatr Soc*. 2013;**61** (2):289–290.
61. Loeb M, Simor AE, Landry L, et al. Antibiotic use in Ontario facilities that provide chronic care. *J Gen Intern Med*. 2001;**16**(6):376–383.
62. Stone ND, Lewis DR, Johnson TM, 2nd. Southeast Veterans Affairs Long-Term Care Methicillin-Resistant Staphylococcus aureus Cooperative. Methicillin-resistant Staphylococcus aureus (MRSA) nasal carriage in residents of Veterans Affairs long-term care facilities: role of antimicrobial exposure and MRSA acquisition. *Infect Control Hosp Epidemiol*. 2012;**33** (6):551–557.
63. Reynolds C, Quan V, Kim D, et al. Methicillin-resistant Staphylococcus aureus (MRSA) carriage in 10 nursing homes in Orange County, California. *Infect Control Hosp Epidemiol*. 2011;**32** (1):91–93.
64. Mody L, Kauffman CA, Donabedian S, Zervos M, Bradley SF. Epidemiology of Staphylococcus aureus colonization in nursing home residents. *Clin Infect Dis*. 2008;**46**(9):1368–1373.
65. Manzur A, Gudiol F. Methicillin-resistant Staphylococcus aureus in long-term-care facilities. *Clin Microbiol Infect*. 2009;**15** Suppl 7:26–30.
66. Lautenbach E, Marsicano R, Tolomeo P, Heard M, Serrano S, Stieritz DD. Epidemiology of antimicrobial resistance among gram-negative organisms recovered from patients in a multistate network of long-term care facilities. *Infect Control Hosp Epidemiol*. 2009;**30**(8):790–793.
67. Han JH, Maslow J, Han X, e t al. Risk factors for the development of gastrointestinal colonization with fluoroquinolone-resistant Escherichia coli in residents of long-term care facilities. *J Infect Dis*. 2014;**209** (3):420–425.
68. Rooney PJ, O'Leary MC, Loughrey AC, et al. Nursing homes as a reservoir of extended-spectrum beta-lactamase (ESBL)-producing ciprofloxacin-resistant Escherichia coli. *J Antimicrob Chemother*. 2009;**64** (3):635–641.
69. Kemper P, Murtaugh CM. Lifetime use of nursing home care. *N Engl J Med*. 1991;**324**(9):595–600.
70. Murtaugh CM, Kemper P, Spillman BC, Carlson BL. The amount, distribution, and timing of lifetime nursing home use. *Med Care*. 1997;**35** (3):204–218.
71. Munoz-Price LS. Long-term acute care hospitals. *Clin Infect Dis*. 2009;**49** (3):438–443.
72. Kahn JM, Benson NM, Appleby D, Carson SS, Iwashyna TJ. Long-term acute care hospital utilization after critical illness. *JAMA*. 2010;**303** (22):2253–2259.
73. Furuno JP, Hebden JN, Standiford HC, et al. Prevalence of methicillin-resistant Staphylococcus aureus and Acinetobacter baumannii in a long-term acute care facility. *Am J Infect Control*. 2008;**36**(7):468–471.
74. Gould CV, Rothenberg R, Steinberg JP. Antibiotic resistance in long-term acute care hospitals: the perfect storm. *Infect Control Hosp Epidemiol*. 2006;**27** (9):920–925.
75. Endimiani A, Depasquale JM, Forero S, et al. Emergence of blaKPC-containing Klebsiella pneumoniae in a long-term acute care hospital: a new challenge to our healthcare system. *J Antimicrob Chemother*. 2009;**64**(5):1102–1110.

Chapter

21

Infection Prevention in the Outpatient Setting

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Over the last three decades, a major shift in the delivery of healthcare from inpatient to outpatient settings has occurred. Outpatient medical facilities provide a diverse array of health services including primary and specialty care, laboratory and radiology diagnostic testing, infusion services, dialysis, and surgical procedures. Currently, over 1 billion visits to physician offices, hospital ambulatory clinics, and emergency departments occur each year in the United States.[1] Furthermore, the majority of surgical procedures are now performed in outpatient settings,[2,3] with more than 50 million outpatient surgical procedures performed each year.[3]

Infection prevention programs have traditionally focused on reducing transmission of infections to hospitalized patients. However, with the shift in healthcare delivery to ambulatory-based care, it is clear that infection prevention programs must also focus on reducing transmission of infections in outpatient settings. Extending infection control principles from inpatient to outpatient settings has many challenges. First, there are organizational hurdles. Ambulatory care settings have historically lacked the infrastructure and dedicated resources for infection prevention.[4,5] Research on epidemiology and prevention of healthcare-associated infections has focused almost entirely on inpatient populations. Second, outpatient settings differ from inpatient settings in terms of risks for transmission of infections. It is therefore not reasonable or feasible to simply extend infection prevention surveillance, policies, and programs from inpatient to outpatient settings. Finally, outpatient settings are heterogeneous, providing a diverse array of services and care for populations with different inherent risks for healthcare associated infections. For example, an ambulatory surgery center that performs sterilization of surgical equipment will need different education, interventions, and oversight from an infection prevention program than an oncology infusion center that provides care for immunocompromised patients receiving intravenous medications.

This chapter provides an overview of infection prevention in ambulatory care settings. For the purposes of this chapter, we define outpatient or ambulatory care as any medical or surgical service provided to patients who are not admitted to inpatient hospital units. The discussion is divided into three main sections: 1) structural and organizational considerations for outpatient settings, 2) general principles of infection prevention that are universally applicable to all patient care settings, and 3) specific considerations that may be relevant in certain ambulatory settings. Readers are also encouraged to review the Centers for Disease Control and Prevention's (CDC) "Guide to Infection Prevention for Outpatient Settings: Minimum Expectations for Safe Care," which was published in 2014 and includes a checklist of items to address the minimal standards of infection prevention for outpatient facilities.[4] This guidance serves as starting point for infection prevention programs in ambulatory care settings.

Structural and Organizational Considerations for Outpatient Settings

Outpatient care settings have distinct structural and organizational characteristics that make infection prevention practice a challenge.[4]

Outpatient healthcare encounters are typically shorter and more problem-focused as compared to inpatient encounters. This leads to higher turnover and volumes of patients per day per facility and numerous locations within a facility where persons are waiting, visiting, or undergoing evaluation and treatment. These factors produce a larger patient population potentially at risk for healthcare-associated infections. The population served in outpatient settings, however, has fewer comorbid conditions and is generally healthier when compared to the inpatient population, with some distinct exceptions (e.g., dialysis centers or hematology/oncology clinics). Thus, the overall susceptibility to infectious adverse events is considered to be lower than in traditional acute care hospital settings. The large size of the population at risk, the brief encounter with the healthcare setting, and the likely infrequent incidence of healthcare associated infections make routine surveillance for adverse events very challenging to measure. These challenges, plus the lack of resources invested in infection prevention, are the reasons that research on prevention of healthcare associated infections in outpatient populations is limited. Outbreaks make up the majority of reports related to poor infection prevention practice in outpatient settings. The high volume and fast turnaround in outpatient settings may also contribute to staff distraction and forgetfulness to follow standard infection prevention practices.

The administrative organization and oversight of infection control for noncontiguous outpatient centers may be a challenge due to geographic location. Larger healthcare organizations may task a central infection prevention program with meeting regulatory requirements for a large number of outpatient clinics. This oversight would require significant travel for periodic site visits. Further, limited contact with infection prevention experts may reduce the number of educational opportunities for on-site staff members. To overcome this geographic barrier, many programs have adopted an infection

prevention liaison model with centralized policies. For example, a facility may identify an individual staff member responsible for overseeing compliance with facility infection prevention policies, who then acts as an extender for the central program. Designated liaisons usually do not have formal certification in infection control and only partial time dedicated to this task. Some states require the presence of at least one individual with training in infection prevention principles per noncontiguous facility to oversee compliance with a facility infection control policy.[6] For example, in 1992, the state of North Carolina passed a law (10A NCAC41A.0206) requiring all healthcare organizations performing invasive procedures to have a written infection control policy and an on-site designated staff member to direct infection control activities. North Carolina does not recognize on-the-job training as being sufficient for compliance with this law and supported the North Carolina Statewide Program for Infection Control and Epidemiology (NC SPICE) to develop a standardized course to meet state requirements. Designated staff in ambulatory settings are required to take this eight-hour course every five years. This educational program addresses the basic epidemiologic principles of infectious diseases, safe injection practices, standard precautions, and sterilization and disinfection.[7] Thus, for smaller organizations, these designated individuals can complete the state training program, develop a facility-specific infection control policy, and meet the minimal state requirements. For larger organizations, these individuals may receive training from the centralized program and then provide on-site oversight using a shared, centralized infection control policy. Regardless of the organizational structure, increasing regulatory interest in outpatient facilities requires attention to policy development, staff education, and adherence.

Ambulatory care facilities have distinct characteristics of their physical structure that make the practice of standard and transmission-based precautions problematic. For example, waiting areas may house many patients, visitors, and staff members over a short time period with varying degrees of contact between individuals. These areas provide many opportunities for person-to-person transmission of communicable disease. Also, environment-to-person transmission can occur in rooms that must be frequently turned over for the next patient with limited time or effort made to clean between patients. Ambulatory care settings may contract with housekeeping services companies that are accustomed to cleaning business offices and unfamiliar with the precautions and processes required for healthcare facilities. Limitations in space may impair the separation of clean and dirty areas. There may be limited or no space for sterilization or high-level disinfection procedures that require careful attention to process and avoidance of potential contamination events. We highlight further examples of these structural considerations with recommendations for management in the discussions below.

Universal Principles of Infection Prevention

The sections below outline the basic principles of infection prevention that apply to all types of practice settings.

Standard Precautions

Standard Precautions are the minimum infection prevention practices that apply to all patients in all care settings, regardless of any suspected or confirmed infection status of the patient.[8] All healthcare personnel in outpatient settings, including all persons who may have direct or indirect contact with patients or infectious material, must be educated on the components of standard precautions, and education must be updated regularly.

The components of standard precautions are:

1. Hand Hygiene
2. Use of Personal Protective Equipment
3. Safe Injection Practices
4. Safe Handling of Potentially Contaminated Equipment or Surfaces in the Patient Environment
5. Respiratory Hygiene/Cough Etiquette

Each component and its applicability to outpatient settings will be discussed in further detail in the sections that follow.

Hand Hygiene

Hand hygiene is critically important for preventing transmission of infections in all healthcare settings. Recommendations for hand hygiene in inpatient settings are directly applicable to outpatient settings. Specifically, the CDC and World Health Organization (WHO) state that hand hygiene should be performed at all of the following times:[4,9–11]

- Before patient contact, even if gloves will be worn
- Before performing an aseptic task
- After contact with blood, body fluids, or wound dressings
- Before moving from a contaminated body site to a clean body site during patient care
- Before exiting the patient's care area after touching the patient or the patient's environment
- After removing personal protective equipment (PPE)

Alcohol-based hand rub is generally preferred over soap and water. Most healthcare personnel find alcohol-based hand rub more convenient and less irritating, especially with frequent and repeated application. Infection prevention programs must therefore ensure that alcohol-based hand rub stations are conveniently located in examination rooms and that supplies are adequate. Soap and water should be used preferentially when hands are visibly soiled and after caring for patients with known or suspected infectious diarrhea (e.g., *C. difficile*, norovirus).

Reported hand hygiene compliance rates in outpatient settings are typically poor (<50 percent).[11–14] Monitoring hand hygiene rates in outpatient settings is particularly challenging. Audits of hand hygiene compliance with regular feedback to providers and other stakeholders are key components of inpatient hand hygiene improvement programs. However, direct observation of hand hygiene performance is not possible in most outpatient clinics where hand washing sinks and alcohol-based hand rub stations are typically located inside patient care rooms. Thus, obtaining reliable data on hand hygiene compliance in outpatient settings for use in performance

Table 21.1 Indications for personal protective equipment

Personal protective equipment	Indication
Gloves	Potential hand contact with blood, body fluids, mucous membranes, nonintact skin, potentially infectious material
Mask with Face Shield	Potential for exposure to splashes or sprays of blood or other body fluids
Gown	Potential for skin or clothing contact with blood or body fluids

improvement programs is a major challenge for infection prevention programs.

Infection prevention programs may use other methods to promote, monitor, and improve hand hygiene performance in outpatient settings. Some outpatient sites have successfully implemented "patient-as-observer" programs, whereby patients are recruited to observe and report hand hygiene performance by healthcare workers.[15,16] In such programs, data from patient observations are fed back to healthcare personnel and used to drive improvement of hand hygiene performance. Additionally, public campaigns with signage and patient education materials may help to improve healthcare worker accountability.

Use of Personal Protective Equipment (PPE)

Personal protective equipment (PPE) is designed to protect healthcare personnel from exposure to infectious agents. PPE should always be worn when there is risk for potential exposure to blood, body fluids, or infectious agents.[8] The specific PPE worn depends on the nature of patient contact and potential exposure (Table 21.1).

An obvious and frequently encountered barrier to appropriate PPE use is lack of adequate or conveniently located supplies. In a busy clinic environment, healthcare workers may be reluctant to take time to find proper equipment, even when it is indicated. PPE should be located where care is provided to facilitate use. PPE should not be stored centrally or in a locked storage area. In the annual risk assessment, infection prevention programs should assess anticipated need for PPE supplies, ensure supplies are adequately and conveniently located, and verify that healthcare workers are educated on appropriate utilization of PPE.

Injection Safety

Safe injection practices are designed to prevent transmission of infections from patient to patient or patient to provider during administration of parenteral medications.[4,8] Key principles of injection safety include:

- Using aseptic technique when preparing and administering medications
- Cleaning the vial diaphragm with 70 percent alcohol solution before inserting needle into vial, even when the vial is new
- Not administering medications from the same syringe to more than one patient, even if the needle or IV tubing set is changed
- Not reusing a syringe or needle to enter a medication vial or solution
- Not administering medication from a single-dose vial to more than one patient
- Dedicating multidose vials to a single patient whenever possible (see below for further discussion)
- Not using IV administration sets for more than one patient
- Disposing of used syringes and needles at the point of use in an appropriate sharps container

Unfortunately, lapses in safe injection practices continue to occur in outpatient facilities and have resulted in devastating consequences for patients, including transmission of hepatitis B and hepatitis C, and serious infections due to bacteria such as *S. aureus*.[17–24] Each year, state health departments and the CDC investigate numerous outbreaks and infection control breaches in outpatient settings. Reuse of syringes to access medication vials and reuse of single-dose vials for more than one patient are the most commonly identified breaches.[24] In addition to causing direct harm to patients, breaches in safe injection practices can lead to notification and testing of thousands of patients who may have been exposed, as well as loss of licensure, lawsuits, and/or criminal prosecution.

A number of factors make outpatient settings particularly vulnerable to patient harm from lapses in safe injection practices. First, the incredible volume of procedures performed in outpatient settings means that there are many opportunities for breaches to occur. Second, surveillance for procedure-related complications is not consistently performed in outpatient settings. Patients may seek follow-up care elsewhere, and thus recognition of a procedural-related complication may be delayed or missed. Additionally, there may be long latency between inoculation and recognition of infection, which may obscure the recognition of an outbreak. If a procedure-related cluster of infections is detected, healthcare facilities must quickly notify local public health officials, so that steps to mitigate further transmission may be taken while an investigation is ongoing.

Multidose vials may be more convenient and cheaper than single dose vials. However, studies have demonstrated that contamination of multidose vials occurs in clinical practice.[25,26] Although the actual risk of infection associated with multidose vials remains unknown, the potential for infection transmission is present, particularly if multidose vials are not stored or accessed properly. For these reasons, the CDC recommends that multidose vials be dedicated for use in a single patient only. If this is not possible, facilities must restrict storage of multidose vials to a centralized medication storage location.[4]

Outpatient facilities require clean work spaces dedicated for medication preparation. Aseptic technique, including hand

hygiene and PPE use must be followed when preparing medications for administration. Medication preparation should not occur in close proximity to sinks where there is potential for water contamination of sterile injection equipment. Finally, medications and injection equipment must be stored safely and securely. Several large-scale outbreaks of hepatitis C have occurred in hospital settings secondary to healthcare worker tampering with controlled substances.[27] Narcotic diversion by healthcare workers is a real threat to injection safety, and healthcare facilities must have well-established policies and practices to prevent opportunities for drug tampering.

Safe Handling of Potentially Contaminated Equipment or Surfaces in the Patient Care Environment

Several studies have determined that environmental contamination with organisms such as methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant enterococcus (VRE) occurs regularly, and the environment may be an important source of pathogen acquisition by noncolonized patients in inpatient settings.[28–32] The role of the environment in transmission of multidrug-resistant pathogens in outpatient settings has not been well studied. In contrast to inpatients, outpatients generally do not have prolonged contact with their environment. However, more patients per day visit the same outpatient environment, and rapid room turnover between patients makes cleaning of clinic spaces challenging. Ambulatory care facilities should prioritize cleaning and disinfection of high-touch surfaces in the patient care environment between patients.

Contract housekeeping services used in ambulatory care settings may be accustomed to cleaning businesses, not healthcare facilities. Written contract agreements must specify appropriate cleaning practices and housekeeper training requirements such as changing mops or using disposable mops and cleaning cloths, how to clean a room where a patient has been on isolation, and training on standard precautions, use of PPE, and bloodborne pathogens. These needs require specific training and must be addressed when contracted cleaning services are utilized.

Appropriate cleaning, disinfection, and/or sterilization of reusable medical equipment are addressed more specifically below (see "Cleaning and Disinfection of Reusable Medical Equipment" in this chapter).

Respiratory Hygiene/Cough Etiquette

Respiratory hygiene and cough etiquette refer to measures to reduce the transmission of respiratory pathogens to susceptible individuals. Respiratory viruses, including influenza, are primarily transmitted via droplet particles produced when an infected individual coughs or sneezes. Indirect transmission through contact with contaminated environmental surfaces may also occur.[33] Some features of outpatient settings that may facilitate transmission of respiratory infections include:

- Congregation of patients in waiting rooms
- High volume of patients, particularly during epidemic seasons
- Inadequate systems to triage patients and maintain separation of unwell and well patients

The following "respiratory hygiene" measures are easily implemented and may help to reduce transmission of respiratory pathogens in outpatient settings:[8]

- Post visual alerts at the entrance to outpatient facilities instructing persons who are reporting for care to report respiratory symptoms
- Provide tissues and no-touch receptacles for disposal of used tissues
- Provide conveniently located hand washing agents
- Ask persons who are coughing to don surgical masks
- Triage coughing individuals out of the common waiting area as soon as possible
- Educate patients with respiratory symptoms to do the following:
  - Cover the nose and mouth when coughing or sneezing
  - Use tissues to contain respiratory secretions and dispose of them in the nearest waste receptacle after use
  - Perform hand hygiene after contact with respiratory secretions and contaminated objects or materials

Transmission-Based Precautions for the Outpatient Setting

Transmission-based precautions (e.g., Contact Precautions, Droplet Precautions, Airborne Precautions) are used in addition to standard precautions to interrupt transmission of certain pathogens. Healthcare personnel in ambulatory care settings must be educated on transmission-based precautions and provided instruction on clinical syndromes that warrant escalation from standard precautions to transmission-based precautions. We recommend that outpatient facilities employ a syndrome-based approach rather than a pathogen-based approach to identify patients who require transmission-based precautions in addition to standard precautions. Identifying patients with history of colonization with multidrug-resistant organisms including MRSA and VRE is not practical in the outpatient settings, nor are there data to suggest that routine use of contact precautions in such patients is effective at reducing transmission of multidrug resistant pathogens. Therefore, outpatient facilities should primarily emphasize use of standard precautions for all patients in ambulatory settings, with addition of transmission-based precautions in specific clinical scenarios. Examples of clinical syndromes and associated recommendations for transmission-based precautions are shown in Table 21.2. For additional information regarding Transmission-Based Precautions, please see Chapter 7, Isolation.

Screening

Failure to identify patients with highly infectious conditions when they encounter the healthcare system is a serious pitfall

Table 21.2 Syndrome-based approach to transmission-based precautions

Clinical presentation	Disease of concern	Transmission-based precautions	Room cleaning
Cough, sore throat, with or without fever	Influenza, Pertussis	Droplet	Routine
Diarrhea	Norovirus *Clostridium difficile*	If continent of stool: Standard If incontinent of stool: Contact-Enteric	Use EPA-approved bleach product
Draining/weeping wound not contained by dressing	MRSA	Contact	Routine
Fever with headache or stiff neck or lethargy	*Neisseria meningitidis*	Droplet	Routine
Rash with fever	Measles Rubella Varicella	Airborne	Room remains closed for 60 minutes after patient leaves, then cleaned per routine
Cough, recent weight loss, hemoptysis	Tuberculosis	Airborne	Room remains closed for 60 minutes after patient leaves, then cleaned per routine
Signs/symptoms of emerging infectious disease plus travel to affected countries	EVD MERS SARS	Airborne Contact	

that leads to potential transmission of infectious diseases to other patients and healthcare workers. Waiting rooms provide potential opportunities for transmission of infections transmitted via droplet and airborne routes. Previous epidemics including Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and Ebola Virus Disease (EVD) raised awareness of the importance of implementing a screening process for patients entering a healthcare environment.

An assessment of patient and community demographics should be included in the annual infection control risk assessment in order to design the best method for screening and triage. This assessment should determine the common, non-English, languages spoken in the community as well as the presence of international travelers. It may be necessary to provide respiratory hygiene signs and patient education in other languages in addition to English and/or heighten awareness of the risk of exposure to communicable diseases imported by international travelers. Provider education should include specific recognition of communicable diseases in countries frequented by clinic patients.

Operationalizing a standardized screening process in ambulatory settings is challenging. Different ambulatory settings pose different risks for encountering patients with highly transmissible or emerging infections. For example, patients with acute onset of fever and respiratory symptoms are more likely to seek care in emergency departments, urgent care clinics, or primary care offices and less likely to seek care in specialty outpatient clinics or ambulatory surgery centers. Still, all healthcare facilities must be prepared to identify individuals with potential highly transmissible infections. We recommend that ambulatory care facilities implement a screening process to determine the following:

- Fever
- Travel in the last 30 days to an area of epidemiologic concern
- Rash
- Respiratory symptoms including cough, hemoptysis

Screening should ideally take place at the time visits are scheduled for outpatient clinics and at the first point of contact for emergency departments and urgent care clinics. Patients who screen positive for risk of highly infectious conditions should be isolated as soon as possible (See "Transmission-Based Precautions" above).

Tuberculosis

Patients and healthcare workers can be infected following exposure to patients with undiagnosed tuberculosis or to patients with known tuberculosis when isolation precautions

are not optimal.[34–38] While the incidence of tuberculosis in the US has declined significantly over the last 2 decades, transmission of tuberculosis in healthcare settings continues to occur.[39,40] A critical element of tuberculosis control programs is early identification and isolation of patients with suspected or confirmed infectious tuberculosis. Failure to suspect tuberculosis leads to delays in implementation of effective infection prevention measures.[41]

Many outpatient facilities are not equipped with Airborne Infection Isolation (AII) rooms for isolation and treatment of patients with suspected tuberculosis or other airborne diseases. When an AII room is not available, patients with suspected or confirmed pulmonary tuberculosis should be asked to don a surgical mask and placed in a single room with the door closed. Healthcare personnel should implement Airborne Precautions. The room must remain closed for 60 minutes following completion of the patient encounter. Outpatient facilities that perform aerosol-generating procedures including sputum induction, bronchoscopy, aerosolized pentamadine treatments, or pulmonary function testing must have adequate facilities meeting ventilation requirements for tuberculosis isolation.

Please see Chapter 27, "Tuberculosis Infection Control in Healthcare Settings," for more information.

Measles

Prior to immunization, 3–4 million cases of measles occurred each year in the US with nearly 50,000 associated hospitalizations and 450 patient deaths each year. Following introduction of single-dose vaccine in the 1960s and subsequent recommendation for the 2-dose series beginning in 1989, endemic transmission of measles was declared eradicated in 2000.[42] However, measles outbreaks continue to occur, and most cases occur among individuals who have not received measles vaccine. Measles is transmitted from person to person with great efficiency. For reasons already discussed, busy emergency departments and primary care clinic waiting rooms present opportunities for healthcare associated measles transmission to occur. In one reported 2008 outbreak of 14 measles cases, 7 individuals acquired measles through healthcare exposure, including 3 who were exposed in emergency departments and 1 who was exposed in a pediatric clinic.[43] Outpatient facilities can reduce risk of facility-associated transmission of measles by requiring staff immunity to measles, adhering to recommended immunization protocols for patients, and promptly triaging patients presenting with fever and rash. Airborne precautions should be used for all patients presenting with clinical syndromes concerning for measles.

Emerging Infectious Diseases

The healthcare system as a whole must be adaptive and responsive to emerging infectious disease threats. In the last 10–15 years, we have observed global and regional epidemics including Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), H1N1 influenza, and Ebola Virus Disease (EVD). Never is our vulnerability to healthcare-associated infection transmission more apparent than during an epidemic of an emerging pathogen. This underscores the importance of having an established system to screen patients on entry to healthcare settings. It is far easier to modify an existing system for screening and triaging patients based on new infectious disease threats than to establish a screening protocol in the midst of an epidemic. Infection preventionists overseeing outpatient departments play key roles in disseminating new information regarding syndrome recognition, mechanisms of disease transmission, and disease prevention.

Cleaning and Disinfection of Reusable Medical Equipment

Readers are encouraged to review Chapter 8, "Disinfection and Sterilization in Healthcare Facilities," and the CDC/HICPAC Guidelines for Disinfection and Sterilization in Healthcare Facilities for a more in-depth review of this topic.[44] All reusable equipment must be cleaned, disinfected, and maintained according to manufacturer's instructions. The level of disinfection or sterilization required depends on the equipment's intended use and potential for transmission of infection. In general, equipment that contacts mucous membranes or non-intact skin requires at least high-level disinfection (HLD) whereas equipment that contacts sterile body sites requires sterilization. The Spaulding Classification System should be utilized to identify what level of disinfection or sterilization is required.[44]

High-Level Disinfection (HLD)

Examples of devices used in outpatient settings that typically undergo HLD include:

- Endoscopes (bronchoscopy, GI, ENT, speech therapy)
- Ultrasound probes (transvaginal, transesophageal)
- Vaginal specula
- Laryngoscope blades

Compared to inpatient settings, outpatient settings provide potential challenges for implementing safe and effective programs for HLD:

- Staff performing HLD may have numerous other responsibilities
- There may not be a formalized process for training and assessing staff competency in performing HLD
- Space for performing HLD may be limited and suboptimal

To overcome these potential challenges, outpatient infection prevention programs should develop formal policies and procedures for performing HLD in their facilities. The policy should clearly delineate who is responsible for performing HLD. Formal staff training and competency evaluation must occur at least annually, and training should be updated when new equipment is introduced. Staff should be made aware that there is little to no room for error with HLD. Manufacturer instructions for cleaning and disinfecting must be strictly followed by each staff member assigned to perform such duties.

These instructions should be accessible for staff performing the disinfection procedures at all times. Facilities should devise a system to monitor and track HLD performance. Finally, construction or renovation of facilities should be done with guidance from infection prevention, so that proper space is allotted for HLD activities.

Cleaning and disinfection of endoscopes present particular challenges for outpatient facilities. More than 11 million endoscopic procedures are performed annually in the US, and many of these are performed in outpatient settings.[45] Although the risk of transmitted infection from a single procedure is extremely low, more outbreaks have been associated with endoscopes than other devices.[45] This is due in part to the complexities of performing adequate high-level disinfection. Flexible endoscopes are heat-sensitive and cannot undergo steam sterilization. These scopes contain long, narrow channels that are difficult to clean and disinfect. Although professional societies have published guidelines for reprocessing endoscopes, the protocols used for those procedures have not been standardized, and different endoscopes must be reprocessed by different methods.[46,47] Moreover, because endoscopes are expensive, endoscopy staff may save money by using a small inventory of endoscopes to evaluate and treat a large number of patients. Staff may not be able to process the equipment properly in the time allowed between patients. Finally, recent outbreaks of multidrug resistant organisms associated with contaminated duodenoscopes further highlight complexities of endoscope HLD.[48,49,50–52] Staff performing HLD of endoscopes must be aware of and adopt new recommendations for reprocessing scopes when such updates are made.

Sterilization

Outpatient facilities may perform steam sterilization on-site, or may contract with a vendor to perform this service off-site. Facilities that perform on-site sterilization of surgical instruments must ensure that all staff are appropriately trained to perform this duty, that instruments are precleaned according to manufacturer instructions for use, that sterilizers are functioning properly, that quality control checks are performed and logs are maintained, and that sterile instruments are stored appropriately to prevent contamination. Furthermore, outpatient facilities that perform sterilization must have adequate space to conduct this practice safely, with clear separation of clean and dirty spaces including a dirty-to-clean processing flow. Facilities that outsource sterilization to a third-party vendor must ensure that instruments are transported in covered containers, appropriately labeled with indicators, and received and stored in a way that maintains sterility. Facilities should verify the third party's competence to perform contracted functions by requiring defined competencies in the written contract as well as reviewing their policies and procedures for performing contracted services. The infection prevention team supporting the facility may also perform a site visit to observe the third-party's processes.

As in inpatient settings, immediate use steam sterilization (IUSS) must be used only when absolutely necessary. IUSS was designed to process items that become contaminated during a sterile procedure but are still needed for that procedure. IUSS should not be used routinely to compensate for inadequate numbers of instruments. The time required for IUSS is very short. Thus, all of the sterilization parameters (e.g., time and temperature) must be met precisely, and careful documentation is required. In addition, IUSS will not work if devices are contaminated with organic matter or if air is trapped in or around the devices. Moreover, because the devices are used immediately (i.e., before the results of biological indicators are known), personnel in ambulatory surgery centers that use IUSS must record which devices were used for specific patients, so that patients can be observed if it is later determined that a device was not processed properly.

Employee and Occupational Health

Employee and occupational health programs for outpatient settings mirror similar programs in inpatient settings (see Chapter 26, "Employee Health and Infection Control"). The annual, facility-specific infection control risk assessment should include at least three considerations for employee health: bloodborne pathogens, employee vaccination programs, and tuberculosis screening programs.

Infection prevention personnel must ensure that outpatient facilities implement policies and procedures to protect healthcare workers from exposure to bloodborne pathogens to meet the OSHA Bloodborne Pathogen standard (see Chapter 26, "Employee Health and Infection Control").[53] In general, bloodborne pathogens policies for outpatient settings are very similar to inpatient facilities with some exceptions based on risk assessments of the patient population served and type of care provided. For example, staff in emergency departments frequently provide acute care for persons who have traumatic injuries or are critically ill, and are therefore at increased risk for contact with blood and body fluids.[54,55] Thus, considerations for this employee group would include educational training in injection safety, provision of and training on needle safety devices, maintenance of a sharps injury log, and a mechanism to provide postexposure prophylaxis along with source patient testing. However, an outpatient clinic with care of a patient population with very infrequent encounters with patients carrying HIV or hepatitis may only require needle and device safety training and maintenance of a sharps injury log. Exposure control plans include ensuring availability of engineering controls (e.g., needleless devices, shielded needle devices), adequate PPE, training, and vaccination against hepatitis B for healthcare personnel. Devices with engineered safety features are required by OSHA and federal legislation in inpatient as well as outpatient settings.[53,56] Infection control professionals face challenges engaging frontline outpatient staff in the selection of particular devices and providing educational programs. Sites of care may be widely scattered, and types of devices available may be diverse. Despite their risk of exposure to blood and body fluids, healthcare workers in the outpatient setting often do not comply with precautions designed to protect them from bloodborne pathogens.[57,58] Like all

educational interventions in infection prevention, reiteration of safety principles and routine retraining is required.

Employee vaccination programs targeted toward pathogens relevant to the practice setting help reduce disease transmission among staff and patients. Provision of employee vaccinations reduces the risk of employees becoming a reservoir for outbreaks or ongoing transmission. Specific pathogens to provide employee vaccinations or requirements for documentation of immunity should be tailored to the practice setting. For example, employees working in dialysis units should be hepatitis B immune. Employees in pediatrics practices or hematology-oncology clinics should be immune to varicella zoster virus. Annual influenza vaccination is one vaccine universally applicable for employees in all practice settings, especially urgent care, primary care, pediatric, and emergency room settings where patients with influenza are likely to seek care.

Employee surveillance programs for tuberculosis exposures may be necessary in some outpatient practice settings, depending on community rates of TB. Routine surveillance for tuberculosis exposures among employees at outpatient centers should be based on a facility-specific risk assessment using CDC definitions of low risk, medium risk, and potential ongoing transmission.[59] This risk assessment should determine which employee groups require screening for tuberculosis exposures, and how often (e.g., only upon hire or annually).

Special Populations

Special considerations for infection prevention needs should be addressed in the three patient populations detailed below.

Dialysis Centers

Patients cared for in hemodialysis centers are a special population with a high level of comorbidity and susceptibility to infection. The number of patients with end-stage renal disease managed with ongoing hemodialysis continues to increase.[60] Historically, infection control concerns for dialysis centers have focused on bloodborne pathogens due to well-documented outbreaks related to poor injection safety and shared equipment.[19,60] However, patients on chronic hemodialysis face multiple infectious risks:

- Bloodborne pathogens (Hepatitis B, C, D and HIV)
- Multidrug-resistant organisms via multiple exposures to antibiotics and inpatient healthcare settings (particularly MRSA, VISA, and VRE)
- Healthcare associated infections due to multiple inpatient healthcare exposures
- Bloodstream infections due to long-term central venous catheters
- Vaccine-preventable bacterial and viral diseases (e.g., pneumococcal disease)

Multiple guidelines used in inpatient settings are also highly relevant for infection prevention practices in dialysis settings including those for intravascular catheter–related infections,[61] prevention of transmission of infectious agents[8] including multidrug-resistant organisms, and environmental controls.[62] CDC has also provided specific guidance for infection prevention in hemodialysis centers since the late 1970s. The current guideline, last updated in 2001, states that infection control programs in the hemodialysis setting must include routine serologic testing and immunization, surveillance, and training and education.[63] In 2008, the Centers for Medicare and Medicaid Services required outpatient dialysis facilities to follow the 2001 CDC recommendations as a condition for receiving Medicare payments.[64]

Standard precautions that limit exposure to blood and body fluids are required for all patients. In hemodialysis settings, contact with blood and body fluids is expected as part of routine care. Thus, standard precautions should be incorporated into routine hemodialysis procedures.[63] Some examples of these procedures are the following:

- Gloves are required whenever touching a patient or a patient's equipment. A supply of clean nonsterile gloves and discard containers should be placed at each dialysis station.
- Items taken to a patient's dialysis station should either be disposed of, dedicated for single use, or cleaned and disinfected before being returned to a common clean area.
- All single-use injectable medications and solutions should be dedicated for use on a single patient and be entered one time only (e.g., erythropoietin). Medications packaged as multidose should be assigned to a single patient whenever possible.[64]
- Staff members should wear gowns, face shields, eye wear, or masks when performing procedures during which spurting or spattering of blood might occur (e.g., during initiation or termination of dialysis and cleaning of dialyzers).

Patients with end-stage renal disease are immune suppressed and particularly susceptible to infections. Vaccination guidelines for patients with chronic kidney disease include vaccination schedules for hepatitis B, influenza, and pneumococcal disease in addition to those routinely recommended for all adults.[65] Hemodialysis centers should require documented serostatus for hepatitis B and C prior to enrollment in their facility for all patients.[63] Provision of hepatitis B vaccine to nonimmune patients is the standard of care given the well-documented bloodborne pathogen risk associated with hemodialysis.

Additional steps must be taken to avoid transmission of hepatitis B virus between seropositive and seronegative patients. Surveillance for change in serostatus from negative to positive must be conducted to determine if breaks in practice have resulted in new infection. CDC guidance recommends the following routine serologic testing:[63]

- Serologic testing for hepatitis B virus and hepatitis C virus infections for all patients upon admission to the dialysis center.
- Vaccination of susceptible patients against hepatitis B.
- Isolation of patients who test positive for hepatitis B surface antigen.
- Monthly hepatitis B surface antigen testing for patients who are nonresponders to the hepatitis B vaccine.

- Annual hepatitis B surface antigen antibody testing for all patients who are hepatitis B surface antigen antibody positive and hepatitis B core antigen antibody negative. Booster dose vaccine if hepatitis B surface antigen antibody level falls below 10 mlU/mL.
- Annual hepatitis C serology testing for all patients who are HCV antibody negative.

Isolation of patients with chronic hepatitis B infection takes particular attention from a staffing perspective and design of the physical space of a dialysis center:[63]

- Dialyze hepatitis B surface antigen positive patients in a separate room using separate machines, equipment, instruments, and supplies.
- Staff members caring for hepatitis B surface antigen positive patients should not care for hepatitis B–susceptible patients at the same time (e.g., during the same shift or during patient changeover).

Dialysis centers should maintain detailed documentation of the following identifying information to assist in investigations of bloodborne pathogen transmission events:

- The lot number of all blood and blood products used
- All mishaps, such as blood leaks or spills and dialysis machine malfunctions
- The location, name, and/or number of the dialysis machine used for each dialysis session
- The names of staff members who connect and disconnect the patient to and from a machine
- Results of serologic tests for hepatitis
- All accidental needle punctures and similar accidents sustained by staff members and patients

Finally, environmental infection control in hemodialysis settings requires attention to the specialized equipment required for hemodialysis. Gram-negative water bacteria are commonly found in water used during hemodialysis, which may form biofilms that are nearly impossible to eradicate if precautions are not taken to reduce bacterial burden. Published methods should be used to clean and disinfect the water treatment and distribution system and the internal circuits of dialysis machines, as well as to reprocess dialyzers for reuse.[60,62] Routine (at least monthly) bacteriologic testing of water and dialysis fluids should be performed according to standards from the Association for the Advancement of Medical Instrumentation (AAMI).[66]

Cystic Fibrosis

Patients with cystic fibrosis (CF) are a unique patient population with specific infection prevention needs. Transmission of clinically important pathogens including *P. aeruginosa, Burkholderia* spp., methicillin-resistant *S. aureus* (MRSA), and *Mycobacteria* spp. occurs between CF patients.[67–69] Additionally, indirect transmission of pathogens can occur between patients via the healthcare environment.

The Cystic Fibrosis Foundation together with the Society of Healthcare Epidemiology of America (SHEA) published updated recommendations for infection prevention and control for CF patients in 2014.[70] Key recommendations for care of CF patients in outpatient settings include:

- Healthcare workers should assume that all CF patients may be colonized with clinically important pathogens, regardless of microbiologic culture data.
- Contact precautions should be used for all patients with CF in both inpatient and outpatient care settings.
- Persons with CF should wear surgical masks in public areas of inpatient and outpatient healthcare settings.
- Congregation of CF patients in common areas and waiting rooms should be minimized. At a minimum, patients with CF should be separated by at least 6 feet from other people with CF in all settings.
- Single-patient use or dedicated equipment (e.g., stethoscope, thermometer) should be used whenever possible for all CF patients.
- Pulmonary function tests should be performed in one of the following manners to prevent airborne transmission:
  - In the exam room, allowing 30 minutes to pass between subsequent CF patients
  - In a negative pressure room
  - In a PFT lab with HEPA filter
  - In a PFT lab without HEPA filter, allowing 30 minutes to pass between subsequent CF patients

In order to implement these recommendations, outpatient facilities require ability to identify CF patients, sufficient supplies of PPE, and education of staff and patients. Additionally, logistical planning is needed to minimize overlap of CF patients in clinic waiting rooms and common areas. Potential strategies include: rooming patients with CF immediately upon arrival to clinic; using a pager or telephone call system to notify patients when their exam room is available; or having patients stay in their assigned room while team members rotate through. Clinics who serve a large number of CF patients (e.g., pulmonary, lung transplant) may be better prepared to implement such a system. On the other hand, outpatient settings that do not provide services specific to CF patients (e.g., emergency departments) may find implementation of such practices more challenging. In all cases, providers should implement standard and transmission-based precautions as primary foundation for infection prevention.

Physical Therapy

Physical therapy facilities may be located in hospitals, in clinics, or can be freestanding. Many of these facilities provide services to outpatients. Often, patients are referred for outpatient therapy following acute care hospitalizations, and patients may have active infections or be colonized with resistant organisms. Thus, the potential for transmission of pathogens among patients in physical therapy settings exists. At the same time, participation in physical therapy is important to post–acute care recovery, and, in general, patients should not be excluded from therapy on the basis of infection transmission risk. There are no standardized guidelines for infection

prevention in physical therapy facilities. We recommend that physical therapy facilities focus primarily on standard precautions, as outlined earlier in this chapter. In addition, we recommend the following general principles:

- All mats, table tops, and equipment handles should be covered with impervious materials, so that these items can be cleaned frequently.
- Cleaning supplies should be stored where they are readily accessible, so that staff can clean the equipment whenever necessary.
- Sinks for hand washing or dispensers of alcohol-based hand rub should be conveniently located such that physical therapists can wash or disinfect their hands easily after caring for each patient, or between caring for patients if they are helping more than one patient at a time.
- Patients should be instructed on how to decontaminate hands and instructed to do so during therapy at appropriate intervals.
- Patients who have active infections caused by transmissible organisms (e.g., draining wound not contained by dressing, uncontrolled pulmonary secretions) should not participate in group therapy. Staff should use appropriate standard and transmission-based precautions when working with these patients to prevent disease transmission.
- Follow all safe injection and medication administration practices as described earlier in this chapter.

Outbreaks have been associated with pulse lavage therapy performed by physical therapists.[71] Facilities providing such therapies should follow manufacturer's instructions for use to ensure adequate cleaning and disinfection of equipment that is shared between patients (e.g., hydrocollators and hydrotherapy tanks).

Summary and Recommendations

The challenge of performing infection prevention in the outpatient setting is clearly the diverse and numerous infectious risks that are specific to each type of practice setting. Thus, the key to producing an effective infection control plan requires careful assessments and routine reassessments of these infectious risks. Only after a clear understanding of the patient population served and the nature of patient interactions occurring at each facility, can one then design an effective control plan. As a first step, infection prevention staff should assess their facilities with the following questions:

- What type of outpatient facilities are present in your medical center (e.g., only hospital-based clinics, units that provide services to both inpatients and outpatients, only freestanding clinics, or a mixture of on-site and off-site clinics owned by the medical center)?
- What types of patients are seen in the outpatient facilities (e.g., young children, immunocompromised patients, or healthy preoperative patients)?
- What types of procedures are performed in the outpatient facilities?
- What types of infectious diseases are diagnosed and treated in the outpatient facilities?
- What are the community characteristics where the outpatient facilities are located? What are the patient population demographics?
- What are the levels of education of personnel in the facility? Is staff turnover a problem?
- Are HLD and/or sterilization processes occurring in any of the outpatient facilities?

Next, an assessment of available resources should inform the design of the control plan:

- What resources are available for infection control?
- Do the administration and the clinicians support the infection control program? What is the chain of command?
- What methods are currently used for staff education and certification?
- Who/what are the third-party contractors involved in cleaning and sterilization processes?

Then, existing infection control policies and current implementation of those policies should be assessed during walking rounds to answer the following questions:

- Does the area have policies, procedures, and engineering controls to prevent transmission of bloodborne pathogens?
- Does the area have appropriate screening, triage, isolation protocols, and engineering controls to prevent the respiratory spread of pathogens?
- Does the area have appropriate screening, triage, and isolation for patients who may be infected or colonized with other infectious agents?
- Does the area have appropriate exposure management plans for bloodborne pathogens, measles virus, *M. tuberculosis*, varicella-zoster virus, *B. pertussis*, lice, and scabies?
- Does the staff understand and practice principles of asepsis, including those required to use multidose vials safely?
- Does the staff understand and practice appropriate cleaning, disinfection, and sterilization?
- Are the policies and procedures in this area consistent in content and intent with those from other areas in the medical center?
- Does the area have educational programs to teach staff precautions for respiratory pathogens, bloodborne pathogens, and other infectious agents? Do they document these programs adequately?

Once you have answered these questions, you should set priorities. We would suggest that all outpatient facilities should first focus on the preventive measures listed below:

- Implement a syndrome-based triage and screening program to identify patients who require transmission-based precautions in addition to standard precautions in order to prevent unnecessary patient and employee exposures.

- Develop a hand hygiene education and surveillance program.
- Ensure that the staff comply with the recommendations of the CDC tuberculosis guideline[59] and the OSHA Bloodborne Pathogen Standard.[53]
- Ensure that the staff and patients have been vaccinated appropriately.
- Ensure that the staff practice good aseptic technique when handling multidose vials.
- Ensure that protocols and practices for cleaning, disinfection, and sterilization are appropriate.

Once these priorities are adequately addressed, infection control personnel then can turn to other facility-specific issues or develop specific control plans based on emerging risks.

Conclusion

Infection prevention and control in the outpatient setting encompasses a large array of practice settings and patient populations. Careful assessment and routine reassessments of infectious risks for each type of practice setting should inform the design of infection control plans. Infection prevention and control personnel who take on this challenge will help to improve safety for both patients and healthcare personnel, as well as the quality of care provided.

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References

1. National Ambulatory Medical Care Survey: State and National Summary Tables (p. 105). Available at: www.cdc.gov/nchs/data/ahcd/namcs_summary/2012_namcs_web_tables.pdf. Accessed August 28, 2012.
2. Barie PS. Infection control practices in ambulatory surgical centers. *JAMA.* 2010;**303**:2295–227.
3. Ambulatory Surgery in the United States, 2006. National Health Statistics Reports, No 11. Center for Disease Control and Prevention, 2009. Available at: www.cdc.gov/nchs/data/nhsr/nhsr011.pdf. Accessed August 28, 2015.
4. Guide to Infection Prevention for Outpatient Settings: Minimum Expectations for Safe Care. Available at: www.cdc.gov/HAI/settings/outpatient/outpatient-care-guidelines.html. Accessed August 29, 2015.
5. Maki DG, Crnich CJ. History forgotten is history relived: nosocomial infection control is also essential in the outpatient setting. *Arch Intern Med.* 2005;**165**:2565–2567.
6. 10A NCAC 41A.0206. Available at: http://reports.oah.state.nc.us/ncac/title percent2010a percent20- percen t20health percent20and percent20hu man percent20services/chapter per cent2041 percent20- percent20epide miology percent20health/subchapter pe rcent20a/10a percent20ncac per cent2041a percent20.0206.html. Accessed October 26, 2015.
7. North Carolina Statewide Program for Infection Prevention and Epidemiology. Available at: http://spice.unc.edu/. Accessed October 26, 2015.
8. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. Available at: www.cdc.gov/hicpac/pdf/isolation/Isolation2007.pdf. Accessed August 31, 2015.
9. WHO Guidelines on Hand Hygiene in Health Care. Available at: http://apps.who.int/iris/bitstream/10665/44102/1/9789241597906_eng.pdf. Accessed August 31, 2015.
10. Centers for Disease Control and Prevention. Guideline for Hand Hygiene in Health-Care Settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *MMWR.* 2002;**51:** 1–45.
11. Hand Hygiene in Outpatient and Home-based Care and Long-term Care Facilities: A Guide to the Application of the WHO Multimodal Hand Hygiene Improvement Strategy and the "My Five Moments for Hand Hygiene" Approach. Available at: www.who.int/gpsc/5may/hh_guide.pdf. Accessed August 31, 2015.
12. Cohen HA, Kitai E, Levy I, Ben-Amitai D. Handwashing patterns in two dermatology clinics. *Dermatology* (Basel, Switzerland). 2002;**205**:358–361.
13. Cohen HA, Matalon A, Amir J, Paret G, Barzilai A. Handwashing patterns in primary pediatric community clinics. *Infection.* 1998;**26**:45–47.
14. Arenas MD, Sanchez-Paya J, Barril G, et al. A multicentric survey of the practice of hand hygiene in haemodialysis units: factors affecting compliance. *Nephrol Dial.* 2005;**20**:1164–1171.
15. Bittle MJ, LaMarche S. Engaging the patient as observer to promote hand hygiene compliance in ambulatory care. *Joint Commission Journal on Quality and Patient Safety.* 2009;**35**:519–525.
16. Le-Abuyen S, Ng J, Kim S, et al. Patient-as-observer approach: an alternative method for hand hygiene auditing in an ambulatory care setting. *Am J Infect Control.* 2014;**42**:439–442.
17. Hlady WG, Hopkins RS, Ogilby TE, Allen ST. Patient-to-patient transmission of hepatitis B in a dermatology practice. *Am J Pub Health.* 1993;**83**:1689–1693.
18. Canter J, Mackey K, Good LS, et al. An outbreak of hepatitis B associated with jet injections in a weight reduction clinic. *Arch Intern Med.* 1990;**150**:1923–1927.
19. Lanini S, Puro V, Lauria FN, Fusco FM, Nisii C, Ippolito G. Patient to patient transmission of hepatitis B virus: a systematic review of reports on outbreaks between 1992 and 2007. *BMC Med.* 2009;**7**:15.
20. Thompson ND, Perz JF, Moorman AC, Holmberg SD. Nonhospital health care–associated hepatitis B and C virus transmission: United States, 1998–2008. *Ann Intern Medi.* 2009;**150**:33–39.
21. Macedo de Oliveira A, White KL, Leschinsky DP, et al. An outbreak of hepatitis C virus infections among outpatients at a hematology/oncology clinic. *Ann Intern Med.* 2005;**142:** 898–902.
22. Acute hepatitis C virus infections attributed to unsafe injection practices at an endoscopy clinic–Nevada, 2007.

MMWR Morbidity and Mortality Weekly Report. 2008;**57:** 513–517.

23. Invasive Staphylococcus aureus infections associated with pain injections and reuse of single-dose vials – Arizona and Delaware, 2012. *MMWR.* 2012;**61:** 501–504.
24. Outbreaks and Patient Notifications in Outpatient Settings, Selected Examples, 2010–2014. Available at: www.cdc.gov/HAI/settings/outpatient/outbreaks-patient-notifications.html#ref2. Accessed October 19, 2015.
25. Mattner F, Gastmeier P. Bacterial contamination of multiple-dose vials: a prevalence study. *Am J Infect Control.* 2004;**32**:12–16.
26. Motamedifar M, Askarian M. The prevalence of multidose vial contamination by aerobic bacteria in a major teaching hospital, Shiraz, Iran, 2006. *Am J Infect Control.* 2009;**37**:773–777.
27. Schaefer MK, Perz JF. Outbreaks of infections associated with drug diversion by US health care personnel. *Mayo Clinic Proceedings.* 2014;**89**:878–887.
28. Huang R, Mehta S, Weed D, Price CS. Methicillin-resistant Staphylococcus aureus survival on hospital fomites. *Infect Control Hosp Epidemiol.* 2006;**27**:1267–1269.
29. Hardy KJ, Oppenheim BA, Gossain S, Gao F, Hawkey PM. A study of the relationship between environmental contamination with methicillin-resistant Staphylococcus aureus (MRSA) and patients' acquisition of MRSA. *Infect Control Hosp Epidemiol.* 2006;**27**:127–132.
30. Drees M, Snydman DR, Schmid CH, et al. Prior environmental contamination increases the risk of acquisition of vancomycin-resistant enterococci. *Clin Infect Dis.* 2008;**46**:678–685.
31. Huang SS, Datta R, Platt R. Risk of acquiring antibiotic-resistant bacteria from prior room occupants. *Arch Intern Med.* 2006;**166**:1945–1951.
32. Martinez JA, Ruthazer R, Hansjosten K, Barefoot L, Snydman DR. Role of environmental contamination as a risk factor for acquisition of vancomycin-resistant enterococci in patients treated in a medical intensive care unit. *Arch Intern Med.* 2003;**163**:1905–1912.
33. Weinstein RA, Bridges CB, Kuehnert MJ, Hall CB. Transmission of influenza: implications for control in health care settings. *Clin Infect Dis.* 2003;**37**:1094–1101.
34. Calder RA, Duclos P, Wilder MH, Pryor VL, Scheel WJ. Mycobacterium tuberculosis transmission in a health clinic. *Bull Int Union Tuberculosis Lung Dis.* 1991;**66**:103–106.
35. Fischl MA, Uttamchandani RB, Daikos GL, et al. An outbreak of tuberculosis caused by multiple-drug-resistant tubercle bacilli among patients with HIV infection. *Ann Intern Med.* 1992;**117**:177–183.
36. Beck-Sague C, Dooley SW, Hutton MD, et al. Hospital outbreak of multidrug-resistant Mycobacterium tuberculosis infections: factors in transmission to staff and HIV-infected patients. *JAMA.* 1992;**268**:1280–1286.
37. Couldwell DL, Dore GJ, Harkness JL, et al. Nosocomial outbreak of tuberculosis in an outpatient HIV treatment room. *AIDS (London, England)* 1996;**10**:521–5.
38. Griffith DE, Hardeman JL, Zhang Y, Wallace RJ, Mazurek GH. Tuberculosis outbreak among healthcare workers in a community hospital. *Am J Respir Crit Care Med.* 1995;**152**:808–811.
39. Tuberculosis outbreak in a community hospital–District of Columbia, 2002. *MMWR Morbidity and mortality weekly report.* 2004;**53:** 214–216.
40. Lee EH, Graham PL, 3rd, O'Keefe M, Fuentes L, Saiman L. Nosocomial transmission of Mycobacterium tuberculosis in a children's hospital. *Int J Tuberculosis Lung Dis.* 2005;**9**:689–692.
41. Moran GJ, McCabe F, Morgan MT, Talan DA. Delayed recognition and infection control for tuberculosis patients in the emergency department. *Ann Emerg Med.* 1995;**26**:290–295.
42. Orenstein WA, Papania MJ, Wharton ME. Measles elimination in the United States. *J Infect Dis.* 2004;**189**:S1–S3.
43. Chen SY, Anderson S, Kutty PK, et al. Health care–associated measles outbreak in the United States after an importation: challenges and economic impact. *J Infect Dis.* 2011;**203**:1517–1525.
44. Guideline for Disinfection and Sterilization in Healthcare Facilities, 2008. Centers for Disease Control and Prevention, 2008. Available at: www.cdc.gov/hicpac/pdf/guidelines/Disinfection_Nov_2008.pdf. Accessed October 26, 2015.
45. Spach DH, Silverstein FE, Stamm WE. Transmission of infection by gastrointestinal endoscopy and bronchoscopy. *Ann Intern Med.* 1993;**118**:117–128.
46. Reprocessing of flexible gastrointestinal endoscopes. American Society for Gastrointestinal Endoscopy. *Gastrointest Endosc.* 1996;**43:** 540–545.
47. Petersen BT, Chennat J, Cohen J, et al. Multisociety guideline on reprocessing flexible GI endoscopes: 2011. *Infect Control Hosp Epidemiol.* 2011;**32**:527–537.
48. Epstein L, Hunter JC, Arwady M, et al. New Delhi metallo-β-lactamase–producing carbapenem-resistant Escherichia coli associated with exposure to duodenoscopes. *JAMA.* 2014;**312**:1447–1455.
49. Interim Duodenoscope Surveillance Protocol. Available at: www.cdc.gov/hai/organisms/cre/cre-duodenoscope-surveillance-protocol.html#ref1. Accessed October 23, 2015.
50. Aumeran C, Poincloux L, Souweine B, et al. Multidrug-resistant Klebsiella pneumoniae outbreak after endoscopic retrograde cholangiopancreatography. *Endoscopy.* 2010;**42**:895–899.
51. Alrabaa SF, Nguyen P, Sanderson R, et al. Early identification and control of carbapenemase-producing Klebsiella pneumoniae, originating from contaminated endoscopic equipment. *Am J Infect Control.* 2013;**41**:562–564.
52. Gastmeier P, Vonberg RP. Klebsiella spp. in endoscopy-associated infections: we may only be seeing the tip of the iceberg. *Infection.* 2014;**42**:15–21.
53. OSHA Compliance Document. Occupational Exposure to bloodborne pathogens; needlesticks and other sharp injuries; Final rule. 29 C.F.R. Part 1910 (January 18, 2001).
54. Kelen GD, Green GB, Purcell RH, et al. Hepatitis B and hepatitis C in emergency department patients. *N. Engl J Med.* 1992;**326**:1399–1404.
55. Kelen GD, Hansen KN, Green GB, Tang N, Ganguli C. Determinants of emergency department procedure- and condition-specific universal (barrier) precaution requirements for optimal provider protection. *Ann Emerg Med.* 1995;**25**:743–750.
56. (2000) FNSaPAPL-.
57. Kelen GD, Green GB, Hexter DA, et al. Substantial improvement in compliance with universal precautions in an emergency department following institution of policy. *Arch Intern Med.* 1991;**151**:2051–2056.
58. Miller KE, Krol RA, Losh DP. Universal precautions in the family physician's office. *J Fam Pract.* 1992;**35**:163–168.

59. Jensen PA, Lambert LA, Iademarco MF, Ridzon R. Guidelines for preventing the transmission of Mycobacterium tuberculosis in health-care settings, 2005. *MMWR Recommendations and reports.* 2005;**54**:1–141.
60. Alter MJ, Tokars JI, Arduino MJ, Favero MS. Nosocomial Infections Associated with Hemodialysis. In: Mayhall CG, ed. *Hospital Epidemiology and Infection Control* 3rd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2004:1139–60.
61. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis.* 2011;**52**:e162–e93.
62. Sehulster L, Chinn RY. Guidelines for environmental infection control in health-care facilities. Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR Recommendations and reports.* 2003;**52**:1–42.
63. Recommendations for preventing transmission of infections among chronic hemodialysis patients. *MMWR Recommendations and Reports.* 2001;**50:** 1–43.
64. Infection control requirements for dialysis facilities and clarification regarding guidance on parenteral medication vials. *MMWR Morbidity and Mortality Weekly Report.* 2008;**57:** 875–876.
65. CDC Guidelines for Vaccinating Kidney Dialysis Patients and Patients with Chronic Kidney Disease. Available at: www.cdc.gov/vaccines/pubs/downloads/dialysis-guide-2012.pdf. Accessed October 26, 2015.
66. Association for the Advancement of Medical Instrumentation (AAMI) Dialysis Standards Collection. Arlington, VA: Association for the Advancement of Medical Instrumentation.; 2014.
67. Aitken ML, Limaye A, Pottinger P, et al. Respiratory outbreak of mycobacterium abscessus subspecies massiliense in a lung transplant and cystic fibrosis center. *Am J Respir Crit Care Med.* 2012;**185**:231–232.
68. Biddick R, Spilker T, Martin A, LiPuma JJ. Evidence of transmission of Burkholderia cepacia, Burkholderia multivorans and Burkholderia dolosa among persons with cystic fibrosis. *FEMS Microbiol Letters.* 2003;**228**:57–62.
69. Aaron SD, Vandemheen KL, Ramotar K, et al. Infection with transmissible strains of Pseudomonas aeruginosa and clinical outcomes in adults with cystic fibrosis. *JAMA.* 2010;**304**:2145–2153.
70. Saiman LMDMPH, Siegel JDMD, LiPuma JJMD, et al. Infection Prevention and Control Guideline for Cystic Fibrosis: 2013 Update. *Infect Control Hosp Epidemiol.* 2014;**35**:S1–S67.
71. Maragakis LL, Cosgrove SE, Song X, et al. An outbreak of multidrug-resistant Acinetobacter baumannii associated with pulsatile lavage wound treatment. *JAMA.* 2004;**292**:3006–3011.

Chapter

22

Infection Prevention in Resource-Limited Settings

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Healthcare-associated infections (HAIs) affect hundreds of millions of people worldwide and are a major patient safety issue.[1–3] Although many institutions, even those in developed countries,[4] can be considered resource-limited settings depending on the definitions applied, resource-limited settings in this chapter are defined as countries with low, llower middle– and upper middle-income economies on the basis of their gross national product per capita in 2014, as reported by the World Bank.[5] With a few exceptions, this categorization includes most countries in the following regions: Africa, Asia (excluding Brunei Darussalam, Japan, Saudi Arabia, South Korea, and Taiwan), some Eastern European countries, Latin America (excluding Argentina and Venezuela), the Caribbean, and Oceania (excluding Australia and New Zealand). Resource-limited countries, including the regions mentioned above, are often called "developing countries." That term is not ideal for discussion of infection prevention issues, because infection prevention programs are impacted not only by economic resources and education but also by sociocultural differences. However, most of the concepts and recommendations discussed in this chapter are presented in a generic manner so that they can be applied in different resource-limited settings by trained infection preventionists (IPs).

In resource-limited settings, the risk of HAI has been estimated to be 2–20 times higher than that in developed countries.[6–12] Prevalence studies conducted in some developing countries have generally reported HAI prevalence of greater than 15 percent (range 6 percent to 27 percent).[7–13] Very few studies have evaluated the mortality associated with HAIs in resource-limited settings, but reported figures in international studies indicate excess mortality rates of 14.3 percent to 27.5 percent for central line–associated bloodstream infection (CLABSI) and 12 percent to 28 percent for ventilator-associated pneumonia (VAP).[14,15] According to some investigators, case-fatality rates for HAI in developing countries may exceed 50 percent among neonates.[16] These figures are particularly sobering in comparison with data from developed countries.[17–19]

Substantial progress has been made in recent years in improving infection prevention programs in resource-limited settings. National infection prevention initiatives have gained considerable importance, particularly in Asia and Latin America.[20–24] Numerous factors have helped focus attention on the importance of infection prevention, including the emergence of multidrug-resistant organisms (MDROs), the increasing perception of occupational hazards among healthcare workers (HCWs), and public demands for improved quality and cost-effectiveness of healthcare.[25] Initiatives from the Centers for Disease Control and Prevention, the World Health Organization (WHO), the Society for Healthcare Epidemiology of America (SHEA), the Association for Professionals in Infection Control and Epidemiology (APIC), and the International Federation of Infection Control have been successful in increasing public and professional awareness of the need for organized infection prevention programs in resource-limited settings, establishing training courses for IPs, and promulgating guidelines. However, the number of trained infection prevention physicians and nurses is currently insufficient in some countries, and training is limited or nonexistent in some regions, especially Sub-Saharan Africa.[26] A growing awareness of the lack of infection prevention programs in resource-limited settings prompted the WHO to create the World Alliance for Patient Safety.[27] Prevention of HAIs is the target of the First Global Patient Safety Challenge from the Alliance, "Clean Care Is Safer Care," which was launched in 2005. The challenge consists of specific actions in five major areas to promote patient safety in healthcare settings: blood safety, clinical procedure safety, injection safety, sanitation and waste management safety, and promotion of safe hand hygiene practices during patient care. A primary objective of this challenge is to launch a practical approach to improve hand hygiene in healthcare throughout the world.[27]

Infection prevention programs are challenged by a lack of standard operating procedures for microbiology laboratories in some resource-limited settings. This may lead to bacterial misidentification and misinterpretation of antimicrobial susceptibility test results, directly impacting patient safety related to inappropriate antibiotic management.[28–31] Furthermore, failure to accurately identify MDROs can undermine standard infection control practices, such as patient isolation, and result in healthcare-associated outbreaks.[31,32] For example, Suwantarat et al.[31] reported misidentification of 7 bacterial isolates during a 1-month period from a university hospital located in the central part of Thailand, a highly endemic region for MDROs and specifically carbapenem-resistant *Acinetobacter baumannii*. In this study, IPs played the critical roles of investigating the discrepancies between patient clinical findings and microbiology results and implementing quality improvement strategies for improving microbiology standards.[31] Accurate microbiological testing is essential to appropriate patient care and effective infection prevention programs.[34–36]

Over the past 15 years, several emerging viral diseases such as Middle East Respiratory Syndrome coronavirus (MERS-CoV),

Ebola virus disease (Ebola), severe acute respiratory syndrome (SARS), and avian influenza have impacted healthcare systems worldwide.[37] The poorly controlled 2014–2015 Ebola outbreak in West Africa highlights both an urgent need for improved infection control practices in intense-transmission resource-limited settings as well as the importance of global preparedness.[37,38]

Epidemiology of Nosocomial Infections

Limited epidemiological data on HAIs are available from developing countries. Existing HAI surveillance and outbreak data from resource-limited settings are difficult to interpret. Some of the limitations of the existing data include the use of different surveillance definitions, the diversity of the patient populations included, variability in the laboratory support available, the range of available expertise in data collection and analysis, and the paucity of peer-reviewed publications in this field. Language barriers, lack of protected time to conduct research, and other obstacles may discourage IPs from publishing their hospital's experiences. The International Nosocomial Infection Control Consortium (INICC)[14,24,39] is a multinational, multicenter, collaborative HAI control program that uses a surveillance system based on that of the US National Healthcare Safety Network (NHSN; formerly called National Nosocomial Infection Surveillance).[18,25,40] The methodology used by this group is quite rigorous, and the data provided come from 98 intensive care units (ICUs) in 18 different developing countries. INICC data are probably the best available representative sample of HAI data from resource-limited settings, although they do not necessarily represent the extent of the impact of HAIs in any entire single country.[18,25]

Results from other important infection surveillance initiatives have been published by other investigators from around the world.[41–47] These groups have reported data according to specific sites of infection, also using the Centers for Disease Control and Prevention's NHSN surveillance definitions. Use of "benchmarking" and comparison with NHSN system data puts significant pressure on developing countries to address specific local problems in order to achieve infection rates comparable with those in the US and Western Europe. Tables 22.1 and 22.2 summarize the data reported by these authors and the INICC for the HAIs occurring most commonly in developing countries.[13,48,49] Recent INICC data demonstrate a declining incidence of nosocomial infections including surgical site infections (SSI) in resource-limited settings compared to previous studies.[48,49] It is likely that effective application of infection control protocols in resource-limited countries has been effective.[50,51] However, rates of device-associated nosocomial infection in the ICUs of the INICC hospitals and SSI rates for most surgical procedures in INICC hospitals, remained higher compared with NHSN data.[48,49]

Table 22.1 shows incidence rates of VAP, catheter-associated urinary tract infection (CAUTI) and CLABSI reported by the INICC and by Starling et al.[13,40,48] compared to NHSN ICUs data in 2006. Recently, INICC conducted a prospective surveillance study from January 2007 through December 2012 in 503 ICUs in Latin America, Asia, Africa, and Europe. Rates of device-associated nosocomial infection were higher in the ICUs of the INICC hospitals than comparable US ICUs. In particular, the pooled rate of CLABSI in the INICC ICUs was nearly fivefold higher than the rate reported from comparable US ICUs (4.9 vs. 0.9 per 1000 central line days), the overall rate of VAP was also higher (16.8 vs. 1.1 per 1000 ventilator-days), as was the rate of CAUTI (5.5 vs. 1.3 per 1000 catheter-days).[48] In a Thai study, on the other hand, CAUTI rates were similar to the rates reported by the NHSN.[46] These data provide a baseline and demonstrate the great potential to design and implement interventions to decrease the incidence of HAIs in resource-limited settings.[52–54]

Table 22.2 shows that SSI following both cardiac and abdominal surgery remain important problems to address in some Latin American countries[49,55] Between January 2005 and December 2010, a prospective INICC surveillance study was performed in 82 hospitals of 66 cities from 30 countries in Latin America, Asia, Africa, and Europe. SSI rates were significantly higher for most surgical procedures in INICC hospitals compared with NHSN data, including the rates of SSI after hip prosthesis (2.6 percent vs. 1.3 percent), coronary bypass (4.5 percent vs. 2.9 percent), abdominal hysterectomy (2.7 percent vs. 1.6 percent), exploratory abdominal surgery (4.1 percent vs. 2.0 percent), and ventricular shunt placement (12.9 percent vs. 5.6 percent).[49]

Risk factors for HAIs have been infrequently studied in resource-limited settings. In a prospective study involving a critically ill pediatric population in Brazil, investigators found an HAI rate of 13 percent (incidence rate, 31.7 HAIs per 1,000 patient-days).[55] Independent risk factors for development of HAI in this study included the device utilization ratio (relative risk, 1.6), receipt of parenteral nutrition (relative risk, 2.5), and greater length of stay (relative risk, 1.7). The authors concluded that the preventive measures should primarily focus on reducing the use of invasive devices, a more restrictive parenteral nutrition policy, and reduction in the length of stay. Length of stay has been reported to be longer in resource-limited settings, compared with US hospitals, for multiple reasons.[56]

Bacterial infections are the most frequent HAIs in resource-limited settings, especially bacterial infections associated with invasive devices or procedures.[2,14,39] In a prevalence survey in Thailand, Gram-negative bacteria were responsible for 70.2 percent and Gram-positive bacteria for only 19.9 percent of a total of 699 HAIs identified.[12] Aggregated data from all INICC ICUs showed that 80.8 percent of all *Staphylococcus aureus* isolates were methicillin-resistant.[2,3] Infections caused by *Enterococcus* species are less common in developing countries than in developed countries; however, vancomycin-resistant enterococci (VRE) have recently emerged as important pathogens in Latin America.[57–60] The most commonly reported Gram-negative bacterial HAIs are due to *Pseudomonas aeruginosa*, *Enterobacter species*, *Klebsiella pneumoniae*, *Escherichia coli*, or *A. baumannii*.[14,39,61] High levels of antimicrobial resistance and high mortality rates have been reported for *P. aeruginosa* and

Table 22.1 Incidence rates of ventilator-associated pneumonia (VAP), catheter-associated urinary tract infection (CAUTI), and catheter-associated bloodstream infection (CA-BSI) in intensive care units (ICUs) in resource-limited settings (RLSs), compared with National Healthcare Safety Network (NHSN) data

Type of infection, reference (year[s]), type of hospital unit	No. of ICU	No. of device-days	Incidence rates by percentile			Pooled mean incidence rate (IQR)[a]	
			10th	50th (median)	90th	In the RLS	NHSN
VAP							
INICC[48] (2007–2012)							
Medical cardiac ICU	33	45,276	0.05	0.32	0.51	11.5 (10.5–12.5)	1.0 (0.8–1.1)
Medical-surgical ICU	151	536,024	0.14	0.45	0.80	16.5 (16.1–16.8)	1.1 (1.0–1.2)
Pediatric ICU	57	134,560	0.10	0.47	0.74	7.9 (7.4–8.4)	0.8 (0.6–0.9)
INICC[39] (2002–2007)							
Medical ICU	2	3,117	6.7	25.5	44.4	40.7 (6.7–44.4)	3.1 (0.9–4.6)
Surgical ICU	4	5,214	5.9	15.1	24.4	18.0 (8.5–21.7)	5.2 (1.8–6.4)
Medical-surgical ICU	60	90,905	0.0	16.5	51.4	19.8 (9.6–24.1)	3.6 (1.3–5.1)
Pediatric ICU	9	7,898	1.3	6.1	15.5	7.8 (3.0–14.2)	2.5 (0.0–2.8)
Danchaivijitr et al.[12] (2003–2004)							
Medical ICU	37	28,174	0.0	11.8	26.4	13.1 (5.0–18.4)	3.1 (0.9–4.6)
Surgical ICU	27	20,295	0.0	11.7	25.5	13.1 (6.0–20.4)	5.2 (1.8–6.4)
Pediatric ICU	23	13,113	0.0	8.7	26.3	11.2 (0.0–18.9)	2.5 (0.0–2.8)
Starling[41] (1996[b])							
Medical-surgical ICU	4	NA	NA	NA	NA	22.7 (NA)	3.6 (1.3–5.1)
Pediatric ICU	1	NA	NA	NA	NA	9.7 (NA)	2.5 (0.0–2.8)
CAUTI							
INICC[48] (2007–2012)							
Medical cardiac ICU	33	86,410	0.23	0.64	0.96	5.9 (5.4–6.4)	2.2 (2.0–2.3)
Medical-surgical ICU	151	921,015	0.35	0.73	0.99	16.5 (16.1–16.8)	1.2 (1.2–1.3)
Pediatric ICU	57	79,832	0.07	0.32	0.61	5.6 (5.1–6.1)	2.7 (2.5–3.0)
INICC[39] (2002–2007)							
Medical ICU	2	6,646	0.0	5.3	10.5	9.6 (0.0–10.5)	4.4 (1.8–5.6)
Surgical ICU	4	8,808	0.3	12.0	27.8	4.2 (3.1–22.9)	4.0 (1.2–6.1)
Medical-surgical ICU	60	155,722	0.0	5.2	22.8	6.61 (2.5–8.3)	3.4 (1.9–4.5)
Pediatric ICU	9	4,777	0.0	0.8	8.0	3.98 (0.0–3.3)	5.2 (0.0–6.0)
Danchaivijitr et al.[12] (2003–2004)							
Medical ICU	37	25,826	0.0	3.7	14.1	5.7 (0.0–8.5)	4.4 (1.8–5.6)
Surgical ICU	27	24,205	0.0	0.0	13.1	3.0 (0.0–5.3)	4.0 (1.2–6.1)
Starling[41] (1996[b])							
Medical-surgical ICU	4	NA	NA	NA	NA	8.55 (NA)	3.4 (1.9–4.5)
Pediatric ICU	1	NA	NA	NA	NA	0.0 (NA)	4.0 (1.2–6.1)

Table 22.1 (cont.)

Type of infection, reference (year[s]), type of hospital unit	No. of ICU	No. of device-days	Incidence rates by percentile			Pooled mean incidence rate (IQR)[a]	
			10th	50th (median)	90th	In the RLS	NHSN
CLABSI							
INICC[48] (2007–2012)							
Medical cardiac ICU	33	89,998	0.11	0.55	1.0	3.5 (3.1–3.9)	1.0 (1.0–1.1)
Medical-surgical ICU	151	809,754	0.21	0.59	1.0	4.9 (4.8–5.1)	0.9 (0.9–1.0)
Pediatric ICU	57	127,825	0.11	0.42	0.89	6.1 (5.7–6.5)	1.4 (1.3–1.6)
INICC[39](2002–2007)							
Medical ICU	2	2,364	2.1	7.4	12.7	10.5 (2.1–12.7)	2.9 (0.8–4.2)
Surgical ICU	4	7,526	1.3	18.2	41.6	17.1 (1.3–41.6)	2.7 (0.9–4.4)
Medical-surgical ICU	60	132,061	0.0	9.7	34.3	8.9 (3.7–16.5)	2.4 (0.6–3.1)
Pediatric ICU	9	16,012	0.0	9.5	24.4	6.8 (7.9–19.2)	5.3 (1.1–6.5)
Danchaivijitr et al.[12] (2003–2004)							
Medical ICU	14	5,567	0.0	0.0	11.7	2.7 (0.0–4.9)	2.9 (0.8–4.2)
Surgical ICU	15	6,763	0.0	0.0	11.5	3.3 (0.0–2.7)	2.7 (0.9–4.4)
Pediatric ICU	14	4,851	0.0	0.0	16.9	5.2 (0.0–6.4)	5.3 (1.1–6.5)
Starling[41] (1996[b])							
Medical-surgical ICU	4	NA	NA	NA	NA	2.13 (NA)	2.4 (0.6–3.1)
Pediatric ICU	1	NA	NA	NA	NA	4.1 c	5.3 (1.1–6.5)

NOTE: INNIC, International Nosocomial Infection Control Consortium; IQR, interquartile range (i.e., 25th and 75th percentile); NA, data not available.
[a] Incidence rates are expressed as follows: for VAP, number of cases per 1,000 ventilator-days; for CAUTI, number of cases per 1,000 catheter-days; for CLABSI, number of cases per 1,000 central line–days.
[b] Only data from 1996 are shown. c Data from 1994.

Table 22.2 Procedure-specific National Nosocomial Infections Surveillance (NNIS) System risk index–adjusted rates of surgical site infection (SSI) in resource-limited settings (RLSs), compared with NNIS benchmarks

Type of procedure, reference (year[s]), risk index category	RLS data		NNIS data[a] (1992–2004)	
	No. of procedures	No. of SSIs per 100 procedures	No. of procedures	No. of SSIs per 100 procedures
Craniotomy				
INICC[49](2005–2010)	12,501	4.4	N/A	2.6[b]
Danchaivijitr et al.[12] (2003–2004)				
Category 0	435	0.69	4,717	0.91
Category 1	800	1.88	14,864	1.72
Category 2	184	3.80	4,666	2.40[c]

Table 22.2 (cont.)

Type of procedure, reference (year[s]), risk index category	RLS data		NNIS data[a] (1992–2004)	
	No. of procedures	No. of SSIs per 100 procedures	No. of procedures	No. of SSIs per 100 procedures
Starling[41] (1994–1996[d])				
Category 0–1	541	2.8	14,864	1.72[e]
Category 2–3	541	2.8	4,666	2.40
Cardiac surgery				
INNIC[49](2005–2010)	14,070	5.6	N/A	1.3[b]
Danchaivijitr et al.[12] (2003–2004)				
Category 0	205	0.98	2,147	0.70
Category 1	175	1.71	49,135	1.50
Category 2	80	2.5	15,215	2.21[c]
Febré et al.[43] (1998–1999[f])				
Category 0	14	0	2,147	0.70
Category 1	161	6.83	49,135	1.50
Category 2	108	9.26	15,215	2.21[c]
Category 3	40	7.5	15,215	2.21[c]
Starling[41] (1994–1996[d])				
Category 0–1	214	5.6	49,135	1.50
Category 2–3	193	5.7	15,215	2.21
Mastectomy				
INICC[49](2005–2010)	4,148	1.7	N/A	2.3[b]
Danchaivijitr et al.[12] (2003–2004)				
Category 0	212	0.47	16,287	1.74
Category 1	140	1.47	10,700	2.2
Starling[41] (1994–1996[d])				
Category 0	369	0.5	16,287	1.74
Category 1	230	2.2	10,700	2.2
Herniorraphy				
INNIC[49](2005–2010)	9,843	1.8	N/A	2.3[b]
Danchaivijitr et al.[12] (2003–2004)				
Category 0	1,296	0.23	12,659	0.81
Category 1	416	0.24	8,397	2.14
Starling[30] (1994–1996[d])				
Category 0	698	0.1	12,659	0.81
Category 1	348	0.9	8,397	2.14
Laparotomy				
INNIC[49](2005–2010)	8,204	4.1	N/A	2.0[b]

Table 22.2 (cont.)

Type of procedure, reference (year[s]), risk index category	RLS data		NNIS data[a] (1992–2004)	
	No. of procedures	No. of SSIs per 100 procedures	No. of procedures	No. of SSIs per 100 procedures
Hernández et al.[44] (1998[g])				
Category 0	56	3.6	6,414	1.71
Category 1	277	22	8,802	3.08
Starling[41] (1994–1996[d])				
Category 0	56	1.8	6,414	1.71
Category 1	135	5.2	8,802	3.08
Abdominal hysterectomy				
INICC[49](2005–2010)	3,875	2.7	N/A	1.6[b]
Danchaivijitr et al.[12] (2003–2004)				
Category 0	112	1.16	49,024	1.36
Category 1	112	1.16	24,064	2.32
Starling[41] (1994–1996[d])				
Category 0	119	0.0	49,024	1.36
Category 1	329	0.9	24,064	2.32

[a] NNIS data given in Danchaivijitr et al.[12]
[b] NNHS (2006-2008) data given in Rhosental VD et al[49]
[c] Risk index category 2–3.
[d] Only data from Hospital A are shown.[25]
[e] Risk index category.
[f] Data on cardiac surgery and thoracic surgery are included.
[g] Data on different types of abdominal surgeries and postdischarge surveillance are included.

A. baumannii in Latin America and Asia.[14,61,62] In addition, carbapenem-resistant Enterobacteriaceae (CRE) have recently emerged and spread globally.[63]

Nosocomial transmission of common communicable infections in resource-limited settings is particularly problematic for pediatric patients.[64–74] There are multiple reports of communicable respiratory viral infections[65,68,69] and bacterial infections,[70] as well as gastrointestinal infections[71-73] and systemic viral infections.[67,74,75] In adults, nosocomial dissemination of multidrug-resistant *Mycobacterium tuberculosis* is also a serious threat.[76–78]

Outbreaks are also significant in resource-limited settings, but they may not be recognized in the absence of effective surveillance systems. Investigators in Mexico described 12 outbreaks of nosocomial infections over a 14-year period,[79] with an outbreak incidence almost 3 times higher than that reported in US hospitals.[80] The overall mortality rate was 25.8 percent; half of deaths were due to pneumonia. The incidence rate was 3 outbreaks per 10,000 hospital discharges, and outbreak-related infections accounted for 1.56 percent of all HAIs. The investigators reported only 2 outbreaks in the years 1985–1991 but 10 outbreaks in the years 1992–1996; the increase was probably the result of improved surveillance.[80,81]

Nosocomial transmission of bloodborne pathogens remains a major but often underappreciated problem in resource-limited settings.[82–84] Despite the WHO Safe Injection Global Network, which has been promoted since 1999,[86] unsafe injection practices – such as reusing disposable needles and syringes, using multidose vials of medication, recapping needles, and discarding needles and syringes into the general waste system – remain common in some developing countries.[86–88] A comprehensive review of all identifiable studies related to injection practices in resource-limited settings reported that, for 14 of these 19 countries, at least 50 percent of injections given were considered unsafe.[82] These findings, and the risk of bloodborne pathogen transmission associated with these practices, reinforce the importance of using standard precautions and educating HCWs about injection safety in resource-limited settings.[90]

Implementing Infection Control Programs

Interventions to Reduce the Incidence of Nosocomial Infections

Reducing the incidence of major nosocomial infections (i.e., VAP, CAUTI, CLABSI, and SSI) is achievable by implementing simple, affordable, non-device interventions that are

feasible and cost-saving in various resource-limited settings.[91–96] Reducing the incidence of VAP can be achieved by means of educational interventions, use of continuous quality improvement models to create a multidisciplinary nosocomial pneumonia team, and implementing a VAP prevention "bundle" (i.e., a combined group of prevention measures). However, they are not widely implemented in resource-limited settings. Factors associated with successful implementation include active participation by respiratory therapists, physicians, nurses and other key leaders; the use of evidence-based educational programs with the VAP prevention bundle; and continuous monitoring of nursing care practices to prevent VAP.[97–100] Together, these findings emphasize the importance of improving the management and care of patients who undergo ventilation, rather than eliminating a particular nosocomial reservoir of infection.

Several non-device interventions have been shown to be effective in reducing the incidence of CAUTI. These simple approaches include providing education, performance feedback to physicians and nurses about catheter care, written reminders for physicians about catheter indications, antibiotic guidelines tailored to specific units, and reminders to physicians to remove unnecessary catheters.[101–106] A recent meta-analysis revealed that these non-device interventions had a significant impact on the duration of catheter use: there were 1.69 fewer catheter-days per patient in the intervention group than in the control group. Additionally, the relative risk of CAUTI was 0.68 (95 percent confidence interval, 0.45–1.02; $P = 0.06$), suggesting a trend toward fewer cases of CAUTI after these interventions.[107]

Educational interventions to reduce the incidence of CLABSI in individual institutions have been examined in several studies.[108–114] These interventions have used didactic training sessions[108,112,114] or a combination of both didactic and hands-on training,[110,111] and have targeted various groups of HCWs, including resident physicians and medical students,[111] physicians-in-training and nursing staff,[108,110,112] intensivists and nurses,[113] and nurses alone.[114] Six of these studies reported a 28 percent to 72 percent decrease in the incidence of CLABSI after the intervention. A multicenter study in the US demonstrated that an educational intervention based on evidence-based practices can be successfully implemented in a diverse group of medical and surgical units and can reduce CLABSI rates.[115] Alternatively, one ICU in the US significantly reduced the incidence of CLABSI by implementing a CLABSI prevention bundle consisting of staff education, use of a mobile catheter-insertion cart, daily inquiries to care providers about whether catheters could be removed, use of a checklist to ensure adherence to evidence-based guidelines for preventing CLABSIs, and empowerment of nurses to stop the catheter insertion procedure if they observe a violation of the guidelines.[116] A CLABSI prevention bundle implemented in one multicenter study[117] included clinician education about practices to control infection and harm resulting from CLABSIs, use of a mobile catheter care cart with necessary supplies, use of a checklist to ensure adherence to infection control practices, stopping catheter insertion (in nonemergency situations) if recommended practices were not being followed, discussion of catheter removal at daily rounds, and providing feedback regarding the number of cases of CLABSI at monthly team meetings and regarding the rate of CLABSI at quarterly team meetings. Implementation of this bundle of measures resulted in a large and sustained reduction in the incidence of CLABSI (up to 66 percent) that was maintained throughout the 18-month study period. Although most of these studies were performed in developed countries,[108–113,115–117] application to resource-limited settings seems feasible.

Strategies that have been successful in reducing the incidence of SSI, regardless of resources, have a common theme: process improvement. Despite several national initiatives and wide dissemination of evidence and guidelines, rates of compliance with recommended prevention measures remain low.[118] However, many unnecessary practices, such as formaldehyde fogging or installation of UV lights in the operating room, have been found to be common in resource-limited settings.[119] Studies have shown that implementing standardized protocols can help increase the reliability of the processes (e.g., reduction in the expenditure for antibiotics used during surgery and reduction in the rate of SSI) in developing countries.[120–122] Thus, evidence-based protocols may serve as a useful tool to help standardize processes for SSI prevention and achieve higher performance. For example, procedure-specific protocols for preoperative antibiotic administration that are implemented by nursing and/or pharmacy staff eliminate the need for surgeons to remember to order the antibiotic and reduce variation in orders written in different ways at different times. Clinical exceptions can be designed into the protocol, providing guidance to staff as to when an alternate treatment path should be followed, such as for a patient allergic to β-lactam agents, or giving instructions to contact the physician. Options to document contraindications can be incorporated into process tools (e.g., preprinted orders), serving as a reminder and making it easy for physicians to note exceptions. Implementing such protocols, together with strict adherence to basic infection control measures (e.g., proper hand hygiene and scrub time), can result in SSI prevention process improvements in resource-limited settings.

Two studies performed in Asia found that many preventive practices geared toward CAUTI, CLABSI, VAP were used infrequently.[123,124] Notably, hospitals with an explicit safety culture, together with participation in a collaborative infection control network, are significantly more likely to implement protocols to prevent HAIs in these studies. Thus, policy implementation with emphasis on specific infection prevention practices to prevent HAIs may be beneficial.

Interventions to Reduce the Incidence of Infections with Multidrug-Resistant Microorganisms

Inappropriate use of antibiotics contributes to a high prevalence of antibiotic-resistant pathogens in resource-limited settings.[125] However, this is poorly documented, because most resource-limited settings lack reliable surveillance systems. It is well demonstrated that appropriate use of

antimicrobials ("antimicrobial stewardship") and infection control programs are essential components in the effort to reduce the incidence of MDRO infections, regardless of resource availability.[126] Although guidelines on preventing the transmission of MDROs, particularly Gram-positive bacteria, are available,[127,128] application of these guidelines in resource-limited settings might not be practical. Issues that complicate guideline implementation in resource-limited settings include the lack of antimicrobial stewardship initiatives, lack of resources to meet the cost of implementing some processes (e.g., use of active surveillance cultures, or providing isolation gowns for patient cohorts), and the lack of evidence-based recommendations to reduce the prevalence of multidrug-resistant Gram-negative bacteria (MDRGNB), which is far higher in developing compared to developed countries.[36,130]

Despite these limitations, several reports from resource-limited settings describe success with multifaceted intervention programs that featured education and use of antibiotic order forms, with or without audits and prescriber feedback, to promote appropriate antibiotic use.[131] It is also important to emphasize that antimicrobial stewardship educational programs should rely on three treatment principles. First, the choice of empirical therapy should be based on the prevalence, patterns, and risks of infection with MDROs in the particular setting. Second, procurement of specimens for culture before the start of treatment is essential for implementing and evaluating strategies for de-escalation of antimicrobial use. Third, subsequent de-escalation should focus on appropriate duration of treatment and monitoring for adverse events.[131–133] Together, these relatively simple interventions have been shown to reduce the incidence of infection with MDROs in various resource-limited settings.[36,129–133]

Several MDRGNB, such as *A. baumannii* and *P. aeruginosa*, have a propensity to cause outbreaks of nosocomial infections.[126,134] Outbreaks of infection with these microorganisms can occur in institutions where an effective antimicrobial stewardship program has been established,[126,130] demonstrating the importance of additional infection control interventions for outbreak control. Although molecular epidemiologic analysis may be unavailable, practitioners in resource-limited settings should adopt (and adapt) other infection control components to help control outbreaks of infection with these microorganisms, such as use of selective environmental cultures guided by epidemiologic data to determine if a common environmental source is present, enhanced contact isolation, enhanced environmental cleaning, and modified active surveillance to identify and isolate colonized patients among high-risk groups.[36,129–132,134] Monitoring adherence to these infection control interventions is also important. These infection control measures, together with antimicrobial stewardship programs, as well as advanced source control have been shown to reduce the rate of transmission of MDRGNB in many resource-limited settings.[36,129–132,134,136]

Likewise, per a national survey in Asia, having a physician as the lead infection control professional and participation in a collaborative effort to prevent MDROs were associated with multifaceted interventions to reduce MDR – *A. baumannii*, and medical school affiliation and participating in a collaborative network to prevent MDROs was associated with multifaceted interventions to reduce MRSA, while participating in a collaborative network, safety culture, and excellent administrative support were positively associated with the implementation of an antimicrobial stewardship program.[137] Future efforts that correlate infection prevention interventions and MDRO trends will help further develop evidence-based practices in resource-limited settings.[138]

Developing a Cost-Effective Infection Prevention Program

Multiple studies have shown that HAIs increase the cost of medical care because of excess lengths of stay and increased morbidity and mortality.[138–151] It is well established that integrated infection prevention programs that include HAI surveillance and multifaceted interventions, including education, can significantly reduce the incidence of HAIs.[12,133,151–155] Thus, it is reasonable to assume that infection prevention programs can reduce healthcare costs. The cost benefit of infection prevention programs has been demonstrated in developed countries.[156–160] The cost-effectiveness of infection prevention interventions is more complex to study, but it too has been demonstrated in some articles.[161–165]

New infection prevention programs in resource-limited settings usually have to prove at least their ability to be cost-neutral in order to receive enough resources to become established. Few studies on this topic from resource-limited settings have been published, and most of them are related to the cost benefit of infection prevention programs. A case-control study in Turkey indicated that HAIs increased the average hospital stay by approximately 4 days. Using an incremental cost estimate, the hospital sector had to spend an additional US$48 million for medical management of HAIs; the benefit-to-cost ratio for an infection prevention program was found to be approximately 4.6.[166] Clearly, a program for preventing HAIs will not only pay for itself but also generate other direct and indirect benefits, both for patients and for society as a whole.

Another recent case-control study, from India, demonstrated that patients with hospital-acquired bacteremia had significantly longer total stays (mean duration, 22.9 days), longer ICU stays (mean duration, 11.3 days), higher mortality rates (mean rate, 54 percent), and greater costs (mean cost, US$14,818) than did uninfected control subjects.[167] The authors estimated that hospital-acquired bacteremia increased costs by a total of US$980,000 in their cardiothoracic unit and illustrated that, although the cost of healthcare is much lower in India than in Western countries, the economic impact of HAIs was similar.[168]

Given this background, we recommend several steps to develop a cost-effective infection prevention program in a resource-limited setting.

1. Perform a risk assessment for your particular setting.
   Initially, it is impossible to do everything. One must first

establish priorities and perform a risk assessment in order to develop a cost-effective infection prevention program. It is necessary to have a baseline assessment of the healthcare system, including the number of beds, the number of procedures performed, the patient population served, and the rate of device utilization, as well as to understand the history of previous efforts to establish infection prevention programs. In the absence of regular surveillance, HAI point-prevalence surveys will be a useful starting point to clarify the extent of the problem and to identify priority areas to target for initial interventions.[12,169]

2. Engage hospital leaders and government authorities. The ultimate responsibility for infection prevention rests within individual facilities, but external political, economic, and social forces may have a significant impact on the development of these initiatives. Healthcare managers must be convinced of the potential to reduce costs and save resources by implementing infection prevention programs, as well as the safety and quality benefits.[170]
3. Establish an infection prevention and control program and committee. The characteristic features of highly effective infection prevention programs have been recognized since 1980.[153,154] In 1998, a consensus panel provided updated and specific recommendations in the following areas: managing critical data and information, including surveillance data; developing, implementing, and monitoring policies and procedures; following guidelines and meeting accreditation requirements; collaborating with the employee health program; applying interventions to prevent transmission of infectious diseases; educating and training healthcare workers; and dedicating resources to infection prevention programs.[171]
4. Adjust the surveillance plan to match the characteristics of your particular setting. Surveillance should focus on high-risk hospital populations: for instance, patients in ICUs and patients with device-associated HAIs.[18,172] Computer and statistical support is desirable, as is a plan to communicate results and implement interventions according to the highest priorities.
5. Implement evidence-based measures first. Hand hygiene programs, standard precautions, and isolation precautions are the basic fundamentals of any infection prevention program to reduce the cross-transmission and spread of infections in healthcare settings.[27,90,173] In addition, unnecessary practices should be eliminated, especially if they are expensive or do not add value – that is, do not aid in preventing infection.[119, 174]
6. Provide education and training in infection prevention for HCWs. Education is a priority, and infection prevention education should first target local infection prevention leaders, then target doctors, nurses, and students.[175,176] Academic centers should develop and implement infection prevention education for the curriculum in medical and nursing schools.[177]
7. Be prepared for obstacles and problems. Multiple barriers have been reported by infection prevention teams during the development of new infection prevention programs. A study from Egypt described numerous constraints, such as non-cooperation of medical staff, underreporting of SSIs and BSIs, lack of communication between the infection prevention team and laboratory staff, and lack of advocacy and political support.[169] In a study from Thailand, the main obstacles for infection prevention programs were a lack of incentives (reported by 66.7 percent of respondents) and lack of support from administrators (reported by 30.2 percent).[178] Many of these same barriers exist in developed countries as well. There are numerous examples of studies on how to build a business case for infection prevention and on establishing priorities in the infection prevention literature from developed countries.[170,179–181] Existing models and tools from developed countries, the CDC, the WHO, and resource-limited settings with successful infection prevention programs should be used to help address these barriers. New infection prevention programs should focus on establishing a track record of reporting infection rates, providing education, and developing interventions to reduce infections, to demonstrate their achievements. Initial successes and cost savings can then be used to provide data to expand the infection prevention program.

Establishing Occupational Health Programs

Healthcare epidemiologists in resource-limited settings should advocate for strong occupational health programs, as HCWs are a scarce resource and are costly to train and replace. Furthermore, communicable diseases are readily transmitted between patients and HCWs and vice versa, and the incidence of occupationally acquired infections reflects the success of a hospital's infection prevention program. Although healthcare workers may be exposed to a number of occupational hazards, this section focuses on selected infectious hazards encountered in resource-limited settings.

Hospitals in resource-limited settings may be unable to implement the use of costly protective measures, such as airborne-infection isolation rooms or safety-engineered needleless devices. Nevertheless, many effective interventions are relatively inexpensive. These include correct use of hand hygiene and standard precautions, vaccination of HCWs, performance of risk assessments, and reducing "presenteeism" (i.e., HCWs working when they are ill with a communicable disease). All HCWs, including physicians, should receive training on hand hygiene and standard precautions. The nosocomial transmission of vaccine-preventable illnesses is well documented; thus, WHO-recommended vaccines should be provided free of charge to all HCWs.[182] Risk assessment – that is, the process of evaluating the risk of potential exposure to an infectious disease before each patient contact – requires that HCWs be educated on the infectious syndromes and patient-care activities that may warrant use of additional protective measures.[89] Presenteeism may be reinforced by hospital policies, peers, or a personal sense of duty, and healthcare

epidemiologists should help policy makers and HCWs understand the risks associated with this practice.

Prevention of *Mycobacterium tuberculosis* Infection

M. tuberculosis infection poses a serious occupational risk in many resource-limited settings. *M. tuberculosis* infection (TB) rates are higher among HCWs with longer length of employment or more exposure to patients infected with M. *tuberculosis*.[78] However, *M. tuberculosis* infection may go unrecognized as an occupational infection if there is a high prevalence of TB in the community or a lack of nosocomial surveillance.

Surveillance for nosocomial TB is useful to evaluate the effectiveness of TB control measures, the ongoing risk of acquisition, and the need for additional interventions. Since most HCWs who acquire *M. tuberculosis* will have latent infection (LTBI), screening for *M. tuberculosis* disease (i.e., active *M. tuberculosis* infection) will greatly underestimate the occupational risk. Surveillance for latent infection can be conducted by use of the tuberculin skin test (TST) or interferon-gamma release assays (IGRAs). A positive result of an IGRAs is more specific for *M. tuberculosis* infection than is a positive tuberculin skin test result, but the assay is costly and not recommended in resource-limited settings.[183] TST results may be affected by previous receipt of BCG vaccine, infection with nontuberculous mycobacteria, or HIV co-infection. Nevertheless, several studies have demonstrated that the tuberculin skin test is a useful tool to quantify the risk of nosocomial *M. tuberculosis* transmission, even among HCWs who have received the BCG vaccine,[78,184,185] and to identify the areas of highest risk to be targeted with control measures.[186] HCWs with a positive tuberculin skin test and/or active *M. tuberculosis* infection should be encouraged to undergo testing for HIV infection. HIV-positive HCWs should be offered antiretroviral therapy as well as treatment for either latent or active *M. tuberculosis* infection, as determined by the clinical assessment.[187]

Although implementing *M. tuberculosis* control measures may be challenging in resource-limited settings, studies from Brazil, Malawi, and Thailand suggest such measures can reduce occupational risk for HCWs.[186,188–190] The WHO recommends that the highest priority be given to administrative control measures; in particular, prompt triage, separation of infectious patients, respiratory hygiene, and minimizing the time infectious patients spend in healthcare facilities.[187] A study from Brazil found that the time from patient presentation to receipt of the first dose of medication active against *M. tuberculosis* can be reduced from days to hours and that implementing administrative control measures, without the use of more costly engineering controls, can result in a significant reduction in the number of HCW TST conversions.[188] Hospitals should also have a program to monitor and maintain effective ventilation. Where mechanical ventilation systems are cost-prohibitive, natural ventilation should be maximized (e.g., by opening windows where climate permits) and augmented by the proper use of fans to improve dilution and direct airflow away from susceptible persons. UV germicidal irradiation (UVGI) devices can be used as a complementary control measure.[187] The use of particulate respirators varies widely between and within resource-limited settings. Because of cost considerations, most hospitals require that HCWs reuse their respirators. If use of respirators is poorly accepted by HCWs, they may wear them improperly, not wear them when use is indicated, or lose them.[78,191] Thus, hospitals that provide respirators should ensure that HCWs are properly trained in their use and should replace lost, torn, or dirty respirators.

Prevention of Transmission of Bloodborne Pathogens and Postexposure Management

Exposure to bloodborne pathogens is a serious occupational hazard in countries with a high prevalence of infection with HIV, hepatitis B virus, and/or hepatitis C virus. The WHO estimates that approximately 3 million HCWs are occupationally exposed to bloodborne pathogens each year, resulting in 66,000 hepatitis B virus infections, 16,000 hepatitis C virus infections, and 1,000 HIV infections; more than 90 percent of these occur in resource-limited settings.[192] Needlestick injuries are the most common source of exposure to bloodborne pathogens, and most of these injuries are preventable. It has been estimated that HCWs in Africa, the Eastern Mediterranean, and Asia sustain on average 4 needle stick injuries per year.[193]

Prevention strategies for reducing occupational exposure to bloodborne pathogens should focus on eliminating unnecessary injections, observing standard precautions, and training HCWs in the safe use and disposal of needles and sharp devices ("sharps").[194] Special efforts should be made to train HCWs who are less experienced, as they are at higher risk of sustaining a needle stick injury. Personal protective equipment (e.g., gloves, gowns, facial protection) should be readily available, and, where feasible, sharps with injury protection features (e.g., needles that autoretract) and reuse prevention features should be used.[195] HCWs should receive hepatitis B vaccine, free of charge, as early in their career as possible and have a protective titer documented. HCWs occupationally exposed to a bloodborne pathogen should have immediate access to a medical assessment, counseling, confidential testing, and follow-up. Hospitals should ensure that medication for HIV postexposure prophylaxis is readily available for workers with exposures deemed high risk.[193,196]

Emerging and Re-Emerging Viruses in Healthcare Workers and Infection Control Implementation

In recent years, emerging and re-emerging viruses have had a devastating effect on hospitals and their communities. Hospitals are often the vanguard for both the recognition and the control of emerging viruses in outbreaks of SARS, novel influenza viruses, MERS-CoV and Ebola. It is estimated that HCWs accounted for 11–57 percent of all SARS cases in 2003, 1–27 percent of all MERS-CoV cases since 2012, and 1–16 percent of all Ebola cases worldwide since 2014, with a fatality

rate of up to 73 percent for Ebola-infected HCWs.[37,38] Additional healthcare transmission involved patients and family members who presented to hospitals for other reasons. The global spread of emerging viruses in HCWs was facilitated by a lack of adherence to standard infection prevention practices.[37,197]

These outbreaks provide several important lessons for future prevention efforts. First, transmission often occurs because of delays in recognizing infectious patients and implementing appropriate infection control measures. Such delays can be reduced by implementing screening, triage, and risk assessment protocols.[37,198] Furthermore, HCWs should be trained to identify unusual clusters of patients with severe febrile respiratory illness or hemorrhagic fevers, particularly if there is a history of contact with other severely ill persons (e.g., a family cluster). These clusters of infection should be reported to local public health authorities.

A second contributing factor in transmission is a lack of availability and inconsistent use of personal protective equipment (PPE). In particular, face and eye protection is often suboptimal.[199,200] HCWs protection can be enhanced by ensuring adequate PPE supply, PPE training (including practice in donning and doffing), use of a designated observer (or "buddy") while donning and doffing to minimize self-contamination, and written protocols for PPE use and disposal.[198,200–202] Changes to PPE supplies and protocols can lead to errors and should be minimized.

Finally, the risk of transmission of emerging pathogens in healthcare settings is associated with high-risk procedures, such as aerosol-generating procedures (e.g., intubation, bronchoscopy) in patients with viral respiratory infections, and phlebotomy or hemodialysis in patients with Ebola. While in principle these procedures should be minimized to reduce HCW risk, in practice, these are often considered life-saving procedures. If high-risk procedures are unavoidable, the number of personnel present during the procedure should be limited. In the case of emerging respiratory viruses, aerosol-generating procedures should be conducted in adequately ventilated single-patient rooms, and HCWs should wear particulate respirators.[198]

In order to prepare for future emerging infectious diseases, healthcare facilities should develop preparedness plans for pandemic avian influenza and implement heightened protective measures.[37,200,202] Pandemic preparedness plans in resource-limited settings should be aligned with their available resources and context. Planning should include the following: healthcare administrative support, mechanisms to rapidly create temporary isolation facilities, systems to restrict exposed HCWs, and involvement of infectious disease specialists who can screen and identify cases early, provide for continuous monitoring to ensure adherence to optimal infection-control practices, and give regular feedback on compliance to HCWs.[37,201] On a national level, the WHO encourages all countries to continue avian influenza surveillance, including surveillance for severe acute respiratory illness, reporting of human infections, and sustained national health preparedness actions.[198] The key factors in controlling avian influenza outbreaks include the rapid and coordinated response of central and regional health and agricultural authorities and the education and performance of HCWs.

In addition to emerging respiratory viruses, hospitals must be prepared to deal with seasonal and endemic respiratory viruses. Annual vaccination against seasonal influenza is recommended for all HCWs.[203] A study from Thailand estimates that the costs incurred in a nosocomial influenza outbreak are 10-fold higher than the costs of a universal annual HCW vaccination program.[204] Thus, vaccination would be cost-effective, particularly in tropical countries where influenza occurs year-round.

Disinfection and Sterilization

The principles of disinfection and sterilization are discussed in Chapter 8. This section focuses on challenges that may confront resource-limited settings more frequently: the impact of water quality on disinfection and sterilization and the reuse of single-use medical devices.

Hospitals in resource-limited settings may face difficulty in ensuring a reliable supply of clean water for cleaning and reprocessing medical devices. The risk of bacterial contamination is lower if deionized or distilled water is used instead of tap water. However, even these sources of water may have high levels of endotoxin. Out breaks of pyrogenic reactions have been linked to the use of water with high endotoxin levels to reprocess cardiac catheters.[205,206] Monitoring the quality of the water used for reprocessing by measuring both bacterial contamination and endotoxin levels is essential for preventing adverse outcomes.

Hospitals may feel compelled to reprocess and reuse medical devices intended "for single use only" as procedures involving increasingly complex and costly medical devices become more widely available in resource-limited settings. This practice raises ethical and patient safety concerns. Safety data supporting the reuse of many such devices are lacking, but not reusing such a device may deny a patient a potentially life-saving procedure, where resources are limited. Inadequate local practices may further increase the risk of adverse patient outcomes.[207] At a minimum, hospitals that reprocess and reuse single-use devices should train the personnel who do the reprocessing; implement a standardized, written reprocessing protocol; ensure adequate cleaning, rinsing, drying, sterilizing, and packaging methods; develop criteria for discarding reused devices so they are not used repeatedly until they malfunction or break; and conduct surveillance for adverse patient events.

Finally, it is important to emphasize that syringes and needles must never be reprocessed or reused. The WHO estimates that as many as 40 percent of injections worldwide are given with reused, unsterilized syringes and needles and that these practices cause an estimated 21 million new HBV cases, 2 million new HCV cases and 260,000 new HIV cases globally, in addition to malaria, Ebola, and Marburg infections.[208]

Table 22.3 Steps to implementing a successful hand hygiene program in a resource-limited setting

Step 1. Seek administrative support ("buy-in")
Promote the World Health Organization campaign (adopt and/or adapt it)
Present an evidence-based case for hand hygiene
Step 2. Provide access to hand hygiene products
Assess the availability of clean water and soap
Implement use of alcohol-based hand rub where it is feasible; place hand hygiene supplies at the point of care
Step 3. Address barriers to good hand hygiene compliance
Lack of understanding: educate healthcare workers about the chain of transmission, the effectiveness of hand hygiene in breaking the chain, and the appropriate moments for hand hygiene
Cultural norms: identify and groom advocates ("champions") and address religious or cultural barriers to use of alcohol-based hand rub
Forgetfulness: use reminders (e.g., posters and promotional materials)
Step 4. Conduct audits and provide feedback on compliance rates

Table 22.4 Infection prevention networks sponsored by professional societies worldwide

Network	URL
Society for Healthcare Epidemiology of America	www.shea-online.org
Association for Professionals in Infection Control and Epidemiology	www.apic.org
International Nosocomial Infection Control Program	www.inicc.org
Asia Pacific Society of Infection Control	www.apsic2009.org
New Zealand National Division of Infection Control Nurses	www.infectioncontrol.co.nz
Eastern Mediterranean Regional Network for Infection Control	www.emro.who.int/emrnic/about.htm
Southeastern Europe Infection Control	None
Baltic Network for Infection Control and Containment of Antimicrobial Resistance	http://balticcare.wordpress.com/
Australian Infection Control Association	www.aica.org.au/
Infection Control Association (Singapore)	www.icas.org.sg/
The Nosocomial Infection Control Group of Thailand	www.idthai.org/
The Hospital Infection Society	www.his.org.uk/
Infection Control Nurses Association	www.ips.uk.net/
Middle Eastern Society of Infection Control	None

Implementing Hand Hygiene Programs

Hospitals in resource-limited settings may face formidable barriers to hand hygiene, including a lack of access to clean (or any) water, lack of administrative support, overworked staff, and crowded wards. A successful hand hygiene program will require a step-by-step approach, with successful completion of each step before moving on to the next (Table 22.3). The first step is to garner the support of hospital administrators. Since the WHO launched the First Global Patient Safety Challenge in 2005, the Ministries of Health in 139 countries have pledged to address hand hygiene in their hospitals.[209] Hospitals in these countries can use this national-level commitment to help convince local administrators of the importance of hand hygiene. Tools and resources from the WHO Global Patient Safety Challenge[210] and the strong association between improved hand hygiene compliance and fewer healthcare-acquired infections may also be useful to rally administrative support (see Chapter 9 on hand hygiene).

Once hospital leadership is supportive, access to appropriate hand hygiene agents must be provided. In most cases, use of plain soap and water is the cheapest method of hand hygiene. However, the feasibility of providing alcohol-based hand rub should be considered, as alcohol-based hand rub has many advantages over soap and water. Alcohol-based hand rub may provide a solution for hospitals without a reliable source of clean, running water, as there is no need for plumbing or concern about water quality. Effective alcohol-based rubs can be made in-house at a fraction of the cost of commercial product. Along with choosing and providing the hand hygiene agent(s) to be made available, careful consideration must be given to their placement. It is essential that HCWs have convenient access to hand hygiene agents at the point where they are providing care to the patient.[211]

Once appropriate hand hygiene agents have been provided, it is necessary to identify and address other potential barriers to compliance. These may include a lack of understanding of the role of hand hygiene in preventing healthcare-acquired infections, lack of awareness of when hand hygiene should be performed, poor hand hygiene practices as a cultural norm, or cultural or religious concerns with the use of alcohol-based hand rub.[212] HCWs should be educated on the importance of hand hygiene in preventing the transmission of infections to patients, as well as protecting themselves from occupational infections. They should be aware of the appropriate moments during patient care activities when hand hygiene should be performed.[213] Cultural norms within a hospital can sometimes be successfully changed by identifying hand hygiene advocates or "champions." Champions should be respected individuals

in the hospital whose hand hygiene practices provide a model for others to follow and who can motivate others to change their attitudes and behavior. Other approaches to changing the cultural norms of a hospital may include poster campaigns, visible support of hospital leadership, and informing patients that hand hygiene is a hospital priority so that patient expectations help drive behavior. In hospitals that promote the use of alcohol-based hand rub, any cultural or religious concerns about the use of this agent should be addressed.[212]

Once the barriers to hand hygiene have been identified and addressed, observing hand hygiene practices and providing feedback to HCWs are an effective method of modifying behavior and further improving compliance. This should be done in a positive and not punitive manner. Performance data may be better received when provided in aggregate fashion (e.g., by unit or occupational group). Competition may drive further improvement (e.g., comparing the performance of one unit or healthcare worker group against another). Hand hygiene compliance rates should become a performance indicator for hospitals committed to improving patient safety and quality of care.

International Infection Control Networks

The first national, multidisciplinary infection prevention societies were formed in the early 1970s and are responsible for much national and global progress; professionals are more likely to be effectively focused on the problem and on education, research, and solutions than are government agencies, and they are less likely to be distracted by political concerns. Just as new IPs need support, education, and a network of more experienced individuals, the new infection prevention societies soon found that they also needed some of these same resources. Infection prevention nurses from the United States, the United Kingdom, Sweden, Canada, and Denmark requested WHO support for an international infection prevention meeting. The WHO sponsored such a meeting in 1978, which was attended by 75 professionals from 25 countries. The development of the International Federation of Infection Control[214] soon followed; the members are the national infection prevention societies of more than 55 countries.[215]

As regional and international societies are an integral parts of the International Federation of Infection Control, so several regional and international infection control networks exist in many regions around the world. These are nonprofit, open, international, professional organizations established to help distribute education on infection control to practitioners in each region, and some offer evidence-based guidelines on infection prevention or offer the opportunity for research networks around the world. Practitioners in resource-limited settings can participate in the activities developed by these societies. Organizations from around the world that sponsor infection prevention networks are listed in Table 22.4.

Conclusions

HAIs infections in resource-limited settings represent a huge unrecognized threat to patient safety. Successful research in resource-limited settings, combined with intensive continuous efforts to more consistently implement simple and inexpensive measures for prevention, will lead to wider acceptance of infection prevention practices in these settings. Existing evidence suggests that infection prevention measures are feasible and effective in reducing the incidence of HAIs and improving healthcare outcomes. In addition, several viral emerging diseases have emerged and are impacting healthcare systems worldwide. However, many unanswered questions remain, and additional studies are required to help understand and improve infection prevention programs in resource-limited settings. Because many interventions do not require expensive technology, resource-limited settings should not delay the implementation of basic infection control interventions while awaiting additional data. Resource-limited countries should develop national infection prevention guidelines to reduce the incidences of nosocomial infections and infections with MDROs. Guidelines to improve the quality of disinfection and sterilization processes, as well as guidelines for pre-exposure and postexposure diagnostic work-ups for occupational exposures, are needed. Resource-limited settings should implement practical, evidence-based, low-cost, and simple preventive strategies first. Additional studies to explore the long-term effect and cost benefit of specific infection prevention interventions in resource-limited settings are needed. Studies of antimicrobial stewardship programs and other interventions to reduce the development and transmission of MDROs are also warranted. Such studies should include analyses of economic, behavioral, communication, and organizational strategies to optimize the implementation of and adherence to best practices.

References

1. Burke JP. Infection control – a problem for patient safety.*N Engl J Med.* 2003;**348:** 651–656.
2. Christenson M, Hitt JA, Abbott G, Septimus EJ, Iversen N. Improving patient safety: resource availability and application for reducing the incidence of healthcare- associated infection. *Infect Control Hosp Epidemiol.* 2006;**27**:245–251.
3. Yokoe DS, Classen D. Improving patient safety through infection control: a new healthcare imperative. *Infect Control Hosp Epidemiol.* 2008;**29** (Suppl 1):S3–S11.
4. Anderson DJ, Kirkland KB, Kaye KS, et al. Underresourced hospital infection control and prevention programs: penny wise, pound foolish? *Infect Control Hosp Epidemiol.* 2007;**28**:767–773.
5. World Bank. Country and Lending Groups. Available at: http://data.worldbank.org/about/country-and-lending-groups. Accessed October 25, 2015.
6. Mayon-White RT, Ducel G, Kereselidze T, Tikomirov E. An international survey of the prevalence of hospital-acquired infection. *J Hosp Infect.* 1988;**11**(Suppl A):43–48.
7. Faria S, Sodano L, Gjata A, et al. The first prevalence survey of nosocomial infections in the University Hospital Centre "Mother Teresa" of Tirana, Albania. *J Hosp Infect.* 2007; **65**:244–250.
8. Farhat CK. Nosocomial infection [in Portugese]. *J Pediatr (Rio J).* 2000;**76**:259–260.

9. Rezende EM, Couto BR, Starling CE, Modena CM. Prevalence of nosocomial infections in general hospitals in Belo Horizonte. *Infect Control Hosp Epidemiol*. 1998; **19**:872–876.
10. Kallel H, Bahoul M, Ksibi H, et al. Prevalence of hospital-acquired infection in a Tunisian hospital. *J Hosp Infect*. 2005;**59**:343–347.
11. Gosling R, Mbatia R, Savage A, Mulligan JA, Reyburn H. Prevalence of hospital-acquired infections in a tertiary referral hospital in northern Tanzania. *Ann Trop Med Parasitol*. 2003;**97**:69–73.
12. Danchaivijitr S, Judaeng T, Sripalakij S, Naksawas K, Plipat T. Prevalence of nosocomial infection in Thailand 2006. *J Med Assoc Thai*. 2007;**90**:1524–1529.
13. Ponce de Leon-Rosales SP, Molinar-Ramos F, Dominguez- Cherit G, Rangel-Frausto MS, Vazquez-Ramos VG. Prevalence of infections in intensive care units in Mexico: a multi-center study. *Crit Care Med*. 2000;**28**:1316–1321.
14. Rosenthal VD, Maki DG, Mehta A, et al. International Noso-comial Infection Control Consortium report, data summary for 2002–2007, issued January 2008. *Am J Infect Control*. 2008;**36**:627–637.
15. Aygun C, Sobreyra Oropeza M, Rosenthal VD, Villamil Gomez W, Rodriguez Calderon ME. Extra mortality of nosocomial infections in neonatal ICUs at eight hospitals of Argentina, Colombia, Mexico, Peru, and Turkey: findings of the International Nosocomial Infection Control Consortium (INICC). *Am J Infect Control*. 2006;**34**:E135.
16. Zaidi AK, Huskins WC, Thaver D, Bhutta ZA, Abbas Z,Goldmann DA. Hospital-acquired neonatal infections in developing countries. *Lancet*. 2005;**365**:1175–1188.
17. Horan TC, Gaynes RP. Surveillance of nosocomial infections. In: Mayall CG, ed. *Hospital Epidemiology and Infection Control*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins;2004:1659–1702.
18. Emori TG, Culver DH, Horan TC, et al. National nosocomial infections surveillance system (NNIS): description of surveillance methods. *Am J Infect Control*. 1991;**19**:19–35.
19. Klevens RM, Edwards JR, Richards CL Jr, et al. Estimating health care–associated infections and deaths in U.S. hospitals, 2002. *Public Health Rep*. 2007;**122**:160–166.
20. Danchaivijitr S. Hospital infection control in Thailand. *Can J Infect Control*. 1991;**6:** 97–99.
21. Danchaivijitr S, Tangtrakool T, Waitayapiches S, Chokloikaew S. Efficacy of hospital infection control in Thailand 1988–1992. *J Hosp Infect*. 1996;**32**:147–153.
22. Ajenjo MC. Infecciones intrahospitalarias: conceptos actuales de prevencion y control. *Rev Chil Urol*. 2006;**72**: 95–101.
23. Marcel JP, Alfa M, Baquero F, et al. Healthcare-associated infections: think globally, act locally. *Clin Microbiol Infect*. 2008;**14**:895–907.
24. Rosenthal VD, Maki DG, Graves N. The International Nosocomial Infection Control Consortium (INICC): goals and objectives, description of surveillance methods, and operational activities. *Am J Infect Control*. 2008;**36**: e1–e12.
25. Starling C. Infection control in developing countries. *Curr Opin Infect Dis*. 2001;**14**:461–466.
26. Newman MJ. Infection control in Africa south of the Sahara. *Infect Control Hosp Epidemiol*. 2001;**22:** 68–69.
27. Pittet D, Allegranzi B, Storr J, et al. Infection control as a major World Health Organization priority for developing countries. *J Hosp Infect*. 2008;**68**:285–292.
28. Drain PK, Hyle EP, Noubary F, et al. Diagnostic point-of-care tests in resource-limited settings. *Lancet Infect Dis*. 2014;**14**:239–249.
29. York M. Challenges encountered when building laboratory capacity in limited-resource hospitals in Vietnam. *Clin Microbiol Newsletter*. 2012;**34**:169–175.
30. Archibald LK, Reller LB. Clinical microbiology in developing countries. *Emerg Infect Dis*. 2001;**7**:302–305.
31. Suwantarat N, Rutjanawech S, Buppajarntham A, Carroll KC, Khawcharoenporn T, Apisarnthanarak A. Bacterial misidentification in a resource-limited microbiology laboratory setting and quality improvement strategies. *J Patient Saf*. 2015 Feb 24. [Epub ahead of print]
32. Siegel J, Rhinehart E, Jackson M, et al. *Management of Multidrug-Resistant Organisms in Healthcare Settings*. Bethesda, MD:Centers for Disease Control and Prevention; 2006.
33. Rand KH, Tillan M. Errors in interpretation of gram stains from positive blood cultures. *Am J Clin Pathol*. 2006;**126**:686–690.
34. Apisarnthanarak A, Buppunharun W, Tiengrim S, et al. An overview of antimicrobial susceptibility patterns for gram-negative bacteria from the National Antimicrobial Resistance Surveillance Thailand (NARST) program from 2000 to 2005. *J Med Assoc Thai*. 2009;**92**:S91–S94.
35. Dejsirilert S, Tiengrim S, Sawanpanyalert P, et al. Antimicrobial resistance of *Acinetobacter baumannii*: six years of National Antimicrobial Resistance Surveillance Thailand (NARST) surveillance. *J Med Assoc Thai*. 2009;**92**:S34–S45.
36. Apisarnthanarak A, Pinitchai U, Thongphubeth K, et al. A multifaceted intervention to reduce pandrug-resistant *Acinetobacter baumannii* colonization and infection in 3 intensive care units in a Thai tertiary care center: a 3-year study. *Clin Infect Dis*. 2008;**47**:760–767.
37. Suwantarat N, Apisarnthanarak A. Risks to healthcare workers with emerging diseases: lessons from MERS-CoV, Ebola, SARS, and Avian Flu. *Curr Opin Infect Dis*. 2015;**28**:349–361.
38. World Health Organization. Ebola report on health worker infections – Special Ebola Situation Report. 20 May 2015. Available at: www.who.int/hrh/documents/21may2015_web_final.pdf?ua=1. Accessed December 8, 2015.
39. Rosenthal VD. Device-associated nosocomial infections in limited-resources countries: findings of the International Nosocomial Infection Control Consortium (INICC). *Am J Infect Control* 2008;**36**:S171.e7–e12.
40. National Healthcare Safety Network (NHSN) Web site. Available at: www.cdc.gov/nhsn/. Accessed September 30, 2009.
41. Starling CE, Couto BR, Pinheiro SM. Applying the Centers for Disease Control and Prevention and National Nosocomial Surveillance system methods in Brazilian hospitals. *Am J Infect Control*. 1997;**25**:303–311.
42. Lopes JM, Tonelli E, Lamounier JA, et al. Prospective surveillance applying the National Nosocomial Infection Surveillance methods in a Brazilian pediatric public hospital. *Am J Infect Control*. 2002;**30**:1–7.
43. Ercole FF, Starling CE, Chianca TC, Carneiro M. Applicability of the National Nosocomial Infections Surveillance system risk index for the

prediction of surgical site infections: a review. *Braz J Infect Dis*. 2007;**11**:134–141.

44. Hernández K, Ramos E, Seas C, Henostroza G, Gotuzzo E. Incidence of and risk factors for surgical-site infections in a Peruvian hospital. *Infect Control Hosp Epidemiol*. 2005; **26**:473–477.
45. Danchaivijitr S, Rongrungruang Y, Pakaworawuth S, Jinta-nothaitavorn D, Naksawas K. Development of quality indicators of nosocomial infection control. *J Med Assoc Thai*. 2005;**88** (Suppl 10):S75–S82.
46. Kasatpibal N, Jamulitrat S, Chongsuvivatwong V. Standardized incidence rates of surgical site infection: a multicenter study in Thailand. *Am J Infect Control*. 2005;**33**:587–594.
47. Coffin SE, Klompas M, Classen D, et al. Strategies to prevent ventilator-associated pneumonia in acute care hospitals.*Infect Control Hosp Epidemiol*. 2008;**29**(Suppl 1):S31–S40.
48. Rosenthal VD, Maki DG, Mehta Y, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary of 43 countries for 2007–2012. Device-associated module. *Am J Infect Control*. 2014;**42**:942–956.
49. Rosenthal VD, Richtmann R, Singh S, et al. Surgical site infections, International Nosocomial Infection Control Consortium(INICC) report, data summary of 30 countries, 2005–2010. *Crit Care Med*. 2014;**40**:3121–3128.
50. Rosenthal VD, Rodrigues C, Álvarez-Moreno C, et al. Effectiveness of a multidimensional approach for prevention of ventilator-associated pneumonia in adult intensive care units from 14 developing countries of four continents: findings of the International Nosocomial Infection Control Consortium. *Crit Care Med*. 2012;**40:** 3121–3128.
51. Rosenthal VD, Álvarez-Moreno C, Villamil-Gómez W, et al. Effectiveness of a multidimensional approach to reduce ventilator-associated pneumonia in pediatric intensive care units of 5 developing countries: International Nosocomial Infection Control Consortium findings. *Am J Infect Control*. 2012;**40**:497–501.
52. Lo E, Nicolle L, Classen D et al. Strategies to prevent catheter-associated urinary tract infections in acute care hospitals. *Infect Control Hosp Epidemiol*. 2008;**29**(Suppl 1): S41–S50.
53. Marschall J, Mermel LA, Classen D et al. Strategies to prevent central line–associated bloodstream infections in acute care hospitals. *Infect Control Hosp Epidemiol*. 2008; **29**(Suppl 1):S22–S30.
54. Anderson DJ, Kaye KS, Classen D et al. Strategies to prevent surgical site infections in acute care hospitals. *Infect Control Hosp Epidemiol*. 2008;**29**(Suppl 1):S51–S61.
55. Gilio AE, Stape A, Pereira CR, Cardoso MF, Silva CV, Troster EJ. Risk factors for nosocomial infections in a critically ill pediatric population: a 25-month prospective cohort study. *Infect Control Hosp Epidemiol*. 2000;**21**:340–342.
56. Barnum H. *Public Hospitals in Developing Countries: Resource Use, Cost, Financing*. Baltimore, MD: Johns Hopkins University Press; 1993.
57. Fica A, Jemenao MI, Bilbao P, et al. Emergency of vancomycin-resistant *Enterococcus* infections in a teaching hospital in Chile [in Spanish]. *Rev Chilena Infectol*. 2007;**24**:462–471.
58. Zárate MS, Gales A, Jordá-Vargas L, et al. Environmental contamination during a vancomycin-resistant enterococci outbreak at a hospital in Argentina [in Spanish]. *Enferm Infecc Microbiol Clin*. 2007;**25**:508–512.
59. Corso AC, Gagetti PS, Rodriguez MM et al. Molecular epidemiology of vancomycin-resistant *Enterococcus faecium* in Argentina. *Int J Infect Dis*. 2007;**11**:69–75.
60. Lizaso D, Aguilera CK, Correa M et al. Nosocomial bloodstream infections caused by gram-negative bacilli: epidemiology and risk factors for mortality [in Spanish]. *Rev Chil Infect*. 2008;**25**:368–373.
61. Bello H, González G, Dominguez M, Zemelman R, Garcia A, Mella S. Activity of selected beta-lactams, ciprofloxacin, and amikacin against different *Acinetobacter baumannii* biotypes from Chilean hospitals. *Diagn Microbiol Infect Dis*. 1997; **28**:183–186.
62. Dutta P, Mitra U, Rasaily R et al. Prospective study of nosocomial enteric infections in a pediatric hospital, Calcutta. *Indian Pediatr* 1993;**30**:187–194.
63. Tang SS, Apisarnthanarak A, Hsu LY. Mechanisms of β-lactam antimicrobial resistance and epidemiology of major community- and healthcare-associated multidrug-resistant bacteria. *Adv Drug Deliv*. 2014, **78**:3–13.
64. Cotton MF, Berkowitz FE, Berkowitz Z, Becker PJ, Heney C. Nosocomial infections in black South African children. *Pediatr Infect Dis J*. 1989;**8**:676–683.
65. Shekhawat PS, Singh RN, Shekhawat R, Joshi KR. Nosocomial infections in pediatric and neonatal ward of Umaid Hospital, Jodhpur: a cross-sectional study. *Indian Pediatr*. 1992;**29**:384–385.
66. Aaby P, Bukh J, Lisse IM, Smits AJ. Introduction of measles into a highly immunised West African community: the role of health care institutions. *J Epidemiol Community Health*. 1985;**39**:113–116.
67. Madhi SA, Ismail K, O'Reilly C, Cutland C. Importance of nosocomial respiratory syncytial virus infections in an African setting. *Trop Med Int Health*. 2004;**9**:491–498.
68. Avendaño LF, Larrañaga C, Palomino MA et al. Community- and hospital-acquired respiratory syncytial virus infections in Chile. *Pediatr Infect Dis J*. 1991;**10**:564–568.
69. Reichler MR, Rakovsky J, Slacikova M et al. Spread of multi drug resistant *Streptococcus pneumoniae* among hospitalized children in Slovakia. *J Infect Dis*. 1996;**173**:374–379.
70. Rodrigues A, de Carvalho M, Monteiro S et al. Hospital surveillance of rotavirus infection and nosocomial transmission of rotavirus disease among children in Guinea-Bissau. *Pediatr Infect Dis J*. 2007;**26**:233–237.
71. Abiodun PO, Omoigberale A. Prevalence of nosocomial rotavirus infection in hospitalized children in Benin City, Nigeria. *Ann Trop Paediatr*. 1994;**14**:85–88.
72. Gusmao RH, Mascarenhas JD, Gabbay YB et al. Rotaviruses as a cause of nosocomial, infantile diarrhoea in northern Brazil: pilot study. *Mem Inst Oswaldo Cruz*. 1995; **90**:743–749.
73. Biellik RJ, Clements CJ. Strategies for minimizing nosocomial transmission of measles [in Spanish]. *Rev Panam Salud Publica*. 1998;**4**:350–357.
74. Navarrete-Navarro S, Avila-Figueroa C, Ruiz-Gutiérrez E, Ramírez-Galván L, Santos JI. Nosocomial measles: a proposal for its control in hospitals [in Spanish]. *Bol Med Hosp Infant Mex* 1990;**47**:495–499.
75. Ritacco V, Di Lonardo M, Reniero A et al. Nosocomial spread of human immunodeficiency virus-related multidrug- resistant tuberculosis in

Buenos Aires. *J Infect Dis*. 1997;**176**:637–642.

76. Harries AD, Kamenya A, Namarika D et al. Delays in diagnosis and treatment of smear-positive tuberculosis and the incidence of tuberculosis in hospital nurses in Blantyre, Malawi. *Trans R Soc Trop Med Hyg*. 1997;**91**:15–17.
77. Wilkinson D, Crump J, Pillay M, Sturm AW. Nosocomial transmission of tuberculosis in Africa documented by restriction fragment length polymorphism. *Trans R Soc Trop Med Hyg*. 1997;**91**:318.
78. Joshi R, Reingold AL, Menzies D, Pai M. Tuberculosis among health-care workers in low- and middle-income countries: a systematic review. *PLoS Med*. 2006;**3**:e494.
79. Ostrosky-Zeichner L, Baez-Martinez R, Rangel-Frausto MS, Ponce-de-Leon S. Epidemiology of nosocomial outbreaks: 14-year experience at a tertiary-care center. *Infect Control Hosp Epidemiol*. 2000;**21**:527–529.
80. Wenzel RP, Thompson RL, Landry SM, et al. Hospital-acquired infections in intensive care unit patients: an overview with emphasis on epidemics. *Infect Control* 1983; **4**:371–375.
81. Simonsen L, Kane A, Lloyd J, Zaffran M, Kane M. Unsafe injections in the developing world and transmission of blood-borne pathogens: a review. *Bull World Health Organ* 1999;**77**:789–800.
82. Kane A, Lloyd J, Zaffran M, Simonsen L, Kane M. Transmission of hepatitis B, hepatitis C and human immunodeficiency viruses through unsafe injections in the developing world: model-based regional estimates. *Bull World Health Organ*. 1999;**77**:801–807.
83. Kermode M. Unsafe injections in low-income country health settings: need for injection safety promotion to prevent the spread of blood-borne viruses. *Health Promot Int*. 2004; **19**:95–103.
84. Kermode M. Healthcare worker safety is a pre-requisite for injection safety in developing countries. *Int J Infect Dis*. 2004;**8**:325–327.
85. Hutin YJ, Chen RT. Injection safety: a global challenge. *Bull World Health Organ*. 1999;**77**:787–788.
86. Lakshman M, Nichter M. Contamination of medicine injection paraphernalia used by registered medical practitioners in south India: an ethnographic study. *Soc Sci Med*. 2000; **51**:11–28.
87. Khan AJ, Luby SP, Fikree F et al. Unsafe injections and the transmission of hepatitis B and C in a periurban community in Pakistan. *Bull World Health Organ*. 2000;**78**: 956–963.
88. Dicko M, Oni AQ, Ganivet S, Kone S, Pierre L, Jacquet B. Safety of immunization injections in Africa: not simply a problem of logistics. *Bull World Health Organ*. 2000; **78**:163–169.
89. Siegel JD, Rhinehart E, Jackson M, Chiarello L. 2007 Guideline for isolation precautions: preventing transmission of infectious agents in health care settings. *Am J Infect Control*. 2007;**35**:S65–S164.
90. Mayhall CG. In pursuit of ventilator-associated pneumonia prevention: the right path. *Clin Infect Dis*. 2007;**45**:712–714.
91. Apisarnthanarak A, Thongphubeth K, Sirinvaravong S et al. Effectiveness of multifaceted hospital-wide quality improvement programs featuring an intervention to remove unnecessary urinary catheters at a tertiary care center in Thailand. *Infect Control Hosp Epidemiol*. 2007;**28**:791–798.
92. Apisarnthanarak A, Suwannakin A, Maungboon P, Warren DK, Fraser VJ. Long-term outcome of an intervention to remove unnecessary urinary catheters, with and without a quality improvement team, in a Thai tertiary care center. *Infect Control Hosp Epidemiol*. 2008;**29**:1094–1095.
93. Gastmeier P, Sohr D, Schwab F et al. Ten years of KISS: the most important requirements for success. *J Hosp Infect*. 2008;**70**(Suppl 1):11–16.
94. Gastmeier P, Geffers C, Brandt C et al. Effectiveness of a nationwide nosocomial infection surveillance system for reducing nosocomial infections. *J Hosp Infect*. 2006;**64**:16–22.
95. McKee C, Berkowitz I, Cosgrove SE et al. Reduction of catheter-associated bloodstream infections in pediatric patients: experimentation and reality. *Pediatr Crit Care Med*. 2008; **9**:40–46.
96. Lobo RD, Levin AS, Gomes LM et al. Impact of an educational program and policy changes on decreasing catheter-associated bloodstream infections in a medical intensive care unit in Brazil. *Am J Infect Control*. 2005;**33**:83–87.
97. Zack JE, Garrison T, Trovillion E et al. Effect of an education program aimed at reducing the occurrence of ventilator-associated pneumonia. *Crit Care Med*. 2002;**30**:2407–2412.
98. Babcock HM, Zack JE, Garrison T et al. An educational intervention to reduce ventilator-associated pneumonia in an integrated health system: a comparison of effects. *Chest*. 2004;**125**:2224–2231.
99. Resar R, Pronovost P, Haraden C, Simmonds T, Rainey T, Nolan T. Using a bundle approach to improve ventilator care processes and reduce ventilator-associated pneumonia. *Jt Comm J Qual Patient Saf*. 2005;**31**:243–248.
100. Institute for Healthcare Improvement (IHI). Implement the Ventilator Bundle. Available at: www.ihi.org/IHI/Topics/Critical- Care/IntensiveCare/Changes/ImplementtheVentilatorBundle.htm. Accessed September 29, 2009.
101. Huang WC, Wann SR, Lin SL et al. Catheter-associated urinary tract infections in intensive care units can be reduced by prompting physicians to remove unnecessary catheters. *Infect Control Hosp Epidemiol*. 2004;**25**:974–978.
102. Rosenthal VD, Guzman S, Safdar N. Effect of education and performance feedback on rates of catheter-associated urinary tract infection in intensive care units in Argentina. *Infect Control Hosp Epidemiol*. 2004;**25**:47–50.
103. Goetz AM, Kedzuf S, Wagener M, Muder RR. Feedback to nursing staff as an intervention to reduce catheter-associated urinary tract infections. *Am J Infect Control*. 1999;**27**:402–404.
104. Stephan F, Sax H, Wachsmuth M, Hoffmeyer P, Clergue F, Pittet D. Reduction of urinary tract infection and antibiotic use after surgery: a controlled, prospective, before-after intervention study. *Clin Infect Dis*. 2006;**42**:1544–1551.
105. Saint S, Kaufman SR, Thompson M, Rogers MA, Chenoweth CE. A reminder reduces urinary catheterization in hospitalized patients. *Jt Comm J Qual Patient Saf*. 2005;**31**:455–462.
106. Garibaldi RA, Mooney BR, Epstein BJ et al. An evaluation of daily bacteriologic monitoring to identify preventable episodes of catheter-associated urinary tract infection. *Infect Control*. 1982;**3**:466–470.

107. Meddings J, Macy M, Rogers MA. Reminder systems to reduce urinary catheter use and catheter-associated urinary tract infection in hospitalized patients: a systematic review and meta-analysis. In: Program and abstracts of the 19th Annual Scientific Meeting of the Society for Healthcare Epidemiology of America; March 19–22, 2009; San Diego, CA. Abstract 141.

108. Parras F, Ena J, Bouza E et al. Impact of an educational program for the prevention of colonization of intravascular catheters. *Infect Control Hosp Epidemiol*. 1994;**15**:239–242.

109. Maas A, Flament P, Pardou A et al. Central venous catheter–related bacteraemia in critically ill neonates: risk factors and impact of a prevention programme. *J Hosp Infect*. 1998; **40**:211–224.

110. Eggimann P, Harbarth S, Constantin MN et al. Impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care. *Lancet*. 2000;**355**:1864–1868.

111. Sherertz RJ, Ely EW, Westbrook DM et al. Education of physicians-in-training can decrease the risk for vascular catheter infection. *Ann Intern Med*. 2000;**132**:641–648.

112. Coopersmith CM, Rebmann TL, Zack JE et al. Effect of an education program on decreasing catheter-related bloodstream infections in the surgical intensive care unit. *Crit Care Med*. 2002;**30**:59–64.

113. Warren DK, Zack JE, Cox MJ et al. An educational intervention to prevent catheter-associated bloodstream infections in a non-teaching, community medical center. *Crit Care Med*. 2003;**31**:1959–1963.

114. Rosenthal VD, Guzman S, Pezzotto SM et al. Effect of an infection control program using education and performance feedback on rates of intravascular device–associated bloodstream infections in intensive care units in Argentina. *Am J Infect Control*. 2003;**31**:405–409.

115. Warren DK, Cosgrove SE, Diekema DJ et al. A multicenter intervention to prevent catheter-associated bloodstream infections. *Infect Control Hosp Epidemiol*. 2006;**27**: 662–669.

116. Berenholtz SM, Pronovost PJ, Lipsett PA et al. Eliminating catheter-related bloodstream infections in the intensive care unit. *Crit Care Med*. 2004;**32**:2014–2020.

117. Pronovost P, Needham D, Berenholtz S et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med*. 2006;**355**:2725–2732.

118. Griffin FA. 5 Million Lives Campaign: reducing methicillin-resistant *Staphylococcus aureus* (MRSA) infections. *Jt Comm J Qual Patient Saf*. 2007;**33**:726–731.

119. Kunaratanapruk S, Silpapojakul K. Unnecessary hospital infection control practices in Thailand: a survey. *J Hosp Infect*. 1998;**40**:55–59.

120. Gomez MI, Acosta-Gnass SI, Mosqueda-Barboza L, Basualdo JA. Reduction in surgical antibiotic prophylaxis expenditure and the rate of surgical site infection by means of a protocol that controls the use of prophylaxis. *Infect Control Hosp Epidemiol*. 2006;**27**:1358–1365.

121. Hermsen ED, Smith Shull S, Puumala SE, Rupp ME. Improvement in prescribing habits and economic outcomes associated with the introduction of a standardized approach for surgical antimicrobial prophylaxis. *Infect Control Hosp Epidemiol*. 2008;**29**:457–461.

122. Apisarnthanarak A, Jirajariyavej S, Thongphubeth K, Yuekyen C, Warren DK, Fraser VJ. Outbreak of postoperative endophthalmitis in a Thai tertiary care center. *Infect Control Hosp Epidemiol*. 2008;**29**:564–566.

123. Apisarnthanarak A, Greene MT, Kennedy EH, Khawcharoenporn T, Krein S, Saint S. National survey of practices to prevent healthcare-associated infections in Thailand. *Infect Control Hosp Epidemiol*. 2012;**33**:711–717.

124. Sakamoto F, Sakihama T, Saint S, Greene MT, Ratz D, Tokuda Y. Health care-associated infection prevention in Japan: the role of safety culture. *Am J Infect Control*. 2014;**42**:888–893.

125. Apisarnthanarak A, Danchaivijitr S, Bailey TC, Fraser VJ. Inappropriate antibiotic use in a tertiary care center in Thailand: an incidence study and review of experience in Thailand. *Infect Control Hosp Epidemiol*. 2006;**27**:416–420.

126. Paterson DL. The role of antimicrobial management programs in optimizing antibiotic prescribing within hospitals.*Clin Infect Dis*. 2006;**42** (Suppl 2):S90–S95.

127. Calfee DP, Salgado CD, Classen D et al. Strategies to prevent transmission of methicillin-resistant *Staphylococcus aureus* in acute care hospitals. *Infect Control Hosp Epidemiol*. 2008;**29**(Suppl 1):S62–S80.

128. Cohen AL, Calfee D, Fridkin SK et al. Recommendations for metrics for multidrug-resistant organisms in healthcare settings: SHEA/HICPAC position paper. *Infect Control Hosp Epidemiol*. 2008;**29**:901–913.

129. Apisarnthanarak A, Warren DK, Fraser VJ. Creating a cohort area to limit transmission of pandrug-resistant *Acinetobacter baumannii* in a Thai tertiary care center. *Clin Infect Dis*. 2009;**48**:1487–1488.

130. Apisarnthanarak A, Danchaivijitr S, Khawcharoenporn T et al. Effectiveness of education and an antibiotic-control program in a tertiary care hospital in Thailand. *Clin Infect Dis*. 2006;**42**:768–775.

131. Apisarnthanarak A, Mundy LM. Inappropriate use of carbapenems in Thailand: a need for better education on de-escalation therapy. *Clin Infect Dis*. 2008;**47**:858–859.

132. Apisarnthanarak A, Fraser VJ. Feasibility and efficacy of infection-control interventions to reduce the number of nosocomial infections and drug-resistant microorganisms in developing countries: what else do we need? *Clin Infect Dis*. 2009;**48**:22–24.

133. Apisarnthanarak A, Pinitchai U, Thongphubeth K et al. Effectiveness of an educational program to reduce ventilator-associated pneumonia in a tertiary care center in Thailand: a 4-year study. *Clin Infect Dis*. 2007;**45**:704–711.

134. Peleg AY, Seifert H, Paterson DL. *Acinetobacter baumannii*:emergence of a successful pathogen. *Clin Microbiol Rev*. 2008;**21**:538–582

135. Apisarnthanarak A, Pinitchai U, Warachan B, Warren DK, Khawcharoenporn T, Hayden MK. Effectiveness of infection prevention measures featuring advanced source control and environmental cleaning to limit transmission of extremely-drug resistant Acinetobacter baumannii in a Thai intensive care unit: an analysis before and after extensive flooding. *Am J Infect Control*. 2014;**42**:116–121.

136. Khawcharoenporn T, Apisarnthanarak A, Mundy LM. National survey of antimicrobial stewardship programs in Thailand. *Am J Infect Control*. 2013;**41**:86–88.

137. Apisarnthanarak A, Khawcharoenporn T, Mundy LM. Practices to prevent multidrug-resistant Acinetobacter baumannii and methicillin-resistant Staphylococcus aureus in Thailand: a national survey. *Am J Infect Control*. 2013;**41**:416–421.

138. Rose R, Hunting KJ, Townsend TR, Wenzel RP. Morbidity/mortality and economics of hospital-acquired blood stream infections: a controlled study. *South Med J*. 1977;**70**:1267–1269.

139. Spengler RF, Greenough WB 3rd. Hospital costs and mortality attributed to nosocomial bacteremias. *JAMA*. 1978;**240**:2455–2458.

140. Kappstein I, Schulgen G, Beyer U, Geiger K, Schumacher M, Daschner FD. Prolongation of hospital stay and extra costs due to ventilator-associated pneumonia in an intensive care unit. *Eur J Clin Microbiol Infect Dis*. 1992;**11**:504–508.

141. Kappstein I, Schulgen G, Fraedrich G, Schlosser V, Schumacher M, Daschner FD. Added hospital stay due to wound infections following cardiac surgery. *Thorac Cardiovasc Surg*. 1992;**40**:148–151.

142. Poulsen KB, Bremmelgaard A, Sorensen AI, Raahave D, Petersen JV. Estimated costs of postoperative wound infections: a case-control study of marginal hospital and social se- curity costs. *Epidemiol. Infect*. 1994;**113**:283–295.

143. Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infection in critically ill patients: excess length of stay, extra costs, and attributable mortality. *JAMA*. 1994;**271**:1598–1601.

144. Coello R, Glenister H, Fereres J et al. The cost of infection in surgical patients: a case-control study. *J Hosp Infect*. 1993;**25**:239–250.

145. Girard R, Fabry J, Meynet R, Lambert DC, Sepetjan M. Costs of nosocomial infection in a neonatal unit. *J Hosp Infect*. 1983;**4**:361–366.

146. Medina M, Martínez-Gallego G, Sillero-Arenas M, Delgado-Rodríguez M. Risk factors and length of stay attributable to hospital infections of the urinary tract in general surgery patients [in Spanish]. *Enferm Infecc Microbiol Clin* 1997;**15**:310–314.

147. Digiovine B, Chenoweth C, Watts C, Higgins M. The attributable mortality and costs of primary nosocomial blood- stream infections in the intensive care unit. *Am J Respir Crit Care Med*. 1999;**160**:976–981.

148. Plowman R, Graves N, Griffin MA et al. The rate and cost of hospital-acquired infections occurring in patients admitted to selected specialties of a district general hospital in England and the national burden imposed. *J Hosp Infect*. 2001; **47**:198–209.

149. Pirson M, Dramaix M, Struelens M, Riley TV, Leclercq P. Costs associated with hospital-acquired bacteraemia in a Belgian hospital. *J Hosp Infect*. 2005;**59**:33–40.

150. Sheng WH, Wang JT, Lu DC, Chie WC, Chen YC, Chang SC. Comparative impact of hospital-acquired infections on medical costs, length of hospital stay and outcome between community hospitals and medical centres. *J Hosp Infect*. 2005;**59**:205–214.

151. Warren DK, Quadir WW, Hollenbeak CS, Elward AM, Cox MJ, Fraser VJ. Attributable cost of catheter-associated bloodstream infections among intensive care patients in a non-teaching hospital. *Crit Care Med*. 2006;**34**:2084–2089.

152. Eickhoff TC. General comments on the study on the efficacy of nosocomial infection control (SENIC Project). *Am J Epidemiol*. 1980;**111**:465–469.

153. Haley RW, Quade D, Freeman HE, Bennett JV. Study on the Efficacy of Nosocomial Infection Control (SENIC Project): summary of study design. *Am J Epidemiol*. 1980;**111**: 472–485.

154. Haley RW, Culver DH, White JW, et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. *Am J Epidemiol*. 1985; **121**:182–205.

155. Harbarth S, Sax H, Gastmeier P. The preventable proportion of nosocomial infections: an overview of published reports. *J Hosp Infect*. 2003;**54**:258–266.

156. Wakefield DS, Helms CM, Massanari RM, Mori M, Pfaller M. Cost of nosocomial infection: relative contributions of laboratory, antibiotic, and per diem costs in serious *Staphylococcus aureus* infections. *Am J Infect Control*. 1988;**16**:185–189.

157. Shulkin DJ, Kinosian B, Glick H, Glen-Puschett C, Daly J, Eisenberg JM. The economic impact of infections: an analysis of hospital costs and charges in surgical patients with cancer. *Arch Surg*. 1993;**128**:449–452.

158. Wenzel RP. The Lowbury Lecture: the economics of nosocomial infections. *J Hosp Infect*. 1995;**31**:79–87.

159. Pittet D, Sax H, Hugonnet S, Harbarth S. Cost implications of successful hand hygiene promotion. *Infect Control Hosp Epidemiol*. 2004;**25**:264–266.

160. Obasanjo O, Perl TM. Cost-benefit and effectiveness of nosocomial surveillance methods. *Curr Clin Top Infect Dis*. 2001;**21**:391–406.

161. VandenBergh MF, Kluytmans JA, van Hout BA et al. Cost- effectiveness of perioperative mupirocin nasal ointment in cardiothoracic surgery. *Infect Control Hosp Epidemiol*. 1996;**17**:786–792.

162. Daschner FD. How cost-effective is the present use of antiseptics? *J Hosp Infect*. 1988;**11**(Suppl A):227–235.

163. Graves N. Economics and preventing hospital-acquired infection. *Emerg Infect Dis*. 2004;**10**:561–566.

164. Graves N, Halton K, Lairson D. Economics and preventing hospital-acquired infection: broadening the perspective. *Infect Control Hosp Epidemiol*. 2007;**28**:178–184.

165. Nyamogoba H, Obala AA. Nosocomial infections in developing countries: cost effective control and prevention. *East Afr Med J*. 2002;**79**:435–441.

166. Khan MM, Celik Y. Cost of nosocomial infection in Turkey: an estimate based on the university hospital data. *Health Serv Manage Res*. 2001;**14**:49–54.

167. Kothari A, Sagar V, Ahluwalia V, Pillai BS, Madan M. Costs associated with hospital-acquired bacteraemia in an Indian hospital: a case-control study. *J Hosp Infect*. 2009;**71**: 143–148.

168. Puskas JD, Williams WH, Mahoney EM et al. Off-pump vs. conventional coronary artery bypass grafting: early and 1-year graft patency, cost, and quality-of-life outcomes: a randomized trial. *JAMA* 2004;**291**:1841–1849.

169. Talaat M, Kandeel A, Rasslan O et al. Evolution of infection control in

Egypt: achievements and challenges. *Am J Infect Control* 2006;**34**:193–200.

170. Murphy DM, Alvarado CJ, Fawal H. The business of infection control and epidemiology. *Am J Infect Control*. 2002; **30**:75–76.
171. Scheckler WE, Brimhall D, Buck AS et al. Requirements for infrastructure and essential activities of infection control and epidemiology in hospitals: a consensus panel report. Society for Healthcare Epidemiology of America. *Infect Control Hosp Epidemiol*. 1998;**19**:114–124.
172. National Healthcare Safety Network (NHSN) Web site. Updated May 11, 2005. Available at: www.cdc.gov/nhsn/. Accessed August 13, 2009.
173. Boyce JM, Pittet D. Guideline for hand hygiene in health-care settings: recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *Infect Control Hosp Epidemiol*. 2002;**23**:S3–S40.
174. Issack MI. Unnecessary hospital infection control practices in developing countries. *J Hosp Infect*. 1999;**42**:339–341.
175. Picheansatian W, Moongtui W, Soparatana P, Chittreecheur J, Apisarnthanarak A, Danchaivijitr S. Evaluation of a training course in infection control for nurses. *J Med Assoc Thai*. 2005;**88**(Suppl 10):S171–S176.
176. Pethyoung W, Picheansathian W, Boonchuang P, Apisarnthanarak A, Danchaivijitr S. Effectiveness of education and quality control work group focusing on nursing practices for prevention of ventilator-associated pneumonia. *J Med Assoc Thai*. 2005;**88** (Suppl 10):S110–S114.
177. Danchaivijitr S, Chakpaiwong S, Jaturatramrong U, Wachiraporntip A, Cherdrungsi R, Sripalakij S. Program on nosocomial infection in the curricula of medicine, dentistry, nursing and medical technology in Thailand. *J Med Assoc Thai*. 2005;**88** (Suppl 10):S150–S154.
178. Danchaivijitr S, Assanasen S, Trakuldis M, Waitayapiches S, Santiprasitkul S. Problems and obstacles in implementation of nosocomial infection control in Thailand. *J Med Assoc Thai*. 2005;**88** (Suppl 10):S70–S74.
179. Perencevich EN, Stone PW, Wright SB, Carmeli Y, Fisman DN, Cosgrove SE. Raising standards while watching the bottom line: making a business case for infection control. *Infect Control Hosp Epidemiol*. 2007;**28**:1121–1133.
180. Furuno JP, Schweizer ML, McGregor JC, Perencevich EN. Economics of infection control surveillance technology: cost-effective or just cost? *Am J Infect Control*. 2008;**36**:S12–S17.
181. Dunagan WC, Murphy DM, Hollenbeak CS, Miller SB. Making the business case for infection control: pitfalls and opportunities. *Am J Infect Control*. 2002;**30**:86–92.
182. World Health Organization (WHO). WHO Recommendations for Routine Immunizations – Summary Tables. Updated February 27, 2015. Available at: www.who.int/immunization/policy/immunization_tables/en/ Accessed November 22, 2015.
183. World Health Organization. Use of tuberculosis interferon-gamma release assays (IGRAs) in low- and middle-income countries: policy statement. 2011. WHO/HTM/TB/2011.18. Available at: http://apps.who.int/iris/bitstream/10665/44759/1/9789241502672_eng.pdf?ua=1&ua=1. Accessed November 21, 2015.
184. Apisarnthanarak A, Thongphubeth K, Yuekyen C, Mundy LM. Postexposure detection of *Mycobacterium tuberculosis* infection in health care workers in resource-limited settings. *Clin Infect Dis*. 2008;**47**:982–984.
185. Khawcharoenporn T, Apisarnthanarak A, Thongphubeth K, Yuekyen C, Mundy LM. Tuberculin skin tests among medical students with prior bacille Calmette Guérin vaccination in a setting with a high prevalence of tuberculosis. *Infect Control Hosp Epidemiol*. 2009;**30**:705–709.
186. Roth VR, Garrett DO, Laserson KF et al. A multicenter evaluation of tuberculin skin test positivity and conversion among health care workers in Brazilian hospitals. *Int J Tuberc Lung Dis*. 2005;**9**:1335–1442.
187. World Health Organization (WHO). WHO policy on TB infection control in health-care facilities, congregate settings and households. 2009. WHO/HTM/TB/2009.419. Available at: http://apps.who.int/iris/bitstream/10665/44148/1/9789241598323_eng.pdf?ua=1. Accessed November 21, 2015.
188. da Costa PA, Trajman A, Mello FC et al. Administrative measures for preventing *Mycobacterium tuberculosis* infection among HCWs in a teaching hospital in Rio de Janeiro, Brazil. *J Hosp Infect*. 2009;**72**:57–64.
189. Harries AD, Hargreaves NJ, Gausi F, Kwanjana JH, Salaniponi FM. Preventing tuberculosis among health workers in Malawi. *Bull World Health Organ*. 2002;**80**:526–531.
190. Yanai H, Limpakarnjanarat K, Uthaivoravit W, Mastro TD, Mori T, Tappero JW. Risk of *Mycobacterium tuberculosis* infection and disease among health care workers, Chiang Rai, Thailand. *Int J Tuberc Lung Dis*. 2003;**7**:36–41
191. Biscotto CR, Pedroso ER, Starling CE, Roth VR. Evaluation of N95 respirator use as a tuberculosis control measure in a resource-limited setting. *Int J Tuberc Lung Dis*. 2005;**9**: 545–549.
192. World Health Organization. Sharp injuries: global burden of disease from sharps injuries to health-care workers. 2003. Available at: www.who.int/quantifying_ehimpacts/publications/9241562463/en/. Accessed November 21, 2015.
193. Wilburn SQ, Eijkemans G. Preventing needlestick injuries among healthcare workers: a WHO-ICN collaboration. *Int J Occup Environ Health*. 2004;**10**:451–456.
194. World Health Organization. Protecting Healthcare Workers: Preventing Needlestick Injuries Toolkit. 2005. Available at: www.who.int/occupational_health/activities/pnitoolkit/en/. Accessed November 21, 2015.
195. World Health Organization. WHO guideline on the use of safety-engineered syringes for intramuscular, intradermal and subcutaneous injections in health-care settings. 2015. WHO/HIS/SDS/2015.5. Available at: www.who.int/injection_safety/global-campaign/injection-safety_guidline.pdf?ua=1. Accessed December 8, 2015.
196. AIDE MEMOIRE. World Health Organization 2003; Panlilio AL, Cardo DM, Grohskopf LA, Heneine W, Ross CS. Updated US Public Health Service guidelines for the management of occupational exposures to HIV and recommendations for postexposure prophylaxis. *MMWR Recomm Rep*. 2005;**54**(RR-9):1–17.
197. Chan-Yeung M. Severe acute respiratory syndrome (SARS) and

healthcare workers. *Int J Occup Environ Health*. 2004;**10**:421–427.

198. World Health Organization. Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care. April 2014. Available at: www.who.int/csr/bioriskreduction/infection_control/publication/en/. Accessed December 11, 2015.
199. Mitchell R, Roth V, Gravel D et al. Are health care workers protected? An observational study of selection and removal of personal protective equipment in Canadian acute care hospitals. *Am J Infect Control*. 2013 Mar;**41**(3):240–244.
200. Fischer WA 2nd, Hynes NA, Perl TM. Protecting healthcare workers from Ebola: personal protective equipment is critical but is not enough. *Ann Intern Med*. 2014; **161**:753–754.
201. Apisarnthanarak A, Mundy LM. Infection control for emerging infectious diseases in developing countries and resource-limited settings. *Infect Control Hosp Epidemiol*. 2006; **27**:885–887.
202. World Health Organization. Interim Infection Prevention and Control Guidance for Care of Patients with Suspected or Confirmed Filovirus Haemorrhagic Fever in Health-Care Settings, with Focus on Ebola. December 2014. Available at: www.who.int/csr/resources/publications/ebola/filovirus_infection_control/en. Accessed December 22, 2015.
203. World Health Organization. Vaccines against influenza WHO position paper – November 2012. *Wkly Epidemiol Rec*. 2012;**47**:461–476. Available at: www.who.int/wer. Accessed December 11, 2015.
204. Apisarnthanarak A, Puthavathana P, Kitphati R, Auewarakul P, Mundy LM. Outbreaks of influenza A among nonvaccinated healthcare workers: implications for resource-limited settings. *Infect Control Hosp Epidemiol*. 2008;**29**:777–780.
205. Duffy RE, Couto B, Pessoa JM, et al. Improving water quality can reduce pyrogenic reactions associated with reuse of cardiac catheters. *Infect Control Hosp Epidemiol*. 2003;**24**:955–960.
206. Archibald LK, Khoi NN, Jarvis WR, et al. Pyrogenic reactions in hemodialysis patients, Hanoi, Vietnam. *Infect Control Hosp Epidemiol*. 2006;**27:** 424–426.
207. Amarante JM, Toscano CM, Pearson ML, Roth V, Jarvis WR, Levin AS. Reprocessing and reuse of single-use medical devices used during hemodynamic procedures in Brazil: a widespread and largely overlooked problem. *Infect Control Hosp Epidemiol*. 2008;**29**:854–858.
208. World Health Organization. WHO guideline on the use of safety-engineered syringes for intramuscular, intradermal and subcutaneous injections in health-care settings. 2015. WHO/HIS/SDS/2015.5. Available at: www.who.int/injection_safety/global-campaign/injection-safety_guidline.pdf?ua=1. Accessed December 8, 2015.
209. World Health Organization. Ten Years of Clean Care is Safer Care: 2005–2015. Available at: www.who.int/gpsc/ccsc_ten-years/en/. Accessed December 11, 2015.
210. World Health Organization. Clean care is safer care: tools and resources. Available at: www.who.int/gpsc/5may/tools/en/. Accessed December 11, 2015.
211. World Health Organization (WHO). World Health Organization guidelines on hand hygiene in health care. Geneva: WHO; 2009. Available at: www.who.int/gpsc/5may/en/. Accessed December 11, 2015.
212. Allegranzi B, Memish ZA, Donaldson L et al. Religion and culture: potential undercurrents influencing hand hygiene promotion in health care. *Am J Infect Control*. 2009;**37**: 28–34.
213. Salmon S, Pittet D, Sax H, McLaws ML. The "My five moments for hand hygiene" concept for the overcrowded setting in resource-limited healthcare systems. *J Hosp Infect*. 2015;**91**:95–99.
214. International Federation of Infection Control (IFIC). Available at: www.theIFIC.org. Accessed December 12, 2015.
215. Hambraeus A. Establishing an infection control structure. *J Hosp Infect* 1995;**30**(Suppl):232–240.

Chapter 23

The Role of the Laboratory in Prevention of Healthcare-Associated Infections

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Because infection prevention requires the ability to detect infections when they occur, the laboratory, particularly the clinical microbiology laboratory, is an essential component of any comprehensive infection prevention program (IPP). As medical technology advances, the need for accurate and rapid detection of organisms and identification of antimicrobial resistance is more important than ever. Emerging molecular and proteomic technologies can increase the speed, accuracy, and sensitivity of detection methods and have allowed the laboratory to identify organisms that were previously unknown or inaccurately identified, as well as those that do not grow readily in culture.[1–5] Molecular and proteomic techniques also enable the microbiologist to identify antimicrobial resistance genes and to perform more discriminating strain typing, thereby facilitating studies of healthcare-associated pathogen transmission.[6–9] However, these new technologies can be costly, and determining the most appropriate and cost-effective use of these powerful new diagnostic approaches can be challenging. We hope in this chapter to outline the key ways in which the laboratory can help prevent healthcare-associated infections (HAIs) and improve antimicrobial stewardship.

The most important roles of the clinical microbiology laboratory in the prevention of HAIs can be divided into five major categories: (1) surveillance, (2) outbreak detection and management, (3) antimicrobial stewardship, (4) advisory, and (5) educational.

Surveillance

Review of the clinical microbiology laboratory records is the most common method for case finding in HAI surveillance: it is estimated that more than 80 percent of HAIs may be identified by a review of positive cultures from the laboratory.[10,11] In addition, the National Healthcare Safety Network (NHSN) now includes metrics for "LabID Events" that track healthcare-associated methicillin-resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* using laboratory- reported data.[12] Reporting of these rates is now mandated by the Centers for Medicare and Medicaid Services (CMS), and the rates are used to reward and penalize healthcare facilities in "pay-for-performance" programs.[13] *Therefore, the most important role of the microbiology laboratory is to promptly and accurately detect healthcare-associated pathogens and their antimicrobial resistance patterns*. The laboratory must also work with the IPP and the hospital's information technology department to determine how microbiology data are delivered and linked to other surveillance data to streamline this process (see Chapter 10).

Major surveillance challenges facing the clinical microbiology laboratory include the continued emergence of novel infectious agents (e.g., new influenza strains, emerging threats such as MERS-COV or Zika virus) and antimicrobial-resistant pathogens (e.g., multidrug-resistant *Acinetobacter* spp., carbapenem-resistant *Enterobacteriaceae*), as well as new governmental and public health mandates that place pressure on the laboratory to provide more robust surveillance support (e.g., mandated active surveillance cultures in some states, pay-for-performance programs, and public reporting of HAI rates).[14]

The spectrum of pathogens causing HAIs continues to evolve, and can significantly vary by region and hospital. Over the past half-century, gram-positive bacteria have become the predominant causes of HAIs, with an increasing incidence of MRSA and vancomycin-resistant Enterococcus (VRE)[11,16,17] (see Chapter 16). *Candida* spp. have also emerged as a major problem.[15] By 2010, eight pathogen groups were implicated in over 80 percent of all HAIs reported to the Centers for Disease Control and Prevention (CDC) NHSN (see Sievert et al.,[18] Table 23.1). The improvement in methods to detect and identify viruses has also led to increased recognition of viral pathogens as common causes of HAI.[19]

Among bacterial causes of HAI, the ESKAPE pathogens (*E. faecium, S. aureus, Klebsiella pneumoniae*, *A. baumannii, Pseudomonas aeruginosa*, and *Enterobacter* spp.) have been identified as being both common and highly problematic due to their rates of antibiotic resistance. These pathogens are responsible for over 70 percent of HAIs in intensive care units.[20, 21] The ESKAPE pathogens that are currently of greatest concern are the multidrug-resistant gram-negative rods (MDR-GNRs;[22–2] see also Chapter 17), which include extended-spectrum beta-lactamase (ESBL) and carbapenemase-producing *Enterobacteriaceae* and multiple-or pan-drug resistant nonfermenters such as *P. aeruginosa* and *A. baumannii*[24] Rapid and accurate identification of these key HAI pathogens, including their multiple, highly complex resistance mechanisms, is important for both optimal patient care and infection prevention efforts.[7,28]

Collection and Transport of Specimens

Providing valid data for HAI surveillance begins with ensuring proper specimen collection, transport, and handling.[29–31] Specimens that are not collected or transported properly may give inaccurate results, even when handled as well as possible

Table 23.1 Rank order of the top eight pathogens associated with HAIs reported to the CDC NHSN program, 2009–2010

	N (%) by infection type									
	Overall		CLABSI		CAUTI		VAP		SSI	
Organisms	N (%)	Rank	N (%)	Rank	N (%)	Rank	N (%)	Rank	N (%)	Rank
S. aureus	12,635 (16)	1	3,735 (12)	4	442 (2)	–	2,043 (24)	1	6,415 (30)	1
Enterococcus spp.	11,207 (14)	2	5,501 (18)	2	3,183 (15)	2	45 (0.5)	–	2,442 (12)	3
Escherichia coli	9,351 (12)	3	1,206 (4)	7	5,660 (27)	1	504 (6)	6	1,981 (9)	4
CoNS	9,261 (11)	4	6,245 (21)	1	467 (2)	–	72 (1)	–	2,477 (12)	2
Candida spp.	7,683 (10)	5	4,439 (15)	3	2,698 (13)	3	183 (2)	–	363 (2)	–
Klebsiella spp.	6,470 (8)	6	2,407 (8)	5	2,365 (11)	5	854 (10)	3	844 (4)	7
P. aeruginosa	6,111 (8)	7	1,166 (4)	8	2,381 (11)	4	1,408 (17)	2	1,156 (6)	5
Enterobacter spp.	3,821 (5)	8	1,365 (5)	6	880 (4)	7	727 (9)	4	849 (4)	6

Adapted from reference 18.
CLABSI: central line associated bloodstream infection; CAUTI: catheter associated urinary tract infection; VAP: ventilator-associated pneumonia; SSI: surgical site infection; CoNS: coagulase negative staphylococci.

once they reach the laboratory. In turn, these inaccurate results may lead to incorrect clinical decisions by physicians, unnecessary labor by laboratory and IPP personnel, and unnecessary patient charges. Many healthcare-associated pathogens (e.g., coagulase-negative staphylococci, *Candida*) also commonly colonize patients' skin or mucous membranes and can easily contaminate cultures if specimens are not collected or handled properly. If contaminants are considered to be infecting organisms and result in a case meeting the HAI surveillance definition, HAI rates may be inflated through misclassification.[10,32] The laboratory must therefore monitor specimen quality carefully and also work closely with inpatient and ambulatory care units to develop and enforce strict criteria for appropriate collection and handling of clinical specimens. These procedures are necessary to ensure that the laboratory information presented to the clinician and the IPP reflects organisms that are actually associated with the site of culture rather than contaminants.

Certain laboratory findings suggest specific handling errors. For example, a persistent failure to isolate organisms from patient specimens with pathogens seen on gram-stain suggests inadequate transport media, delay or inappropriate refrigeration of specimens in transit, errors in staining, contaminated reagents, or inadequate culture techniques. Likewise, the frequent recovery of three or more different organisms in clean-voided, midstream urine specimens suggests unsatisfactory methods of specimen collection, delay in transporting specimens to the laboratory, or delay in culturing. Specimen collection and handling should be assessed regularly to detect and correct such problems; the frequency with which probable contaminants are isolated from clinical specimens can be a measure of the quality of specimen collection in a specific hospital unit. Addressing these issues is another area where laboratory and IPP personnel can work together to improve results, including decreasing contamination rates. Many hospitals also monitor specimen transport time and use this information to avoid culturing of old, inadequate specimens. Evaluation of test turnaround time has become an important element of laboratory quality assurance.[33]

Initial Evaluation of Specimens

Assessing the quality of specimens at the time that they are received in the laboratory is one of the best ways to evaluate their suitability for further microbiologic work up. Microscopic review of gram stain of sputum specimens is a proven means for determining the adequacy of these specimens;[29,34] specimens that are identified as inadequate (multiple squamous epithelial cells, no neutrophils) are not processed further and thereby prevent confusion by the clinician or epidemiologist in interpreting the results. Scoring systems for use in determining acceptable wound, vaginal, cervical, or other specimens have also been described.[29,35] Application of such criteria ensures that the information generated from the specimens that are processed completely will

more likely correlate with true infecting organisms and will reduce unnecessary laboratory costs.

The initial screening of specimens that takes place in the laboratory can have a significant impact on surveillance and HAI rates. For example, some hospital laboratories have implemented "reflex" testing algorithms for urine culture orders, whereby a urine culture is performed only for those samples that are abnormal using specific urinalysis or urine microscopy criteria.[36] This approach, meant to reduce detection of asymptomatic bacteriuria, will also impact catheter-associated urinary tract infection (CAUTI) rates. Similarly, rejection of formed stool specimens for *C. difficile* testing will reduce the number of *C. difficile*–colonized patients who are included in hospital-reported *C. difficile* infection (CDI) rates.[37]

Rapid Tests for Organism Detection and Identification

Rapid availability of laboratory test results can greatly enhance infection prevention and antimicrobial stewardship efforts. Early receipt of data allows both for timely delivery of directed antibiotic therapy, as well as rapid implementation of transmission-based precautions, if indicated. Although no formal definition of "rapid" exists for describing the time required for results to be generated, most clinicians and microbiologists consider rapid results to be those available within 2 to 4 hours.[38]

It is important to distinguish the analytic turnaround time (TAT) from the actual TAT of a test – the time from when a test is ordered to when the result is translated into a change in patient care. As Figure 23.1 outlines, both pre-analytic and post-analytic processes can result in delays in the actual TAT of even the most rapid test. For example, a rapid test for bacterial detection with analytic TAT of 2 hours that is batched and performed once daily represents little improvement in TAT over some agar-based methods. Similarly, tests that require an isolated bacterial colony to perform are not actually "rapid," given that it often takes 24 hours or more to grow the organism. Thus, the most useful rapid tests are those that can be applied directly to patient samples (or to broth cultures after an abbreviated incubation). If rapid testing is to provide any benefit, there must be a postanalytic system in place for the results to be translated into action (e.g., institution of isolation, discontinuation of isolation, decolonization, change in antibiotic therapy). Unless the performance characteristics are significantly better, there is no reason to convert to a more expensive test with shorter analytic TAT if the actual TAT of the test will not be meaningfully reduced.

There are several rapid immunologic methods that allow for prompt diagnosis when applied directly to patient samples, including detection of *Legionella pneumophila* serogroup 1 (urine), *C. difficile* (stool), *Cryptococcus neoformans* (serum or CSF), *Streptococcus pneumoniae* (urine or CSF), and *Plasmodium* spp. (serum).[39] Such tests are easy to perform, inexpensive, and can often be made available in most clinical microbiology laboratories. However, some are limited by lower sensitivity than more traditional assays.

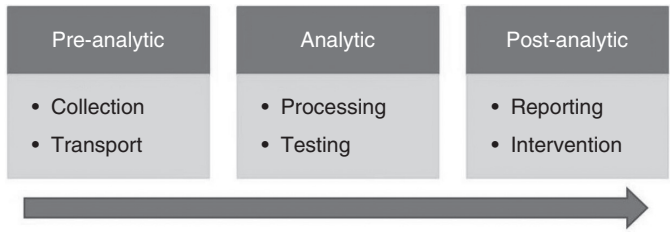


Figure 23.1 Steps included in the actual turnaround time (TAT) of a laboratory test. For infection control and antimicrobial stewardship, reductions in analytic TAT will only have an impact if promptly linked to an active intervention arm (postanalytic process). Adapted from reference 50.

Although long considered to be of great potential for enhancing the ability of the microbiology laboratory to rapidly detect and identify infections agents,[38] the use of rapid molecular methods in infectious disease diagnosis has increased substantially only in the past 5 to 10 years. The growth in the number of commercially available test kits and analyte-specific reagents (ASRs) has facilitated the use of this technology in the clinical laboratory.[40] Technological advances in real-time PCR techniques, automation, nucleic acid sequencing, multiplex analysis, and mass spectrometry promise to continue to expand the availability of rapid and accurate infectious disease diagnosis. A detailed review of currently available technologies is beyond the scope of this chapter and can be found elsewhere,[40] but the most common general approaches include nucleic acid probes, PCR (or other nucleic acid amplification technologies), and mass spectrometry.

Peptide nucleic acid fluorescent in situ hybridization (PNA- FISH) probes have been used for more rapid identification of *S. aureus*, coagulase-negative staphylococci, *E. faecalis*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *C. albicans*, *C. glabrata*, *C. tropicalis*, *C. parapsilosis*, and *C. krusei* from positive blood culture bottles and *S. agalactiae* from Lim broth cultures.[41–43] Although the use of PNA-FISH probes can provide identification within 3 hours, the requirement for prior organism growth in culture lengthens the overall TAT of this technology.

PCR-based approaches have already revolutionized the diagnosis of viral infections, with most laboratories having replaced viral culture with molecular diagnostics. For example, the availability of sensitive multiplex PCR panels now allows for syndromic testing that includes detection of more than a dozen respiratory viral targets at once, and some panels include selected bacterial targets as well (e.g., *Bordetella pertussis*, *Mycoplasma pneumoniae*). These tests have greatly advanced our ability to identify and track respiratory pathogens that have potential for nosocomial spread, provide opportunity for earlier implementation of appropriate transmission-based precautions, and may also reduce unnecessary antibiotic prescribing.[44] Such multiplex panels are also now available for direct testing of stool for multiple gastrointestinal pathogens,[45] and of positive blood cultures for both organism and resistance gene targets.[46] Just as for rapid respiratory viral diagnostics, these assays have obvious benefits for infection prevention and antimicrobial stewardship by allowing for earlier targeted

interventions to both prevent transmission and to optimize therapy.[46]

PCR coupled with nucleic acid sequencing has also proven to be an excellent means of rapidly identifying bacteria and fungi from blood culture or other culture materials, and is considered the new standard for bacterial and fungal identification.[40] Using ribosomal gene sequencing kits for bacteria and fungi, a sequence from an unknown organism can be compared with either a full or partial 16S rRNA (D2 large-subunit rRNA for fungi) sequence from over 1,000 type strains.[47] Computer analysis provides percent base pair differences between the unknown agent and the 20 most closely related organisms, alignment tools show differences between the related sequences, and phylogenetic tree tools verify that the unknown organism clusters with the 20 closest organisms in the database. Continual refinements in methods and software, and decreases in cost, should lead to more widespread use of sequence-based approaches for microbial identification.

The most recent approach to the rapid identification of bacteria and fungi from culture is the use of proteomics facilitated by matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS).[1,5] MALDI-TOF systems produce detailed spectra, based upon mass-to-charge ratios of the small molecules produced by laser desorption of bacteria or fungi, and have emerged as robust, rapid and inexpensive methods to detect and characterize a wide range of organisms. The use of MALDI-TOF MS to identify bacteria has been shown to be highly accurate relative to 16S rRNA sequencing and capable of delivering an identification of a precultured organism in 6 minutes at a cost that is one-quarter of that of conventional identification.[1] Some methods for the processing of positive blood culture samples have been published, but direct testing of other samples such as urine will require additional development.[5,48,49] Novel applications for this technology are being developed and include microbial strain typing, antimicrobial susceptibility testing, and the study of virulence profiles.[5]

Rapid molecular methods for detecting important antimicrobial resistance genes have also been developed, with most of the current focus being on rapid detection of the *mec*A gene in MRSA and the *van*A/*van*B genes of VRE, directly by PCR on patient samples (e.g., nares or perirectal swab).[50,51] A positive result from any of these tests allows clinicians to implement or adjust infection prevention interventions in a timely manner. Real-time PCR tests for detection of emerging MDR-GNRs, primarily assays that target the most common carbapenemase-encoding genes, are still in development[52–54] but should soon be available for clinical use.

Although most clinicians and microbiologists enthusiastically welcome the introduction of rapid tests for infectious diseases, it may be challenging to perform such testing with quick turnaround times because of the financial advantages of batch testing and the difficulty of staffing the laboratory for frequent testing. It is often stated that rapid results obtained by molecular testing are associated with improved patient outcomes, reduced length of hospital stay and duration of antimicrobial administration as well as substantial cost savings.[55,56] However, rapid microbiologic testing does not always have demonstrable patient care or financial benefit,[57] and in order to realize these potential benefits, such tests must be available around the clock. For example, if testing hours are restricted, rapid reporting of results will be compromised and the clinical impact, as well as cost savings to the institution gained by a shorter length of patient stay or reductions in unnecessary treatments, will not be fully realized.[2] Buehler and colleagues performed a systematic review and meta-analysis of the effectiveness of rapid identification of bloodstream pathogens in reducing morbidity, mortality, length of patient stay, and antibiotic use. While they found that rapid molecular testing with direct communication to clinicians improved timeliness of targeted antibiotic therapy, and demonstrated a trend toward reduced mortality, there was insufficient evidence to make a recommendation about rapid testing approaches.[46] Clearly, better outcomes studies are needed to support the ongoing development and introduction of rapid diagnostic testing.[58]

The clinical microbiologist, in consultation with appropriate clinicians and members of the IPP team, should determine which rapid microbiological tests should be offered and provide the necessary restrictions and guidelines for use. The group should base their decisions on data from the literature, data generated by their laboratory, and data on their target patient population. Ideally, these assays should be used as part of a well-designed and carefully planned strategy for the reduction of HAIs and antimicrobial resistance in the healthcare setting. Given the added expense of such testing, the group should try to determine whether the test would improve patient care substantially. More expensive testing procedures may be justified if they help reduce the use of less sensitive and specific tests and eliminate unnecessary diagnostic procedures and ineffective therapies.[38]

Automated Identification and Susceptibility Testing

The clinical microbiology laboratory's ability to identify HAI pathogens accurately is challenged continuously by the expanding spectrum of organisms that colonize and infect seriously ill patients. Whereas the more common ESKAPE pathogens are readily identified by the available automated systems, many nonfermentative GNR and other less common or fastidious organisms that cause HAIs can be more difficult to identify. Consequently, the laboratory frequently must update the methods used to identify and characterize HAI pathogens.

Unusual microorganisms or common microorganisms with atypical phenotypic properties often cannot be reliably identified by commercial systems and may require the use of molecular or proteomic methods to obtain an accurate identification.[40,59] As mentioned earlier, the increased adoption of proteomic approaches (MALDI-TOF MS) has greatly enhanced the ability of many laboratories to identify organisms accurately to the species level. However, even these systems are challenged by some organisms or organism groups (e.g., *S. pneumoniae* and *S. mitis, E. coli* and *Shigella* spp.[60, 61]

Therefore, as pathogens continue to evolve and taxonomic classifications are revised, microbiologists must pay attention to the manufacturers' communications about products, such as letters, notices, or test exclusions regarding the accuracy of the test methods, as well as the published literature describing the potential problems encountered by others using these identification systems. Prompt notification of IPP personnel of such issues will avoid confusion.

A couple of potential unintended consequences of increasingly accurate species identifications are relevant to the IPP. First, some species that were previously lumped into large categories (e.g., "diphtheroids") can now be reliably and accurately identified by MALDI-TOF MS. In rare cases, giving an organism a species name may impact whether a case meets an NHSN definition for HAI. For example, if a blood culture grows a "diphtheroid" that can now be given an accurate species name for an organism that is not on the NHSN list of "common commensals," it could change the classification from "contaminant" to CLABSI. In addition, some of the rare species within the coagulase-negative staphylococci are not listed on the NHSN organism databases, which can confuse IPs or auditors as they review classification of HAIs. Finally, the reporting of species names with which clinicians are not familiar may result in overtreatment or confusion (e.g., *Staphylococcus pettenkoferi* versus the more familiar "coagulase-negative staphylococcus"). Thus the laboratory and IPP personnel should consider options to limit confusion, including in some cases to "lump" some species groups back into the more familiar categories to which clinicians and IPs have become accustomed.

Commercial antimicrobial susceptibility testing (AST) systems were introduced into clinical microbiology laboratories during the 1980s and have been used in the majority of laboratories since the 1990s.[62,63] The AST systems generally include data management software that may be interfaced with a laboratory information system (LIS) and often various levels of expert system and epidemiological analysis. A laboratory may choose to use an automated AST system for several reasons, including labor savings, test reproducibility, data management with expert system analysis, and the opportunity to generate results more rapidly.

Laboratory directors must keep current with the literature regarding automated systems' ability to detect emerging resistances, and they must implement, if necessary, additional methods to detect or confirm particular resistance patterns. Increasingly, such confirmatory testing will be performed using molecular methods.[6,64] Laboratory personnel must notify IPP staff immediately when key resistant organisms are identified and when new or unusual phenotypic resistance patterns are detected so that appropriate interventions can be taken. Molecular methods may be used to detect specific antimicrobial resistance genes (resistance genotyping) in many organisms.[6]

Despite its many potential advantages, genotyping will not completely replace phenotypic methods for detecting antimicrobial resistance in the clinical laboratory in the near future. Molecular methods for resistance detection may be applied directly to the clinical specimen, providing simultaneous detection and identification of the pathogen plus resistance characterization.[1,3,4] Likewise, they are useful in detecting resistance in viruses, slow-growing or nonviable organisms, or organisms with resistance mechanisms that are not reliably detected by phenotypic methods.[4,40] However, because of their high specificity, molecular methods will not detect newly emerging resistance mechanisms and are unlikely to be useful in detecting resistance genes in species where the gene has not been observed previously. Furthermore, the presence of a resistance gene does not mean that the gene will be expressed, and the absence of a known resistance gene does not exclude the possibility of resistance from another mechanism. Phenotypic antimicrobial susceptibility testing methods allow laboratories to test many organisms and detect newly emerging as well as established resistance patterns.

Active Surveillance Cultures

The laboratory often serves as an early warning system by identifying clusters of organisms with unique phenotypic characteristics and communicating the observations promptly to IPP personnel. Although this mode of surveillance may be sufficient to detect patients with infection, it is unlikely to detect those patients who may be colonized with an MDRO and who may serve as a reservoir for MDRO transmission.[22,25,65] Therefore, during outbreaks, when new MDROs are emerging, or if transmission of an MDRO continues despite the use of standard infection prevention practices, "active surveillance" cultures may be utilized to identify patients colonized (but not clinically infected) with an MDRO.[66] In addition, some states (as well as the Veterans Affairs healthcare system) have mandated the routine use of active surveillance for MRSA.[65,67]

In contrast to the extensive experience with MRSA active surveillance, there is less known about how to apply active surveillance to prevent transmission of MDR-GNRs.[14,22,25] MDR-GNRs are vastly different from MRSA in terms of the diversity of species and resistance mechanisms, optimal screening methods for various MDR-GNRs are still being developed, and several important questions about MDR-GNR transmission remain to be answered before the utility of active surveillance can be established for these organisms.[22] Thus the role of active surveillance for MDR-GNRs remains unclear.[25]

Large-scale active surveillance efforts are complex and resource intensive.[65,67] In addition to the cost of the screening test itself, there are costs associated with sample acquisition and transport, laboratory validation and reporting, process and outcome monitoring, personal protective equipment, bed management, and patient/ family education.[67] Indeed, the prospect of performing active surveillance cultures for a large number of diverse MDROs (which requires that culture samples be obtained from several different anatomic sites of each patient) threatens to overwhelm and divert the resources of microbiology laboratories, IPPs, and hospital units. Broader application of active surveillance will require the development

of molecular or other novel approaches to identify multiple MDROs simultaneously and at low cost in patient samples.

Currently, active surveillance cultures for MDROs should be limited to certain situations, including new introduction of problematic pathogens (e.g., carbapenem-resistant *Enterobacteriaceae*), continued transmission of a problematic MDRO despite implementation of standard and enhanced infection prevention practices, or outbreak settings.[66] Furthermore, the use of active surveillance should always be seen as an adjunct measure, and should not draw attention away from those well-established practices for infection prevention that are applied to all at-risk patient populations and are designed to prevent infections due to all pathogens (e.g., hand hygiene and bundled practices for prevention of device-associated infections).[67]

Laboratory Information Systems and Reporting of Data

A Laboratory Information System (LIS) that can mine data prospectively and interface with other parts of the electronic health record can help IPP staff perform surveillance, monitor patient-to-patient spread of pathogens, and provide earlier detection of outbreaks.[68–70] Thus, individuals selecting an LIS must consult with both laboratory and IPP personnel before purchasing the optimal system for the hospital.

The laboratory should report all results as quickly as possible. In most situations, routine reporting on the hospitals' LIS will be adequate for clinical and epidemiological purposes. However, the detection of certain epidemiologically important pathogens requires immediate notification of IPP personnel so that transmission prevention measures can be initiated immediately (including, if applicable, notification of public health authorities). Examples of organisms for which urgent notification should occur include *Mycobacterium tuberculosis*, *Neisseria meningitidis*, *Legionella*, enteric pathogens such as *Salmonella* or *Shigella*, and MDROs such as MRSA, glycopeptide-intermediate and -resistant *S. aureus*, VRE, and ESBL- or carbapenemase-producing *Enterobacteriaceae*. In addition, new or unusual pathogens, or potential agents of bioterrorism (e.g., *Bacillus anthracis*, *Yersinia pestis*, and orthopoxviruses) should be reported immediately to the IPP. The list of organisms for immediate notification may vary from one institution to another. For example, an MDRO may have become endemic in one hospital, to the point that the IPP no longer requires immediate notification, while another hospital has not yet had introduction of the MDRO and needs such notification.[14]

In addition to the above, laboratory staff should meet regularly with IPP staff to ensure that their communication is direct and clear. They can discuss areas of mutual concern, such as the status of epidemiological and microbiological investigation of clusters or outbreaks. Together they can determine whether supplementary studies such as molecular typing or environmental cultures will be necessary. If special studies are necessary, they can determine exactly what needs to be done, who will do these procedures, and when they will be performed.

Outbreak Detection and Management

Whenever an HAI outbreak is detected, the IPP must act quickly to characterize and define the extent of the outbreak, to identify possible causes, and to design and implement effective control measures (Table 23.2; see Chapter 11, "Outbreak Investigations"). The clinical microbiology laboratory plays an important role in any potential outbreak situation, including early recognition of possible infection clusters, rapid notification and collaboration with the IPP staff, additional case finding, and provision of molecular typing for determination of relatedness, which requires maintenance of an organism bank. The laboratory should also act in a consultative capacity with the IPP staff to help determine whether an outbreak is "real" or a potential pseudo-outbreak due to false-positive diagnostic tests or contamination of specimens. In addition, the laboratory can help generate hypotheses as to the potential source of an outbreak, its reservoir, and mode of spread, through molecular typing of the suspected organisms and through testing of the environment and/or personnel as necessary.

Outbreak investigations can be facilitated if the IPP team prepares in advance. One step in this process is to identify the most common types of outbreaks that have occurred in the hospital. Laboratory and IPP personnel can then determine what resources (e.g., personnel, time, funds, materials, space, or special tests) would be required to investigate a "typical" outbreak. Laboratory staff should also anticipate the extra costs associated with outbreak investigations so that they can work with hospital administration to include funds for those efforts in annual budgets.

Outbreaks are often detected retrospectively, either after they have resolved or when they are already beginning to wane. Therefore, a major challenge to the clinical microbiology laboratory is in detecting outbreaks early enough to allow effective intervention and impact morbidity and mortality. Computer decision support may assist in identifying clustering of infections with the same organisms that occur at the same time in the same patient care area,[71, 72] but outbreaks are often first detected by an observant laboratorian at the bench. Thus effective and regular communication between laboratory personnel and the IPP staff is essential to this effort. Given the stress inherent in an outbreak investigation and the speed with which important decisions must be made, the IPP team, including laboratory personnel, might need to meet daily to discuss new findings and make decisions. In the future, efforts at early detection will likely be facilitated by real-time data-mining programs that can raise flags based upon subtle changes in rates of test ordering or of positive test results.

Staff members in both the IPP and the laboratory have important unique responsibilities during outbreak investigations. One of the laboratory's critical responsibilities is to save all potentially relevant organisms in case further analysis is needed. Regardless of their ability to perform special tests to characterize the organisms, all microbiology laboratories should save isolates during outbreaks. If the laboratory cannot perform the necessary tests, the isolates can be sent to a reference laboratory. Similarly, the laboratory should save all organisms that

Table 23.2 Steps in healthcare-associated outbreak investigation, and the role of the laboratory at each step[a]

Investigative step	Role of the clinical microbiology laboratory
RECOGNIZE PROBLEM	Surveillance and early warning system – ideally part of the Laboratory Information System. Notify infection control personnel of infection clusters, unusual resistance patterns, possible patient-to-patient transmission.
ESTABLISH CASE DEFINITION	Assist and advise regarding inclusion of laboratory diagnosis in case definition.
CONFIRM CASES	Perform laboratory confirmation of diagnosis.
COMPLETE CASE FINDING	Characterize isolates with accuracy. Store all sterile site isolates and epidemiologically important isolates. Search laboratory database for new cases.
ESTABLISH BACKGROUND RATE OF DISEASE, COMPARE TO ATTACK RATE DURING SUSPECTED OUTBREAK	Provide data for use in ongoing surveillance, including baseline rates for selected units and infection sites. Search laboratory database for all prior cases of the entity if baseline rate is not prospectively monitored.
CHARACTERIZE OUTBREAK (DESCRIPTIVE EPIDEMIOLOGY)	Perform typing of involved strains, compare to previously isolated endemic strains to determine if the outbreak involves a single strain. This can only be done if selected pathogens are routinely stored (see above).
GENERATE HYPOTHESES ABOUT CAUSATION: RESERVOIR MODE OF SPREAD VECTOR CASE CONTROL STUDY OR COHORT STUDY	Perform supplementary studies or cultures as needed, but only if justified by epidemiologic link to transmission: Personnel Patients Environment
INSTITUTE CONTROL MEASURES	Adjust laboratory procedures as necessary.
ONGOING SURVEILLANCE TO DOCUMENT EFFICACY OF CONTROL MEASURES	Maintain surveillance and early warning function of the laboratory.

[a] Adapted from reference 11.

might be even remotely related to the outbreak, because organisms can be discarded if they are not needed but cannot be retrieved once they have been thrown away.

The microbiology laboratory should plan ahead and save all epidemiologically important isolates from routine cultures. Laboratory and IPP personnel should decide which isolates should be banked and how long they should be stored based upon their epidemiological importance and the available resources. We recommend that all isolates from normally sterile sites (e.g., blood and cerebrospinal fluid), important MDROs (MRSA, VRE, MDR-GNRs) from any site and other epidemiologically important pathogens (e.g., *M. tuberculosis, Legionella*) be saved for a period of 3 to 5 years.

Supplementary Cultures

The clinical microbiology laboratory is often called upon to detect potential HAI pathogens that may be colonizers of patients, healthcare workers (HCWs), and the hospital environment. For example, patients and HCWs increasingly are being screened for carriage of epidemiologically significant organisms. The most common organisms for which screening is performed are the MDROs (MRSA, VRE, and MDR-GNRs), often as one aspect of an enhanced program for MDRO control.[66] Screening for other organisms (e.g., Group A streptococci) may be performed as part of an HAI or outbreak investigation. Finally, hand cultures may be performed as part of educational efforts in support of a hand hygiene campaign or to confirm the mechanism of cross- infection during an outbreak investigation.[73]

For some organisms (e.g., MRSA, VRE), screening methods are standardized and well established, while for others (e.g., MDR-GNRs), such methods are evolving and will continue to evolve as more complex resistance phenotypes emerge.[51,74] Table 23.3 outlines current approaches to screening patients and HCWs for organisms of epidemiologic significance.

When performing screening cultures of personnel and the environment, special culture media might improve the

Table 23.3 Screening patients and healthcare workers for asymptomatic carriage of organisms of epidemiologic significance[a,b]

Organism (s)	Diagnostic procedures	Turnaround time (h)	Optimum specimens
S. aureus, including MRSA	Aerobic culture and AST Chromogenic agar medium Real-time PCR	48–96 [c] 18–48 [e] 1–4	Nares,[d] throat, perirectal, skin, wounds Nares, throat, perirectal, skin, wounds Nares[f]
VRE	Aerobic culture and AST Real-time PCR	48–72 1–4	Perirectal or stool swab Perirectal or stool swab
Multiresistant GNR (*P. aeruginosa, Acinetobacter* spp., *S. maltophilia*, ESBL-and carbapenemase-producing organisms)	Aerobic culture using selective media and AST[g] Real-time PCR[i]	48–72 1–4	Perirectal or stool swab, endotracheal or sputum sample, sites of prior infection or colonization.[h] Perirectal or stool swab
Group A streptococci	Aerobic culture	24–48	Rectal, vaginal, skin, throat
Various organisms carried on hands	Aerobic cultures with selective medium, Contact agar plates, Broth-based glove-juice technique	48–96	Hand cultures Direct imprint on agar plate Culture of broth after 1 min of hand immersion with agitation of broth

[a] Adapted from reference 11.
[b] Such cultures should only be done for the following reasons: (1) as part of an outbreak investigation, to identify carriage of an organism among patients or healthcare workers who are epidemiologically linked to cases; (2) to identify carriers of MDROs as part of enhanced MDRO control strategies; (3) to identify *S. aureus* carriers in order to proceed with a decolonization strategy to decrease risk for acquisition of *S. aureus* infection during a period of vulnerability (e.g., perioperative).
[c] The gold standard method includes overnight broth enrichment and confirmation of species identification and antimicrobial susceptibility, which can increase turnaround time to 96 hours. Most conventional agar-based screens (e.g. mannitol salt agar with or without oxacillin), without broth enrichment, provide a turnaround time of approximately 48 hours.
[d] The nares provides the best sensitivity and specificity of any single site for detection of *S. aureus* (including MRSA). However, several studies have shown that sampling of additional sites, including oropharynx and perirectal sites, may increase yield by 10 to 40%.
[e] Positive results for chromogenic agar medium can be reported at 18 to 24 hours, but negative results require 48 hours.
[f] Currently available real-time PCR assays are FDA approved only for nares samples but have been used in some studies for oropharyngeal, skin, and perirectal samples.
[g] Several modifications of culture methods may enhance recovery by increasing medium selectivity for MDROs (e.g., addition of ceftazidime for ESBL-producing *Enterobacteriaceae*, levofloxacin for fluoroquinolone-resistant *E. coli*).
[h] Sample site choice should be guided by likely reservoirs, gastrointestinal (e.g., *E. coli*) and respiratory (e.g., *Acinetobacter, P. aeruginosa*).
[i] Real-time PCR assays for selected carbapenemase genes are not yet FDA approved, but in development.

laboratory's ability to identify the reservoir and the pathogens of interest. For example, selective media (i.e., which inhibit the growth of species other than that of interest) or differential media (i.e., which reveal distinctive morphological features [pigmentation, colony type] that differentiate the species of interest from other species), or both, might allow the laboratory staff to process specimens quickly and efficiently. In addition, enrichment cultures might be necessary to optimize the laboratory's ability to detect specific HAI pathogens present in low numbers (Table 23.3).

Laboratory and IPP should weigh two important factors before deciding to culture hospital personnel during an outbreak investigation: (1) finding the outbreak strain on the hands or in the nares of a HCW does not establish the direction of transmission or definitively implicate a HCW as the source or reservoir for the outbreak, (2) culturing hospital personnel indiscriminately can lead to confusing results and can generate ill will toward the IPP. In general, only HCWs epidemiologically linked to cases should be cultured. With these caveats in mind, we recommend that IPPs obtain cultures of hospital personnel only after consulting with a hospital epidemiologist experienced in outbreak investigation.[11]

At one time, the hospital environment was considered to be the major source of HAI pathogens. More recently it has been recognized that patients most often acquire infection from their own endogenous (colonizing) flora.[75,76] Nonetheless, the hospital environment serves as an important source of potential nosocomial pathogens[74] (see Chapter 8), and there are specific circumstances in which environmental sampling for quality assurance (QA) or for detection of potential pathogens is required. Routine sampling for QA should be limited to biologic monitoring of sterilization processes and monthly cultures of water and dialysate for hemodialysis. On some occasions, it may be helpful to perform a short-term evaluation of the effectiveness of hospital cleaning and disinfection (for example, sampling surfaces for VRE or *C. difficile* after terminal room cleaning). Similarly, sampling the hospital potable

Table 23.4 Microbiologic studies of the hospital environment (air, water, and surfaces) for organisms of epidemiological significance[a,b]

Source and organism(s)	Procedure(s)	Turnaround time	Optimum specimen
Air			
Fungi (molds)	Fungal culture on selective medium	48 h–7 days	Air processed with large- volume air sampler[c]
Bacteria [d]	Routine aerobic cultures	48–72 h	Air processed with large- volume air sampler
Water			
Legionella spp.	Culture on selective media[e]	5–10 days	500-mL-1-liter water samples.[f] Swabs of internal surfaces of faucets, shower heads, and aerators.[f]
Fungi[g]	Fungal culture on selective medium	48–96 h	500-mL-1-liter water samples.[f] Swabs of internal surfaces of faucets, shower heads, and aerators.[f]
Bacteria	Routine aerobic cultures	48–72 h	Water and dialysate samples as outlined by AAMI.[h]
Surfaces			
Aerobic bacteria (including MDROs)	Aerobic cultures using selective and nonselective media	48–72 h	Surface swab or sponge, contact agar plate (Rodac) [i]
C. difficile	Anaerobic cultures	48–72 h	Surface swab or sponge, contact agar plate (Rodac) [j]
VRE	Selective aerobic cultures	48–72 h	Surface swab or sponge, contact agar plate (Rodac)

[a] Adapted from reference 97.
[b] With the exception of water and dialysate cultures for monitoring of hemodialysis, and potable water cultures for *Legionella* spp., environmental cultures should be performed only when an epidemiologic investigation suggests the environment may be involved in pathogen transmission.
[c] Large-volume air samples are preferred for air sampling for mold spores: settle plates should not be used.
[d] There are no standards for acceptable levels of bacteria in air samples, nor is there any evidence correlating bacterial burden to infection risk. Air sampling for bacteria should be performed only rarely, either as part of an outbreak investigation or a research protocol.
[e] *Legionella* spp. will not grow on routine aerobic culture media. Buffered charcoal yeast extract agar in a CO_2-enriched atmosphere is required for isolation of *Legionella*.
[f] The larger volume (1 liter) is preferred. If the water source is chlorinated, 0.5 mL of 0.1 N sodium thiosulfate should be added to each liter sample to neutralize the chlorine. Water samples are filter concentrated. Swabs should be immersed in 3 to 5 mL of water taken during sampling of the same site, to prevent drying.
[g] The role of waterborne fungi in infection transmission in the hospital environment remains poorly described, but cultures may be indicated as part of a search for environmental sources during an outbreak of invasive fungal infections in an immunocompromised patient population.
[h] AAMI, Association for the Advancement of Medical Instrumentation, whose standards govern microbiological monitoring of hemodialysis water and dialysate.
[i] The sterile swab or sponge should be moistened (e.g., with nutrient broth or sterile saline) before sample collection.
[j] For *C. difficile*, the contact agar plate should be optimized for anaerobic recovery (selective, prereduced media, promptly placed in an anaerobic environment).

water supply for *Legionella* spp. is indicated after diagnosis of nosocomial legionellosis or as part of a comprehensive program to decrease risk of nosocomial legionellosis.[75,77,78] Air sampling for mold spores can also be an important step in determining the source of invasive fungal infection in highly immunocompromised patients. On rare occasions, sampling of other inanimate objects or surfaces may be indicated and then only when a careful epidemiologic investigation suggests that a particular object or surface may be implicated in pathogen transmission. Table 23.4 outlines current approaches to screening the hospital environment for organisms of epidemiologic significance.

In general, routine undirected cultures of HCWs or the hospital environment should be discouraged. Both IPP and laboratory personnel must understand that such cultures are labor intensive and nonstandardized, and they rarely provide useful information.[75] With few exceptions (see above), such sampling should only be performed as part of an epidemiologic investigation in consultation with the hospital epidemiologist. When such an investigation reveals a common organism in the patient, HCW, and/ or environmental samples, the laboratory should also provide access to epidemiologic strain typing methods.

Molecular Typing to Support Infection Prevention Activities

There are several circumstances in which it is important to determine if two or more organisms are genetically related, and thus likely to have a common source. These circumstances include (1) outbreaks, clusters and other transmission investigations, where evidence for patient-to-patient transmission or a common reservoir of infection is sought; (2) determination of pathogenesis or origin of an individual infection (e.g., comparison of an infecting isolate to strains previously found as colonizers of the patient or environment); and (3) surveillance for emergence or spread of a particularly virulent or epidemic clone (e.g., USA300 MRSA, BI/NAP1 strain of *C. difficile*, etc.). In many situations, species identification and AST results may provide evidence for (or against) an epidemiological link. However, because many organisms have predictable resistance patterns, AST patterns are not discriminatory enough, and

Table 23.5 Selected genotypic methods for epidemiological strain typing of nosocomial pathogens[a,b]

Typing Method	Comments
Plasmid profiling	Simple, low-cost method that is useful as a supplement to other typing methods. Only useful if organism has plasmids. Restriction endonuclease analysis of plasmid DNA enhances discriminatory power of the method, and can help determine if resistance elements expressed by distinct strains are due to plasmid dissemination.
Ribotyping	Labor-intensive method of moderate discriminatory power. Manual ribotyping of historical interest. Automated ribotyping may serve as a first-level (expensive) screening method or library typing method.
PFGE	Labor-intensive method with excellent discriminatory power. Has been considered the gold standard for highly discriminatory bacterial subtyping for most common HAI pathogens. Useful in outbreak surveillance. Interlaboratory reproducibility can be achieved with standardized protocols (e.g., PulseNet) for development of large-scale library subtyping databases.
RAPD	Poorly reproducible method that is best used to answer specific limited epidemiological questions. May be useful in small-scale outbreak investigations.
rep-PCR	Relatively rapid and easy to perform, moderate discriminatory power (not sufficient for highly clonal pathogens such as MRSA). A semiautomated method (DiversiLab System, bioMérieux, Marcy l'Etoile, France) may be useful for laboratories that do not have access to more discriminatory methods.
PCR-ribotyping	A simple, low-cost approach that is the first line method for subtyping of *C. difficile*.
AFLP	Moderately complex method suitable for local library subtyping and outbreak surveillance. Excellent discriminatory power and reproducibility.
MLST	One of the first DNA sequence-based typing methods. Limited discriminatory power, 100% typability and high reproducibility. Best used for phylogenetic studies and large-scale library typing.
MLVA	MLST approach using virulence-associated genes to improve discriminatory power. Moderately labor-intensive with excellent discriminatory power. May be used in outbreak surveillance and large-scale library subtyping if standardized.
Whole-genome sequencing	The gold standard for discriminatory power. Not widely available currently, but cost and speed of sequencing continue to decrease – thus, once informatics for rapid automated interpretation are available, will likely replace most other methods.

[a] Adapted from reference 97.
[b] Abbreviations: AFLP, amplified fragment length polymorphism; MLST, multilocus sequence typing; MLVA, multivirulence locus sequence typing; PFGE, pulsed field gel electrophoresis; RAPD, random amplification of polymorphic DNA; rep-PCR, repetitive-element PCR; SNP, single-nucleotide polymorphisms.

additional tests are required to determine whether the isolates are truly related. Thus genotypic or DNA-based typing methods have replaced phenotypic typing methods (e.g., AST, biochemical profiles, and bacteriophage susceptibility patterns), that discriminate poorly among isolates.

General Principles Regarding Use of Molecular Strain Typing

The most important concept to understand when using molecular typing techniques is that of "clonality." Organisms that demonstrate evidence of genetic relatedness by one or more molecular typing approaches are often described as belonging to the same "clone," which is another way of stating that they have recently arisen from a common ancestor.[79] It must be understood, however, that most molecular typing methods are more powerful at determining the *absence* of clonality than its presence, for several reasons. First, the advent of whole genome sequencing (WGS) is now demonstrating that the discriminatory power of many typing methods may be worse than previously thought. A recent study comparing WGS to pulsed field gel electrophoresis (PFGE) for several common HAI pathogens (MRSA, VRE, and multiple-drug resistant *Acinetobacter*) found that in almost 30 percent of cases in which PFGE yielded no band differences (indistinguishable patterns), WGS revealed the organisms to be nonclonal.[9] Conversely, in all cases where PFGE found organisms to be definitely unrelated, WGS confirmed that finding.[9] Second, many common HAI pathogens belong to a relatively few closely related clonal lineages, the best example being MRSA,[80,81] where the vast majority of infections are now due to strains belonging to USA100 and USA300 lineages.[81] Thus typing methods with limited discriminatory capability may falsely suggest that two strains have a recent common source when they do not. Finally, some outbreaks may be due to resistance determinants that are carried on mobile genetic elements (e.g., plasmids) that can be readily transferred between strains and even across species of bacteria. Of course, in such situations the finding of genetically distinct strains (or even different species) does not exclude the possibility that a common resistance element is spreading.[82] Therefore,

the results of molecular typing should always be interpreted in the context of the rest of the epidemiologic investigation (the setting, the duration of the outbreak, the organism or resistance determinant implicated, etc.), and of the performance characteristics of the typing method used.

There are many techniques used in molecular strain typing, and we have summarized some of them in Table 23.5. More detailed discussion of the specific techniques used in each method can be found in recent reviews.[83,84] The most important characteristics to consider when selecting a typing method include (1) typeability: the ability to provide a result for all isolates tested; (2) reproducibility: the ability to provide the same result each time the same isolate is tested (such reproducibility can be evaluated both within the same laboratory (intralaboratory) and between laboratories (interlaboratory); (3) discriminatory power: the ability to differentiate among organisms that are not epidemiologically related; (4) ease of performance: including how easily the approach can be incorporated into the clinical microbiology laboratory; (5) ease of interpretation: including the degree to which interpretation is automated or objective, versus visually interpreted and occasionally involving some subjectivity; and (6) cost: including both initial and ongoing investments.

As outlined in Table 23.5, WGS is now the gold standard for molecular strain typing, based upon the fact that it provides the greatest possible discriminatory power. WGS technology also provides promise for the rapid detection of antimicrobial resistance and virulence determinants.[85] The cost and turnaround time of WGS are now equivalent or better than those of other common typing methods, but several hurdles still remain before WGS is routinely available in the clinical microbiology laboratory to support infection prevention activities. First, there is a need to determine the rate of genomic change in the various organisms that cause HAI, and the degree of genomic diversity that exists within and between hosts during infections and outbreaks.[86] While data are accumulating to help answer these questions for selected common pathogens (e.g., *S. aureus*), less is known for other organisms. Such data are needed in order to establish agreed-upon criteria for defining clonal lineages. These criteria are likely to be situation. and species-specific – for example, more variability is expected over the course of a year-long, hospital-wide outbreak versus one that occurs within a 1–2 week period in a single ICU, and some bacterial species have more rapid mutation rates than others. Second, and equally important, an automated bioinformatics pipeline is required to allow for rapid and reliable data analysis and interpretation.[86] Nonetheless, we expect WGS to become increasingly available and affordable, and to replace most other molecular strain typing methods within the next 5–10 years.

Antimicrobial Stewardship

Every hospital in the US must now have an antimicrobial stewardship program (ASP), guidelines for which have been published by the Infections Disease Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA)[87] (see Chapter 19). Antimicrobial stewardship efforts are directly dependent on reports from the clinical microbiology laboratory, so good communication among the laboratory, pharmacy, IPP, and a stewardship team is essential. For guiding empirical antimicrobial therapy, unit-specific and tailored antibiograms should be updated on a regular basis and provided to clinicians. Such antibiogram data can also be used for evaluation of trends in important antimicrobial resistance rates and for education of clinicians regarding optimal antimicrobial use. These results can be presented in a tabular format that includes the antibiograms of the most common HAI pathogens by anatomical site and hospital service location and also includes antimicrobial dosing and cost information. This information will help clinicians select empiric antimicrobial therapy for patients with HAIs. The Clinical and Laboratory Standards Institute (CLSI) has developed guidelines for the preparation of antibiograms.[88]

Directed antimicrobial therapy requires patient-specific culture and susceptibility data. This allows for a prospective audit of antimicrobial use with feedback to the prescriber. A major challenge to effective stewardship is the ability to obtain antimicrobial susceptibility data from the laboratory in a timely manner. As outlined in the previous section, rapid molecular and proteomic approaches to detection and identification of microbial pathogens and antibiotic resistance determinants will help reduce the TAT for these data and should lead to more prompt targeting of antimicrobial therapy. However, efforts to reduce the analytical TAT are only helpful if they are linked to rapid incorporation of the information into antimicrobial management decisions. An active ASP using a computer decision-support system can streamline this process by automatically alerting the stewardship team when restricted drugs are ordered, indicating where the patient resides, other medications the patient is receiving, and pertinent microbiology laboratory results.[69,89] Other alerts may include notification if a patient was receiving double antimicrobial coverage or no antimicrobial coverage for an identified pathogen and identification of potential candidates for a switch from intravenous to oral therapy or for discontinuation of therapy when cultures fail to detect a potential pathogen. One ASP projected that a decision-support system saved the institution more than $600,000 annually compared to the ASP without the decision-support system.[89] Further details regarding antimicrobial stewardship and the importance of laboratory support can be found in Chapter 19.

Advisory

The clinical microbiologist (doctoral-level microbiologist, pathologist, microbiology supervisors, or designated laboratory personnel), hospital epidemiologist and infection preventionist (IP) must work as a team to prevent and control HAIs effectively. Given continuous changes in healthcare-associated pathogens, antimicrobial resistance, medical care, and healthcare delivery, staff members from the laboratory and from the IPP must work to ensure collaboration and open communication. The relationship between the microbiology laboratory, the IPP, and increasingly the antibiotic stewardship program,[10,26,90] is critical to the success of these important efforts to improve patient care, control costs, and preserve options for effective antimicrobial therapy.

The clinical microbiologist (or microbiology supervisor in an institution that does not have a doctoral-level microbiologist) must be an active member of the infection prevention committee. Because the infection prevention committee frequently bases decisions on the results of microbiological tests, the clinical microbiologist must guide the committee in integrating culture results and selecting appropriate microbiological approaches to solve specific problems. The microbiology laboratory can benefit if IPP personnel understand the routine processes in microbiology (e.g., timelines for the processing of blood, wound, or urine cultures and related techniques).[10] Specimen processing timelines enable IPP staff to set expectations of turnaround times for specific results and time constraints of microbiology test services, thus minimizing premature phone calls to the laboratory requesting culture information. Conversely, while serving on the committee, the microbiologist will learn about the problems confronting the IPP and thus will be better able to organize the laboratory's response to such problems.

The microbiologist must educate the committee about several important issues. Because most IPP personnel have not worked in laboratories, the microbiologist should ensure that these individuals understand basic microbiology principles and techniques. The microbiologist must also explain the advantages and limitations, the scope and accuracy (i.e., sensitivity and specificity), and the costs of microbiologic methods used to detect, identify, and assess the antimicrobial susceptibility of HAI pathogens.

In addition, the microbiologist should inform the committee about changes in methods, reagents, or instrumentation that may substantially affect the laboratory's ability to detect and characterize healthcare-associated pathogens. These include changes in the sensitivity and specificity of diagnostic methods, changes in antimicrobial susceptibility testing interpretive criteria, and taxonomic changes that may create confusion. An example of changes in testing and reporting criteria that directly affect infection prevention efforts is the recent change in the interpretive breakpoints for the *Enterobacteriaceae* and cephalosporins and carbapenems enacted by the CLSI.[91] The new (lower) breakpoints are intended to obviate the need for ESBL confirmatory testing or modified Hodge testing (confirmation of carbapenemase) for clinical use. The result of this change in testing and interpretive criteria has been the loss of epidemiologic data for some IPPs that have come to rely on these confirmatory tests to guide prevention activities,[92] and has also led to an increase in the number of isolates characterized as resistant to cephalosporins and carbapenems, and therefore potentially MDR, with major implications for infection prevention.[93,94] One institution reported that this change resulted in a 35 percent increase in the number of MDR-GNRs identified and a concomitant increase in the hospitals' use of contact precautions.[93]

Communication may be enhanced if the IPP staff regularly round in the laboratory to ask questions, review microbiological and molecular testing results, and discuss current problems and views. Likewise, the microbiology staff should attend conferences at which IPP personnel discuss epidemiological principles and contemporary topics. Unfortunately, several ongoing trends challenge these valuable personal interactions between the microbiology and IPP personnel.[14] Consolidation of clinical microbiology laboratory services, off-site moves of microbiology laboratories, and total reliance on the electronic medical records to the exclusion of first-hand observation (e.g., review of plates or gram stains) too often keep clinicians and infection prevention personnel out of the microbiology laboratory and keep microbiologists confined to the laboratory.

Budgetary Considerations

Given that most laboratories have limited financial and staff resources, the microbiologist must help the IPP staff and the committee understand the costs and appropriate indications for the microbiological tests most commonly used to support epidemiological investigations so that these limited resources are used effectively. Costs for laboratory procedures that are not related directly to the care of patients (e.g., bacteriologic sampling of personnel or the environment) should be borne by a budget separate from the laboratory. To facilitate all of the microbiologic activities necessitated by an outbreak, the laboratory (or the hospital epidemiologist or the infection prevention committee, depending on the hospitals' organizational structure) should have a contingency fund to enable personnel, materials, and space to be temporarily assigned to support the outbreak investigation.[11] An investigation of an outbreak should not be financed by charging individual patients for cultures taken during the investigation. Viewing the clinical microbiology laboratory as an integral component of the IPP may help healthcare administrators understand the importance of adequate funding for the clinical microbiology laboratory, particularly as the laboratory's activities increase to meet infection prevention priorities. Effective prevention saves not only lives but money, and these savings are rarely credited to the clinical microbiology laboratory.[14]

Educational

Education in clinical microbiology is an essential element of training for hospital epidemiologists and IPs, and is required as part of graduate medical education for the infectious diseases specialists who often serve as hospital epidemiologists,[95] as well as for those IPs seeking certification in infection control.[96] Advances in diagnostic microbiology require that this educational role continue beyond the training years, as many practicing hospital epidemiologists and IPs are not familiar with all of the emerging technologies that impact the field. Continuing education is therefore essential, and provides an important role for professional societies (e.g., Society for Healthcare Epidemiology of America [SHEA], Association of Practitioners in Infection Control [APIC], and American Society for Microbiology [ASM]).

Local options for education are also needed, so that IPP personnel understand the performance characteristics and advantages and disadvantages of new approaches to the detection of healthcare-associated pathogens. Educational opportunities should be ongoing and should take many forms, including IPs

and hospital epidemiologists rounding in the laboratory, microbiology lab directors providing updates at weekly IPP work rounds or monthly infection control meetings, periodic cross-departmental grand rounds presentations, e-mail updates regarding changes in testing practices that link to more detailed information, and regional or national meeting attendance.

Conclusions

The clinical microbiology laboratory is an essential component of an effective infection prevention program. The laboratory can provide a broad range of technologies, from conventional culture-based methods to modern molecular, immunologic, and proteomic methods for detection and characterization of HAI pathogens, which can be used to support and enhance the efforts of the IPP. If the IPP and antimicrobial stewardship teams work with laboratory personnel to apply these techniques appropriately, they can prevent and solve problems efficiently and effectively. The better the collaborative relationship between the laboratory and the IPP, the more effective each will be in helping to reduce the risk for HAIs and the rate of antimicrobial resistance.

References

1. Bizzini A, Greub G. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry, a revolution in clinical microbial identification. *Clin Microbiol Infect.* 2010;**16**:1614–1619.
2. Mosammaparast N, McAdam AJ, Nolte FS. Molecular testing for infectious diseases should be done in the clinical microbiology laboratory. *J Clin Microbiol.* 2012;**50**:1836–1840.
3. Petti CA. Detection and identification of microorganisms by gene amplification and sequencing. *Clin Infect Dis.* 2007;**44**:1108–1114.
4. Tenover FC. Rapid detection and identification of bacterial pathogens using novel molecular technologies: infection control and beyond. *Clin Infect Dis.* 2007;**44**:418–423.
5. Van Belkum A, Welker M, Erhard M, Chatellier, S. Biomedical mass spectrometry in today's and tomorrow's clinical microbiology laboratories. *J Clin Microbiol.* 2012;**50**:1513–1517.
6. Abbott A, Fang F. Molecular detection of antibacterial drug resistance. In: Jorgensen J, Pfaller M, Carroll K, et al. eds. *Manual of Clinical Microbiology*, 11th ed. Washington, DC: American Society for Microbiology, 2015:1379–1389.
7. Okeke IN, Peeling RW, Goossens H, et al. Diagnostics as essential tools for containing antibacterial resistance. *Drug Resist Updat.* 2011;**14**:95–106.
8. Rice LB, Bonomo RA. Mechanisms of resistance to antibacterial agents. In: J Versalovic, KC Carroll, G Funke, et al; eds. *Manual of Clinical Microbiology*, 10th ed. Washington, DC: American Society for Microbiology, 2011:1082–1114.
9. Salipante SJ, SenGupta, DJ, Cummings LA, Land TA, Hoogestaat DR, Cookson BT. Application of whole-genome sequencing for bacterial strain typing in molecular epidemiology. *J Clin Microbiol.* 2015;**53**:1072–1079.
10. Barenfanger J, Bente J, Havener G. Optimal performance for clinical microbiologists and their interaction with infection control staff. *Clin Microbiol Newsl.* 2009;**31**:9–15.
11. Diekema DJ, Pfaller MA. Prevention of healthcare associated infections. In: Jorgensen J, Pfaller M, Carroll KC, et al, eds. *Manual of Clinical Microbiology*, 11th ed. Washington, DC: American Society for Microbiology, 2015:106–119.
12. Centers for Disease Control and Prevention. Available at: www.cdc.gov/nhsn/pdfs/cms/cms-reporting-requirements.pdf. Accessed December 1, 2015.
13. Centers for Medicare and Medicaid Services. Available at: www.medicare.gov/hospitalcompare/linking-quality-to-payment.html. Accessed December 1, 2015.
14. Diekema DJ, Saubolle MA. Clinical microbiology and infection prevention. *J Clin Microbiol.* 2011;**49**:557–560.
15. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: a persistent public health problem. *Clin Microbiol Rev.* 2007;**20**:133–163.
16. Cormican MG, Jones RN. Emerging resistance to antimicrobial agents in gram- positive bacteria: enterococci, staphylococci, and nonpneumococcal streptococci. *Drugs.* 1996;**51**(Suppl 1):6–12.
17. Wisplinghoff H, Bischoff T, Tallent SM, et al. Nosocomial bloodstream infections in U.S. hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. *Clin Infect Dis.* 2004;**39**:309–317.
18. Sievert DM, Ricks P, Edwards JR, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009–2010. *Infect Cont Hosp Epidem.* 2013;**34**:1–14.
19. Aitken C, Jeffries DJ. Nosocomial spread of viral disease. *Clin Microbiol Rev.* 2001;**14**:528–546.
20. Rice LB. Progress and challenges in implementing the research on ESKAPE pathogens. *Infect Control Hosp Epidemiol.* 2010;**31**(Suppl 1):S7–S10.
21. Vincent JL, Rello J, Marshall J, et al. International study of the prevalence and outcomes of infection in intensive care units. *JAMA.* 2009;**302**:2323–2329.
22. Harris AD, McGregor JC, Furuno JP. What infection control interventions should be undertaken to control multidrug-resistant Gram-negative bacteria? *Clin Infect Dis.* 2006;**43**(Suppl 2):S57–S61.
23. Hawkey PM, Jones AM. The changing epidemiology of resistance. *J Antimicrob Chemother.* 2009;**64**(Suppl 1):i3–i10.
24. Kallen AJ, Srinivasan A. Current epidemiology of multidrug-resistant Gram- negative bacilli in the United States. *Infect Control Hosp Epidemiol.* 2010;**31**(Suppl 1):S51–S54.
25. Maragakis LL, Perl TM. How can we stem the rising tide of multidrug-resistant Gram-negative bacilli? *Infect Control Hosp Epidemiol.* 2010;**31**:338–340.
26. Opal SM, Calandra T. Antibiotic usage and resistance: gaining or losing ground on infections in critically ill patients? *JAMA.* 2009;**302**:2367–2368.
27. Walsh TR, Toleman MA. The emergence of pan-resistant Gram-negative pathogens merits a rapid global political response. *J Antimicrob- Chemother.* 2012;**67**:1–3.
28. Humphries RM, McKinnell JA. Continuing challenges for the clinical laboratory for detection of carbapenem-resistant *Enterobacteriaceae*. *J Clin Microbiol.* 2015;**53**:3712–3714.
29. Baron EJ. Specimen collection, transport, and processing: bacteriology. In: Jorgensen J, Pfaller M, Carroll KC,

et al, eds. *Manual of Clinical Microbiology*, 11th ed. Washington, DC: American Society for Microbiology, 2015:270–315.

30. Dunn J. Specimen collection, transport, and processing: virology. In: Jorgensen J, Pfaller M, Carroll KC, et al, eds. *Manual of Clinical Microbiology*, 11th ed. Washington, DC: American Society for Microbiology, 2015:1405–1421.
31. McGowan KL. Specimen collection, transport, and processing: mycology. In: Jorgensen J, Pfaller M, Carroll KC, et al, eds. *Manual of Clinical Microbiology*, 11th ed. Washington, DC: American Society for Microbiology, 2015:1944–54.
32. Beekmann SE, Diekema DJ, Doern GV. Determining the clinical significance of coagulase-negative staphylococci isolated from blood cultures. *Infect Control Hosp Epidemiol.* 2005;**26**:559–566.
33. Valenstein P. Laboratory turnaround time. *Am J Clin Pathol.* 1996;**105**:676–688.
34. Flournoy DJ, Beal LM, Smith MD. What constitutes an adequate sputum specimen? *Lab Med.* 1994;**25**:456–459.
35. Baron EJ. Quality management and the clinical microbiology laboratory. *Diagn Microbial Infect Dis.* 1995;**23**:23–34.
36. Stovall RT, Haenal JB, Jenkins TC, et al. A negative urinalysis rules out catheter-associated urinary tract infection in trauma patients in the ICU. *J Am Coll Surg.* 2013;**217**:162–166.
37. Koo HL, Van JN, Zhao M, et al. Real-time PCR detection of asymptomatic *Clostridium difficile* colonization and rising *C. difficile* associated disease rates. *Infect Cont Hosp Epidem.* 2014;**35:**667–673.
38. Pfaller MA. Molecular approaches to diagnosing and managing infectious diseases: practicality and costs. *Emerg Infect Dis.* 2001;**7**:312–318.
39. Theel ES, Carpenter AB, Binnicker MJ. Immunoassays for diagnosis of infectious diseases. In: Jorgensen J, Pfaller M, Carroll KC, et al, eds. *Manual of Clinical Microbiology*, 11th ed. Washington, DC: American Society for Microbiology, 2015:91–105.
40. Nolte F. Molecular microbiology. In: Jorgensen J, Pfaller M, Carroll KC, et al, eds. *Manual of Clinical Microbiology*, 11th ed. Washington, DC: American Society for Microbiology, 2015:54–90.
41. Oliveira K, Brecher SM, Durbin A, et al. Direct identification of *Staphylococcus aureus* from positive blood culture bottles. *J Clin Microbiol.* 2003;**41**:889–891.
42. Rigby S, Procop GW, Haase G, et al. Fluorescence in situ hybridization with peptide nucleic acid probes for rapid identification of *Candida albicans* directly from blood culture bottles. *J Clin Microbiol.* 2002;**40**:2182–2186.
43. Sogaard M, Stender H, Schonheyder HC. Direct identification of major blood culture pathogens, including *Pseudomonas aeruginosa* and *Escherichia Coli*, by a panel of fluorescence in situ hybridization assays using peptide nucleic acid probes. *J Clin Microbiol.* 2005;**43**:1947–1949.
44. Schreckenberger P, McAdam A. Point-counterpoint: large multiplex PCR panels should be first-line tests for detection of respiratory and intestinal pathogens. *J Clin Microbiol.* 2015;**53**:3110–3115.
45. Binnicker MJ. Multiplex molecular panels for the diagnosis of gastrointestinal infection: Performance, result interpretation, and cost-effectiveness. *J Clin Microbiol.* 2015;Aug 26 (Epub ahead of print).
46. Buehler SS, Madison B, Snyder SR, et al. Effectiveness of practices to increase timeliness of providing targeted therapy for inpatients with bloodstream infections: a laboratory medicine best practices systematic review and meta-analysis. *Clin Microbiol Rev.* 2016;**29**:59.
47. Tang YW, Ellis NM, Hopkins MK, et al. Comparison of phenotypic and genotypic techniques for identification of unusual aerobic pathogenic gram-negative bacilli. *J Clin Microbiol.* 1998;**36**:3674–3679.
48. Bille E, et al. MALDI- TOF MS Andromas strategy for the routine identification of bacteria, mycobacteria, yeasts, *Aspergillus* spp. and positive blood cultures. Clin Microbiol Infect doi:10.1111/j. 1469–0691. 2011. 03688. x.
49. Ferreira L, Dauphin B, Leto J, et al. Direct identification of urinary tract pathogens from urine samples by matrix-assisted laser desorption ionization- time of flight mass spectrometry. *J Clin Microbiol.* 2010;**48**:2110–2115.
50. Diekema DJ, Pfaller MA. Rapid detection of antibiotic-resistant organism carriage for infection prevention. *Clin Infect Dis.* 2013;**56**:1614–1620.
51. Ota-Sullivan K, Diekema DJ. Overview of molecular diagnostics in multiple-drug resistant organism prevention: focus on multiple-drug resistant gram-negatives. In: *Molecular Microbiology: Diagnostic Principles and Practice*, 3rd ed. Ed. Persing D, Tenover F, Tang YW, et al. Washington DC: ASM Press,2014.
52. Hofko M, Mischnik A, Kaase M, Zimmermann S, Dalpke AH. Detection of carbapenemases by real-time PCR and melt curve analysis on the BD Max system. *J Clin Microbiol.* 2014;**52**:1701–1704.
53. Nijhuis R, Samuelsen O, Savelkoul P, van Zwet A. Evaluation of a new real-time PCR assay (Check-Direct CPE) for rapid detection of KPC, OXA-48, VIM, and NDM carbapenemases using spiked rectal swabs. *Diagn Microbiol Infect Dis.* 2013;**77**:316–320.
54. Tenover FC, Canton R, Kop J, et al. Detection of colonization by carbapenemase-producing Gram negative bacilli in patients by use of the Xpert MDRO assay. *J Clin Microbiol.* 2013;**51**:3780–3787.
55. Brown J, Paladino JA. Impact of rapid methicillin-resistant *Staphylococcus aureus* polymerase chain reaction testing on mortality and cost effectiveness in hospitalized patients with bacteremias: a decision model. *Pharmacoeconomics.* 2010;**28**:567–575.
56. Huizing KMN, Swanink CMA, Landstra AM, van Zwet AA, van Setten PA. Rapid enterovirus molecular testing in cerebrospinal fluid reduces length of hospitalization and duration of antibiotic therapy in children with aseptic meningitis. *Pediatr Infect Dis.* 2011;**30**:1107–1109.
57. Wishaupt JO, Russcher A, Smeets LC, Versteegh FGA, Hartwig NG. Clinical impact of RT-PCR for pediatric acute respiratory infections: a controlled clinical trial. *Pediactrics.* 2011;**128**: e1113–e1120.
58. Doern GV. The value of outcomes data in the practice of clinical microbiology. *J Clin Microbiol.* 2014;**52**:1314–1316.
59. Petti CA, Weinstein MP, Carroll KC. Systems for detection and identification of bacteria and yeasts. In: J Versalovic, KC Carroll, G Funke, et al., eds. *Manual of Clinical Microbiol*, 10th ed. Washington, DC: American Society for Microbiology, 2011:15–26.
60. Ikrayannikova LN, Filimonova AV, Malkhova MV, et al. Discrimination between *Streptococcus pneumoniae* and *Streptococcus mitis* based upon sorting

of their MALDI mass spectra. *Clin Microbiol Infect.* 2013;**19**:1066–1071.

61. Shaumann R, Knoop N, Genzel GH, et al. Discrimination of *Enterobacteriaceae* and non-fermenting Gram negative bacilli by MALDI-TOF mass Spectrometry. *Open Microbiol J.* 2013;7:118–122.
62. Jorgensen JH, Ferraro MJ. Antimicrobial susceptibility testing: a review of general principles and contemporary practices. *Clin Infect Dis.* 2009;**49**:1749–1755.
63. Richter SS, Ferraro MJ. Susceptibility testing instrumentation and computerized expert systems for data analysis and interpretation. In: J Versalovic, KC Carroll, G Funke, et al. eds. *Manual of Clinical Microbiology*, 10th ed. Washington, DC: American Society for Microbiology, 2011:1144–1154.
64. Kollef MH, Golan Y, Micek ST, Shorr AF, Restrepo MI. Appraising contemporary strategies to combat multidrug resistant Gram-negative bacterial infections: proceedings and data from the Gram- negative resistance summit. *Clin Infect Dis.* 2011;**53**(Suppl 2):S33–S55.
65. Peterson LR, Diekema DJ. To screen or not to screen for methicillin-resistant *Staphylococcus aureus*. *J Clin Microbiol.* 2010;**48**:683–689.
66. Siegel JD, Rhinehart E, Jackson M, Chiarello L. Healthcare Infection Control Practices Advisory Committee. Management of multidrug- resistant organisms in healthcare settings, 2006. Available at : http://www.cdc.gov/ncidod/dhqp/pdf/ar/mdroGuideline2006.pdf.
67. Diekema DJ, Edmond MB. Look before you leap: active surveillance for multidrug-resistant organisms. *Clin Infect Dis.* 2007;**44**:1101–1107.
68. Brossette SE, Hacek DM, Gavin PJ, et al. A laboratory-based, hospital-wide, electronic marker for nosocomial infection. *Am J Clin Pathol.* 2006;**125**:34–39.
69. McGregor JC, Weekes E, Forrest GN, et al. Impact of a computerized clinical decision support system on reducing inappropriate antimicrobial use: a randomized controlled trial. *J Am Med Inform Assoc.* 2006;**13**:378–384.
70. Peterson LR, Brossette SE. Hunting healthcare-associated infections from the clinical microbiology laboratory: passive, active, and virtual surveillance. *J Clin Microbiol.* 2002;**40**:1–4.
71. Hacek DM, Suriano T, Noskin GA, et al. Medical and economic benefit of a comprehensive infection control program that includes routine determination of microbial clonality. *Am J Clin Pathol.* 1999;**111**:647–654.
72. Heisterkamp SH, Dekkers AL, Heijne JC. Automated detection of infectious disease outbreaks: hierarchical time series models. *Stat Med.* 2006;**25**:4179–4196.
73. Widmer AF, Wenzel RP, Trilla A, et al. Outbreak of *Pseudomonas aeruginosa* infections in a surgical intensive care unit: probable transmission via hands of a healthcare worker. *Clin Infect Dis.* 1993;**16**:372–376.
74. Weintrob AC, Roediger MP, Barber M, et al. Natural history of colonization with gram-negative multidrug-resistant organisms among hospitalized patients. *Infect Control Hosp Epidemiol.* 2010;**31**:330–337.
75. Centers for Disease Control and Prevention. Guidelines for the environmental infection control in healthcare facilities. *MMWR Morb Mortal Wkly Rep*. 2003;**52**:1–42.
76. Maki DG, Alvarado CJ, Hassemer CA, Zilz MA. Relation of the inanimate hospital environment to endemic nosocomial infection. *N Engl J Med.* 1982;**25**:1562–1566.
77. Centers for Disease Control and Prevention. Guidelines for preventing health-care associated pneumonia, 2003. *MMWR Recommend Rep.* 2004;**53**(RR- 03):1–36.
78. O' Neill E, Humphreys H. Surveillance of hospital water and primary prevention of nosocomial legionellosis: what is the evidence? *J Hosp Infect.* 2005;**59**:273–279.
79. Orskov F, Orskov I. From the National Institutes of Health: summary of a workshop on the clone concept in the epidemiology, taxonomy, and evolution of the Enterobacteriaceae and other bacteria. *J Infect Dis.* 1983;**148**:346–357.
80. Chambers HF, Deleo FR. Waves of resistance: *Staphylcoccus aureus* in the antibiotic era. *Nat Rev Microbiol.* 2009;7:629–641.
81. Diekema DJ, Richter SS, Heilmann KP, et al. Continued emergence of USA300 MRSA in the United States: results from a nationwide surveillance study. *Infect Cont Hosp Epidemiol.* 2014;**35**:285–292.
82. Won S, Munoz Prices, LS, Lolans K, Hota B, Weinstein RA, Hayden MK. Emergence and rapid regional spread of KPC-producing *Enterobacteriaceae*. *Clin Infect Dis.* 2011;**53**:532–540.
83. Singh A, Goering RV, Simjee S, Foley SL, Zervos MJ. Application of molecular techniques to the study of hospital infection. *Clin Microbiol Rev.* 2006;**19**:512–530.
84. Trees E, Rota PA, Maccannell D, Gerner-Smidt P. Molecular epidemiology. In: Jorgensen J, Pfaller M, Carroll KC, et al, eds. *Manual of Clinical Microbiology*, 11th ed. Washington, DC: American Society for Microbiology, 2015:131–160.
85. Koser CU, Holden MT, Ellington MJ, et al. Rapid whole-genome sequencing for investigation of a neonatal MRSA outbreak. *N Engl J Med.* 2012;**366**:2267–2275.
86. Robilotti E, Kamboj M. Integration of whole-genome sequencing into infection control practices: the potential and the hurdles. *J Clin Microbiol.* 2015;**53**:1054–1055.
87. Dellit TH, Owens RC, McGowan JE Jr, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis.* 2007;**44**:159–177.
88. Clinical and Laboratory Standards Institute. Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data: Document M39-A4. Wayne, PA: CLSI, 2014.
89. Standiford HC, Chan S, Tripoli M, Weekes E, Forrest GN. Antimicrobial stewardship at a large tertiary care academic medical center: cost analysis before, during, and after a 7-year program. *Infect Control Hosp Epidemiol.* 2012;**33**:338–345.
90. Bartlett JG. A call to arms: the imperative for antimicrobial stewardship. *Clin Infect Dis.* 2011;**53** (Suppl 1):54–57.
91. Clinical and Laboratory Standards Institute. Performance Standards for antimicrobial susceptibility testing: 20th Informational Supplement. Wayne, PA: CLSI, 2010.
92. Livermore DM, Andrews JM, Hawkey PM, et al. Are susceptibility tests enough, or should laboratories still seek ESBLs and carbapenemases directly? *J Antimicrob Chemother.* 2012;**67**:1569–1577.
93. Covington LE, Nasrallah H, Behta M, et al. New CLSI recommendations: practical implications of eliminating ESBL testing and implementing new

MIC breakpoints for Enterobacteriaceae at a major teaching hospital, abstr 632. Abstr Soc Healthcare Epidemiol Am 2011 Annu Sci Meet 1 to 4 April 2011 Dallas, TX. Available at: http://shea.confex.com/shea/2011/webprogram/Paper4335.html.

94. Rodriguez- Bano J, Picon E, Navarro MD, et al. Impact of changes in CLSI and EUCAST breakpoints for susceptibility in bloodstream infections due to extended- spectrum β-lactamase-producing *Escherichia coli*. Clin Microbiol Infect 2011; doi:10. 111/j. 1469–0691. 2011. 03673. x.

95. ACGME. Program Requirements for Graduate Medical Education in Infectious Diseases. Available at: www.acgme.org/acgmeweb/Portals/0/PFAssets/2013-PR-FAQ-PIF/146_infectious_disease_int_med_07132013.pdf.

96. Certification Board of Infection Control. Available at: http://www.cbic.org/certification/2015-examination-content-outline Accessed December 1, 2015.

97. Pfaller MA, Diekema DJ. The role of the laboratory in prevention of healthcare-associated infections. In: Jarvis WR, ed. *Bennett and Brachman's Hospital Infections*, 6th ed. Philadelphia, PA. Lippincott, Williams and Wilkins, 2014, p. 119–138.

Chapter

24 Biological Disasters

Sandro Cinti and Eden Wells

Biological disasters, including bioterrorism, severe acute respiratory syndrome (SARS), Middle East Respiratory Syndrome (MERS), Ebola, and pandemic influenza present a unique set of challenges for the hospital epidemiologist (HE). These events appear suddenly, cause high morbidity and mortality, and produce high levels of fear and, potentially, panic. The response to a biological disaster requires coordination of many local, state and federal entities. As such, it is important for the HE to be familiar not only with the biological agents, but also with his/her role in responding to a biological disaster. This chapter will review the National Incident Management Structure (NIMS), the role of the HE in a biological disaster, the early characteristics of a biological disaster, and, finally, the agents of a biological disaster including Category A Bioterrorism Agents (smallpox, anthrax, tularemia, botulinum toxin, viral hemorrhagic fevers, and plague), SARS, MERS, and pandemic influenza.[1]

The National Incident Management Structure (NIMS)

The hospital epidemiologist (HE) will have an important role within a healthcare facility's disaster response plan to a biological disaster. In the event of a large-scale infectious disease outbreak, as may be seen with a bioterrorist attack, an emerging infectious disease outbreak, or with an influenza pandemic, hospitals and their emergency departments will be on the front line for response. Hospital planners must collaborate with other community responders so that the overall response is delivered in a coordinated fashion. Interagency, hospital, and community response during a disaster event can become extremely complex, and in 2003 Homeland Security Presidential Directive-5 (HSPD-5) created the National Incident Management System (NIMS).[2] NIMS enhances the ability of the United States to manage any domestic incident by establishing one single, comprehensive national incident management system.[2]

NIMS provides a national template for all government and private organizations to work together in a coordinated fashion to prepare for, prevent, respond to and recover from domestic incidents, including acts of terrorism.[2] In 2006, the NIMS Integration Center and Department of Health and Human Services (DHHS) released the "NIMS Implementation Activities for Hospitals and Healthcare Systems" guide, which contains seventeen elements for hospital planning.[3] These have been updated by the Hospital Preparedness Program (HPP) and the DHHS Assistant Secretary of Preparedness and Response (ASPR) over the years to 11 NIMS Implementation Objectives (Table 24.1) as of 2015. While the American Hospital Association strongly encourages all hospitals to become NIMS-compliant, only hospitals that receive federal preparedness and response funds are required to do so.[4,5] Regardless, emergency responders from surrounding agencies are themselves operating under NIMS-compliant response systems, and it is important for hospitals to coordinate planning and response with these agencies.[5] Hospitals will need to interact with numerous response partners in a bioterrorism event, including prehospital emergency services, the local emergency operations center, other hospitals, the regional hospital coordination center, public safety and public health agencies, to name just a few (Figure 24.1).[6] Hospitals and hospital systems that are recipients of federal hospital preparedness funds work together in local and regional groups to coordinate their disaster and bioterrorism response plans, regardless of whether the HE's facility is a recipient of these funds. It will be important for the HE to identify these preparedness activities within his or her community and healthcare region.

The Hospital Incident Command System

A critical element for hospital response in a disaster such as a bioterrorism event is the incident command structure. The Hospital Incident Command System (HICS) is one example of a NIMS-compliant incident command system (ICS) methodology for healthcare systems. HICS was adapted from the Hospital Emergency Incident Command System HEICS, which was developed in the 1980s and was used by over 6, 000 US hospitals to prepare and respond to a variety of disasters.[6] HICS, however, can be implemented for both emergent and non-emergent incidents. A sample HICS command structure is outlined in Figure 24.2.[6]

The HE is part of the hospital's ICS response, either in developing the hospital response plan, in surveillance for the detection of a bioterrorism, outbreak, or pandemic event, or in the control and management of the disease agent within the hospital facility. Therefore, the HE may be asked to assume a role within the Operations or Planning sections of the ICS (see Figure 24.1). These roles may be different from the HE's usual roles, and regular training and exercise of the hospital facility's ICS or HICS is important for all involved healthcare personnel. Furthermore, as a subject matter expert in infection prevention and infectious diseases, the HE may be asked to provide information to the Incident Commander or Section

Table 24.1 NIMS Implementation for Healthcare Organizations Guidance January 2015[4]

Adoption
1. Adopt NIMS throughout the healthcare organization to include appropriate departments and business units.
2. Ensure Federal Preparedness grants and cooperative agreements support NIMS Implementation (in accordance with the eligibility and allowable uses of the awards).
Preparedness: Planning
3. Revise and update emergency operations plans (EOPs), standard operating procedures (SOPs), and standard operating guidelines (SOGs) to incorporate NIMS and National Response Framework (NRF) components, principles and policies, to include planning, training, response, exercises, equipment, evaluation, and corrective actions.
4. Participate in interagency mutual aid and/or assistance agreements, to include agreements with public and private sector and nongovernmental organizations.
Preparedness: Training and Exercises
5. Implement ICS-700: NIMS, An Introduction, ICS-100: Introduction to ICS, and ICS-200: ICS For Single Resources training to appropriate personnel.
6. Implement ICS-800 National Response Framework (NRF): An Introduction training to appropriate personnel.
7. Promote and integrate, as appropriate, NIMS concepts and principles (i.e., trie Incident Command System) into all healthcare organization-related training and exercises.
Communications and Information Management
8. Promote and ensure that hospital processes, equipment, communication, and data interoperability facilitate the collection and distribution of consistent and accurate information with local and state partners during an incident or event.
9. Apply common and consistent terminology as promoted in NIMS, including the establishment of plain language communications standards.
Command and Management
10. Manage all emergency incidents, exercises, and preplanned (recurring/special) events with consistent application of ICS organizational structures, doctrine, processes, and procedures.
11. Adopt the principle of Public Information, facilitated by the use of the Joint Information System (JIS) and Joint Information Center(J 1C) ensuring that Public Information procedures and processes gather, verify, coordinate, and disseminate information during an incident or event.

Chiefs in the Emergency Operation Center during any serious facility, or community, disaster event.

Role of the Hospital Epidemiologist in Biological Disasters

The HE will play a large role in the preparation for and response to any biological disaster. Within the HICS, the HE will be a key consultant to the incident commander. Particular duties that will fall on the HE before and during a biological disaster include surveillance for infection, infection prevention and communication of infectious risk to healthcare personnel.

Surveillance for infection

The HE is responsible for developing surveillance protocols within the hospital but must also monitor external sources for up-to-date information on potential biological threats. During the SARS outbreak of 2003, many US hospitals screened patients presenting to emergency departments for clinical symptoms and exposure history based on the CDC case definition.[7] Had SARS become more widespread in the US, more stringent surveillance might have been necessary. In Toronto, where SARS was more widespread, hospitals instituted strict temperature checks for both healthcare personnel and patients.[8] Regarding laboratory surveillance, the HE must guide clinicians and hospital laboratories on which laboratory tests should be used for surveillance and diagnosis of a biological threat. As an example, early in an influenza pandemic, rapid influenza tests may help to signal the arrival of influenza in a particular hospital. However, given the relative insensitivity of rapid influenza tests,[9] it may not make sense to use this test later in the pandemic or as a means of identifying infected patients that should be treated.

Regarding external surveillance, the HE will be called upon to interpret information coming from multiple sources including the community, the state, the federal government and the World Health Organization (WHO). Rapid decisions will have to be made about activating biological disaster plans within the hospital. As an example, an increase in the WHO pandemic alert phase from 3 to 4 would indicate increased human-to-

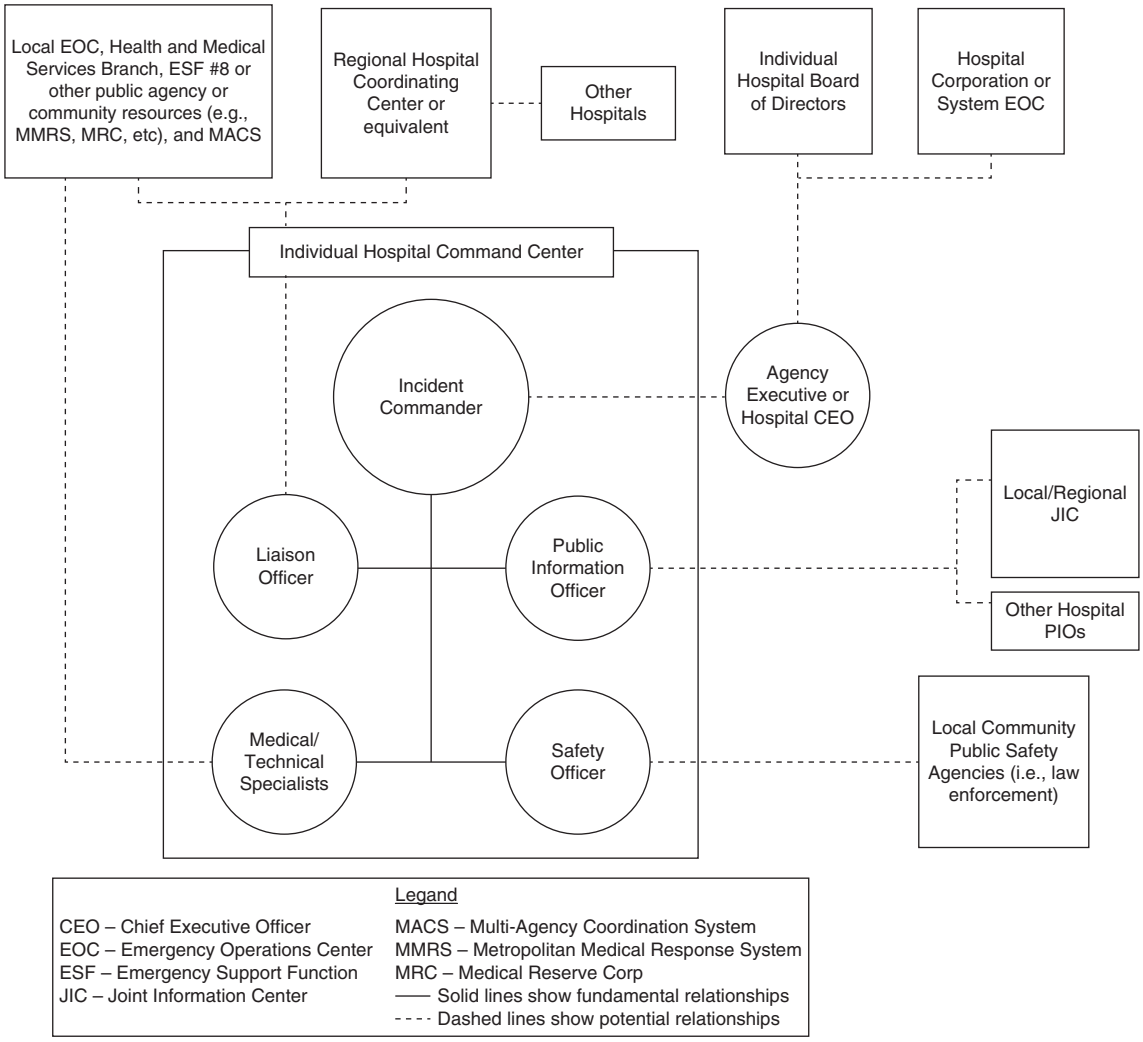


Figure 24.1 Hospital Community Response Partners.[6] © 2014 by California Emergency Medical Services Authority (EMSA), reproduced with permission.

human transmission of a pandemic strain of influenza.[10] Even if increased transmission is not occurring in the US, certain actions such as stockpiling vaccine, personal protective equipment, and antimicrobials might be important for a hospital. If the pandemic progresses, strategies to improve hospital capacity such as curtailing elective procedures and clinic appointments, or reassigning staff to influenza wards, might need to be instituted. Gathering accurate information on disease activity locally, statewide, nationwide, and worldwide will be crucial to a successful hospital response. The Ebola epidemic of 2014 is another example of the need for external surveillance. HEs all over the US had to keep in close contact with state health departments in order to follow CDC monitoring guidelines for travelers returning from Guinea, Sierra Leone, or Liberia.[11]

Infection Prevention

Although infection prevention is the daily task of the HE, biological disasters present unique challenges. Pre-event duties of the HE in planning for a biological disaster include 1) helping to develop stockpiles of personal protective equipment (PPE), vaccines, and antimicrobials; 2) establishing protocols for the use of PPE, isolation procedures, and cohorting of patients to prevent disease transmission; 3) helping to establish priority groups and develop mechanisms for the distribution of vaccines, and antimicrobials; and 4) helping to develop treatment, prophylaxis, and immunization protocols that will be used within the hospital.

Stockpiling of antimicrobials, PPE and, possibly, vaccine will be very important as these will be scarce resources during a biological disaster. During the SARS outbreak in Toronto, Canada, N95 masks became scarce even in the US where very few cases and no fatalities had occurred.[12] There has been enough concern about bioterrorism and pandemic influenza that the states and federal government have stockpiled antimicrobials.[13,14] In anticipation of a biological event, the HE must work with material services, pharmacy, infectious diseases, and the hospital leadership to determine which resources and how much of each resource should be stockpiled. The input of the HE is particularly crucial when it comes to stockpiling of PPE, as protocols for fit-testing of N95 masks

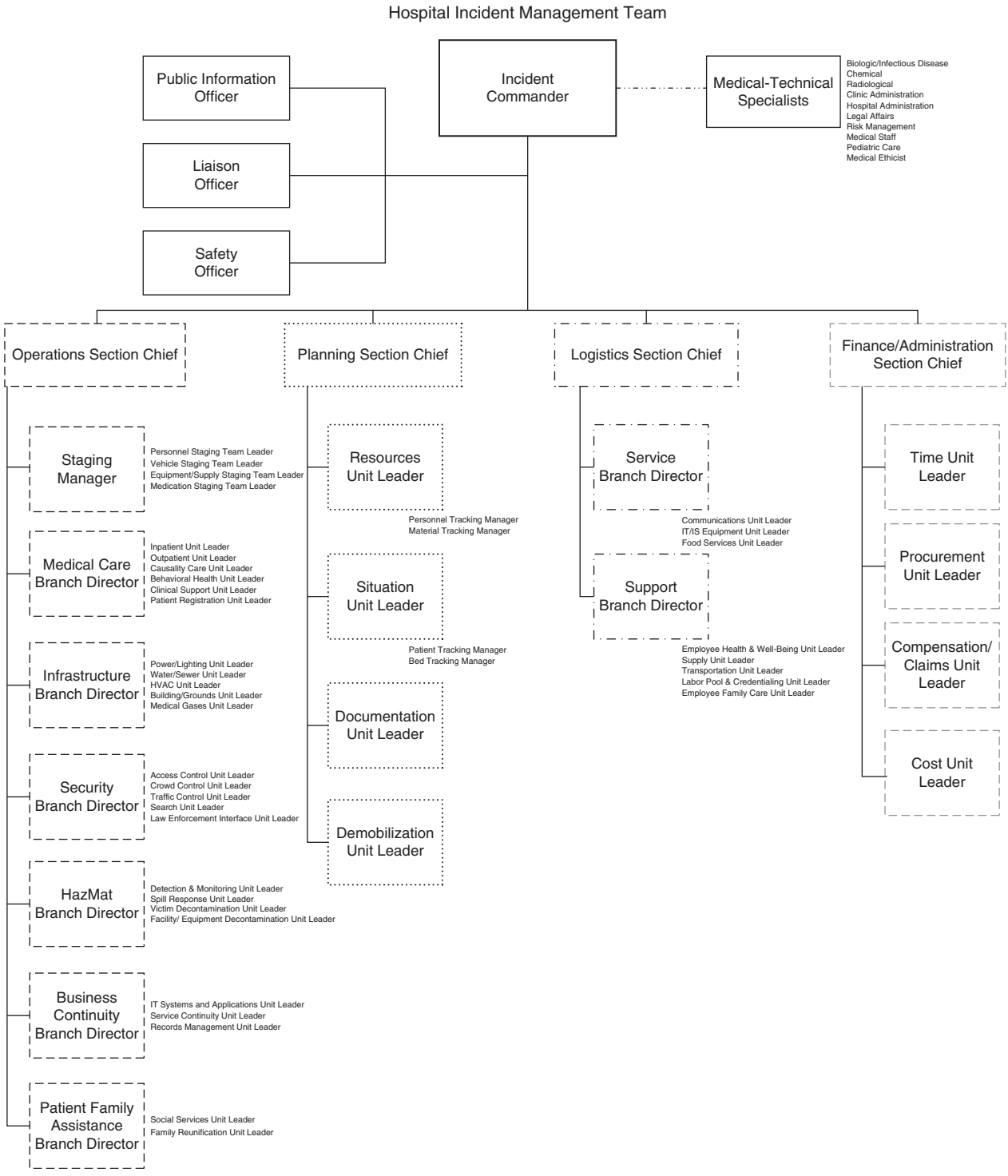


Figure 24.2 Hospital Incident Management Team-Sample Organizational Chart.[6] © 2014 by California Emergency Medical Services Authority (EMSA), reproduced with permission.

and proper use of PPE will be crucial determining the numbers that should be held on site.

Hospital leadership will look to the HE to develop protocols for PPE use, isolation procedures, and cohorting strategies in all areas of the hospital. Each biological threat has different clinical presentations and requirements for infection prevention (see Tables 24.2 and 24.3), and many biological agents such as anthrax, plague, SARS, MERS, Ebola, or H5N1 influenza have rarely or never been seen in most hospitals. Thus the HE must develop strategies for infection prevention in a mass casualty biological event. Although SARS requires airborne isolation precautions, a huge influx of patients might force a hospital to cohort SARS-infected patients to a certain ward, section of the hospital, or even off site.[15] Plans for cohorting

Table 24.2 Clinical presentation and diagnosis of biological disaster agents*

Agent	Clinical presentation	Incubation	Diagnosis
Anthrax *(Bacillus anthracis)*	**Cutaneous** • Papule to vesicle to eschar, painless, extensive surrounding edema • Lymphangitis may occur with painful lymphadenopathy • Fevers and chills may occur with dissemination • Eschar dries and falls off over 1–2 weeks **Inhalational** • Stage 1: fever, dyspnea, cough, headache, vomiting, chills, weakness, abdominal pain, and chest pain. May improve slightly after a few days. • Stage 2: abrupt fever, dyspnea, stridor, cyanosis, diaphoresis, and shock with rapid death. Lymphadenopathy may occur. 50% get meningitis. **Gastrointestinal** • Upper symptoms: sore throat, dysphagia, oral or esophageal ulcers, nausea, vomiting, fevers, hemoptysis • Lower symptoms: fevers, abdominal pain, bloody stools, lymphadenopathy, ascites, acute abdomen, sepsis **Meningitis** • Headache, neck stiffness, photophobia, fever, chills, altered mental status	**Cutaneous**: 1–10 days **Inhalational**: 1–6 days (residual spores may cause disease up to 60 days later) **Gastrointestinal**: 3–7 days (residual spores may cause disease up to 60 days later) **Meningitis:** 1–6 days (residual spores may cause disease up to 60 days later)	**Cutaneous** • Culture of vesicular fluid, skin biopsy or blood may grow *B. anthracis* • Gram stain of vesicular fluid, wound exudate or punch biopsy may show gram positive bacilli • PCR or IHS of punch biopsy of the skin (send to CDC) **Inhalational** • Gram stain of blood buffy coat and/or blood showing gram positive rods may be the earliest sign of infection. • Blood culture positive for gram positive rod within 6–24 hours of infection (unless antibiotics given before) and positive for *Bacillus* species within 48 hours . Antimicrobial susceptibilities should be performed • Blood, pleural fluid, spinal fluid for PCR, IHS (send to CDC) • Bloody pleural fluid • Send suspicious samples to CDC for confirmation of diagnosis • Sputum culture and gram stain are rarely helpful • Radiology-CXR with widened mediastinum and/or pleural effusion and/or infiltrates, CT chest with mediastinal lymphadenopathy, pleural effusion and/or pulmonary infiltrates • Nasal swabs and blood antibody levels are only useful for epidemiologic purposes **Gastrointestinal** • Same lab tests as inhalational anthrax • Stool cultures not helpful • Radiology-abdominal X-ray with bowel obstruction, CT abdomen with lymphadenopathy and thickened bowel

Table 24.2 (cont.)

Agent	Clinical presentation	Incubation	Diagnosis
			Meningitis • Bloody CSF • Positive gram stain for gram positive rods • Positive culture of CSF for gram positive rod within 6–24 hours of infection (unless antibiotics given before) and positive for *Bacillus* species within 48 hours **Postmortem** • Hemorrhagic necrotizing lymphadenitis, meningitis, mediastinitis

Smallpox (Variola major)	**Prodrome (duration 2–4 days)**
	• Sometimes contagious
	• Fever, in the range of 101°F to 104°F
	• Malaise
	• Head and body aches, prostration
	• Abdominal pain and delirium may be present
	• Occasionally, vomiting
	Early Rash (duration about 4 days)
	• Most contagious period
	• Rash appears as small red spots on the tongue and in the mouth (enanthem)
	• Rash develops into sores that break open and spread large amounts of the virus into mouth and throat
	• Rash then appears on the skin, starting on the face and spreading to the arms and legs and then to the hands and feet
	• By the third day of the rash, the rash becomes papular
	• By the fourth day, the vesicles become pustular and fill with a thick, opaque fluid; often will be umbilicated
	• Fever often will rise again at this time and remain high until scabs form over vesicles
		12–14 days (range 7–17 days)	• CDC rash protocol
			• Laboratory diagnostic testing for variola virus should be conducted in a CDC Laboratory Response Network (LRN) laboratory utilizing LRN-approved PCR tests and protocols for variola virus
			• Culture of vesicular or pustular fluid
			  ▪ Specimen should be collected by someone who has recently been vaccinated and who is wearing appropriate PPE
			  ▪ To obtain vesicular or pustular fluid, lesions may need to be opened with the blunt edge of a scalpel; the fluid can then be harvested on a swab
			• Diagnostic laboratory criteria:
			  ▪ PCR identification of variola DNA in a clinical specimen
			  ▪ Isolation of smallpox (variola) virus from a clinical specimen with variola PCR confirmation
			• Initial confirmation of a smallpox outbreak requires additional confirmatory testing at CDC

	• Patient may appear critically ill **Pustular Rash (duration about 5 days)** • Contagious • Rash becomes more vesicular, round, tense, and deeply embedded in the dermis • Patient appears critically ill **Pustules and Scabs (duration about 5 days)** • Contagious • Crusts begin to form on about the eighth or ninth day of rash **Resolving Scabs (duration about 6 days)** • Contagious • The scabs begin to fall off, leaving pitted scars. • Most scabs will have fallen by three weeks after rash onset • The patient is contagious until all of the scabs have fallen off **Scabs Resolved** • Scabs have fallen off • Patient is no longer contagious **Other Forms** • Hemorrhagic, flat smallpox ▪ Difficult to diagnose, high mortality		
Plague (*Yersinia pestis)*	**Bubonic** • Abrupt onset of fever and chills • Intense pain and swelling in lymph node area; exquisite tenderness without fluctuation • If untreated can lead to disseminated infection	**Bubonic** (from flea bite): 2–8 days **Pneumonic, septicemic, pharyngeal, meningitis:** 1–6 days	**Bubonic** • Lymph node aspirate with gram-negative bacilli or coccobacilli with bipolar (safety pin) staining • Culture of lymph node aspirate with gram-negative bacilli or coccobacilli after 24–48 hours growth with later identification as *Yersinia* species

Table 24.2 (cont.)

Agent	Clinical presentation	Incubation	Diagnosis
	Pneumonic • Can be primary from inhalation of respiratory droplets of infected individuals or secondary due to dissemination of bubonic plague (more common) • Sudden onset of high fever, dyspnea, pleuritic chest pain, and cough which may be productive of bloody sputum • Rapidly fatal if not treated **Septicemic** • Fever and sepsis without other characteristic clinical clues • Difficult to diagnose in a timely manner and rapidly fatal if not treated **Pharyngeal** • Pharyngitis/tonsillitis with anterior cervical lymphadenitis after ingestion of *Y. pestis* **Meningitis** • Can occur from bacteremia associated with other forms of plague • Symptoms typical of bacterial meningitis		**Pneumonic** • Gram stain of sputum, blood, or lymph node aspirate with gram-negative bacilli or coccobacilli with bipolar (safety pin) staining • Culture of sputum, blood, or lymph node aspirate with gram-negative bacilli or coccobacilli after 24–48 hours growth with later identification as *Yersinia* species ▪ Antimicrobial susceptibilities should be performed • Antigen detection, IgM EIA, immunostaining, and PCR only available through CDC or state labs • Leukocytosis, coagulation abnormalities, aminotransferase elevations, azotemia, and other evidence of multiorgan failure • Radiology-CXR with lobar pneumonia or bilateral infiltrates and/or pleural effusions **Septicemic** • Same as for pneumonic except CXR may not show pneumonia and there may be no buboes **Pharyngeal** • Throat culture with gram-negative bacilli or coccobacilli • Culture of lymph node aspirate with gram-negative bacilli or coccobacilli after 24–48 hours growth with later identification as *Yersinia* species **Meningitis** • CSF culture and gram stain with gram-negative bacilli or coccobacilli with bipolar (safety pin) staining

			Postmortem • Lobular exudation, bacillary aggregation, and areas of necrosis in pulmonary parenchyma

Tularemia (*Francisella tularensis*)	**Pneumonic**
	• Abrupt onset fever, headache, chills, myalgias, sore throat
	• Dry or slightly productive cough, substernal chest pain or tightness
	• Nausea, vomiting, diarrhea
	• Symptoms can last weeks to months
	Typhoidal
	• Fevers, chills, myalgias, abdominal pain, diarrhea
	• No regional lymphadenopathy or skin lesions
	Oropharyngeal
	• Exudative pharyngitis, tonsillitis, oral ulcerations
	• Cervical lymphadenopathy
	• Fevers, headache, chills, myalgias
	Glandular
	• Regional lymphadenopathy without skin or ocular lesions
	• Fevers, headache, chills, myalgias
	Ulceroglandular and Oculoglandular.
	• Less likely to occur from a biological attack
	• Ulcerative skin or ocular lesions with regional lymphadenopathy
	• Fevers, headache, chills, myalgias
		All forms: 1–14 days	**Pneumonic**
			• High index of suspicion given nonspecific symptoms
			• Gram stain of blood, sputum, lymph node:*F. tularensis* is a gram-negative coccobacillus that stains poorly
			• Culture of sputum, pharyngeal swabs, lymph node and rarely blood-difficult to culture and requires cysteine-enriched agar
			  ▪ Highly infectious so microbiology lab must be notified if tularemia is suspected
			  ▪ Antimicrobial susceptibilities should be performed
			• Fluorescent antibody stain performed in special laboratories
			• Antigen detection assays, PCR, EIA, immunoblotting, pulse field gel electrophoresis only done in special laboratories
			• Serum antibodies-fourfold rise in titer or single IgG titer of 1:160 (these only appear after 10 days of illness)
			• Leukocytosis, coagulation abnormalities, aminotransferase elevations, azotemia, and other evidence of multiorgan failure
			• Radiology-CXR/chest CT with bronchopneumonia in 1 or more lobes, hilar adenopathy, pleural effusion
			• Pathology/Postmortem: acute necrosis in involved tissues (lungs, lymph nodes, spleen, liver, and kidney) with a granulomatous reaction

Table 24.2 (cont.)

Agent	Clinical presentation	Incubation	Diagnosis
			Typhoidal, Glandular, Ulceroglandular, Pharyngeal, Oculogalndular • Same as above without pulmonary tests and including skin and/or ocular specimens
Botulinum Toxin (*Clostridium botulinum)*	**Foodborne** • Gastrointestinal: . Initial symptoms can include nausea, vomiting, abdominal cramps, or diarrhea . Constipation (after neurological symptom onset) • Neurological: . Initial-dry mouth, blurred vision, and diplopia . Dysphonia, dysarthria, dysphagia, and peripheral muscle weakness. . Characteristic proximal-to-distal pattern: symmetric descending paralysis, begins with the cranial nerves, affects upper extremities, then respiratory muscles, and then the lower extremities **Wound** • Gastrointestinal: none • Neurological: Same as above **Infant** • Gastrointestinal: . Constipation . Poor feeding • Neurological: . Weak cry . Poor muscle tone, floppy head . Decreased sucking, lethargy	2 hours–8 days depending on toxin dose absorbed Inhalational form has effect by 3 days	• Clinical diagnosis • Routine testing is unremarkable • Serum, stool, gastric aspirates, vomitus, and suspected food or liquid should be sent to CDC or state lab for testing for mouse bioassay (detects 0.03 ng of botulinum toxin in 1–2 days); also culture will grow anaerobically in 7–10 days • Electromyogram (EMG): normal nerve conduction velocity, normal sensory nerve function, a pattern of brief, small amplitude motor potentials, and an incremental response (facilitation) to repetitive stimulation often seen only at 50 Hz • CSF-normal • Rule out Guillain-Barré Syndrome (GBS), myasthenia gravis-GBS is ascending paralysis, myasthenia gravis and GBS have characteristic EMG findings

	Intentional, or bioterror, event • Gastrointestinal: Similar to foodborne, above • Neurological: Similar to foodborne, above • Inhalational events may not be associated with gastrointestinal symptoms, just neurological		
Viral Hemorrhagic Fever (VHF)	**Filovirus** (Marburg, Ebola) • Fever, headache, myalgias, abdominal pain, nausea, vomiting • Maculopapular rash 5 days after onset of symptoms, jaundice • Hemorrhagic complications: petechiae, hematemesis, hemoptysis, purpura, bloody diarrhea, bleeding at puncture sites, shock, DIC • Delirium, coma, seizures **Arenevirus** (Lassa Fever) • Fever, headache, malaise, arthralgias, back pain, nonproductive cough • Maculopapular rash, prostration, exudative pharyngitis • Hemorrhagic complications- see filovirus above **Bunyavirus** (Rift Valley Fever) • Fever, headache, photophobia, retro-orbital pain • Hemorrhagic complications- see filovirus above • Encephalitis-confusion, lethargy, tremors, ataxia, coma, seizures, meningismus, vertigo, and choreiform movements. • Retinitis-bilateral: hemorrhages, exudates, and cotton wool spots may be visible on macula; retinal detachment may occur • Hepatitis	**Filovirus** (Marburg, Ebola): 2–21 days **Arenavirus** (Lassa Fever): 5–16 days **Bunyavirus** (Rift Valley Fever): 2–6 days **Flavivirus** (Yellow Fever): 3–6 days	• World Health Organization surveillance standards for VHF (all must be present) ◦ Acute onset of fever of less than 3 weeks' duration in a patient who is severely ill ◦ No known predisposing host factors for hemorrhagic manifestations ◦ Any 2 of the following: hemorrhagic or purpuric rash, epistaxis, hematemesis, hemoptysis, blood in stool, or other hemorrhagic symptom • Organism identification of any VHF agent must be performed at the CDC, and specimens should be collected and sent in consultation with local public health and the CDC ◦ Serology (ELISA), PCR, viral isolation (requires Biosafety Level 4 facility) **Fiovirus** (Marburg, Ebola) • Laboratory: leukopenia, thrombocytopenia, elevated liver enzymes and amylase, DIC (prolonged bleeding time, prothrombin time, and activated partial thromboplastin time; elevated fibrin degradation products; decreased fibrinogen)

Table 24.2 (cont.)

Agent	Clinical presentation	Incubation	Diagnosis
	Flavivirus (Yellow Fever) • Fever, headache, myalgias, facial flushing, conjunctival injection, relative bradycardia • Hemorrhagic complications: see filovirus above • Malignant disease: severe hepatic involvement, bleeding manifestations, renal failure, shock, and death		**Arenevirus** (Lassa Fever) • Laboratory-elevated liver enzymes, hemoconcentration **Bunyavirus** (Rift Valley Fever) • Laboratory: thrombocytopenia, leukocytosis initially followed by leukocytopenia, DIC (see filovirus above), elevated hepatic enzymes **Flavivirus** (Yellow Fever) • Laboratory: leukopenia, thrombocytopenia, liver enzyme elevation, and hyperbilirubinemia
Severe Acute Respiratory Syndrome (SARS)	**Prodrome:** influenza-like symptoms including fever, myalgias, headache, and diarrhea **Early Respiratory Phase**: dry, nonproductive cough and mild dyspnea **Late Respiratory Phase:** progressive hypoxia, dyspnea on exertion (10–20%) require mechanical ventilation	**Prodrome**: 2–7 days **Early Respiratory Phase**: 1–5 days **Late Respiratory Phase**: 7 days	**Case Definition** • Clinical, epidemiological, and laboratory criteria (www.cdc.gov/ncidod/sars/guidance/b/app1.htm) **PCR** • Positive test must be confirmed by testing for another region of the SARS virus genome • Nasopharyngeal swabs (high sensitivity even in first 5 days), pharyngeal, and stool specimens • Serum PCR is not as sensitive but should be sent • Viral quantification may be helpful in infection prevention **Antibody Assays** • IgM is not positive until 7 days after symptoms begin; IgG is positive after 20–26 days so serologic testing in the acute setting is not helpful • Serologic testing can be done by immunofluorescent assay, ELISA, and Western blot assay **Antigen Detection** • Serum EIA for SARS N protein-good for early disease (<7 days) • Sensitivity decreases after 7 days

			• Antigen EIA not as sensitive for nonserum specimens as RT-PCR **General laboratory tests are not helpful Radiology**: CXR and CT with nonspecific bilateral infiltrates
Middle Eastern Respiratory Syndrome Coronavirus (MERSCoV)	• **Symptoms:** Fever, chills/rigors, headache, non-productive cough, dyspnea, and myalgia • **Other symptoms:** sore throat, coryza, nausea and vomiting, dizziness, sputum production, diarrhea, vomiting, and abdominal pain	**5 days** (range 2–14)	• Confirmatory laboratory testing requires a positive PCR on at least two specific genomic targets or a single positive target with sequencing on a second
Pandemic Influenza	**Influenza-like illness:** • Fever (>38°C) • Sore throat • Cough **Other possible signs/symptoms:** • Headache • Fatigue • Rhinorrhea, nasal congestion • Myalgias • Gastrointestingal symptoms may occur (more commonly in children), such as nausea, vomiting, and diarrhea • More severe presentations, such as shortness of breath/dyspnea, hyppotension, pneumonia, "cytokine storm," shock or death may occur • Presentation may also be altered by secondary or underlying infections	**1–7 days**	• Respiratory specimens, best collected within first 3 days of illness onset: 1) nasopharyngeal wash/aspirates, 2) nasopharyngeal swabs, 3) oropharyngeal swabs, 4) broncheoalveolar lavage, 5) tracheal aspirate, 6) pleural fluid tap, 7) sputum, and 8) autopsy specimens • Nasopharyngeal wash/aspirates are specimen of choice for respiratory virus detection • Other specimen sources may be requested depending upon pandemic strain • Viral isolation is usually the gold standard for influenza diagnostics • Real-time PCR is the preferred assay for influenza A (H5N1) testing • BSL2 conditions required: CDC has made H5-specific primers and probes available to state health department laboratories[24] • Immunofluorescence antibody (IFA) staining following virus isolation to identify influenza types (A, B) and influenza A HA subtypes using a specific antisera panel • Some rapid diagnostic tests may be able to detect the pandemic strain with adequate sensitivity and

Table 24.2 (cont.)

Agent	Clinical presentation	Incubation	Diagnosis
			specificity during an influenza pandemic • Sera for ELISA, hemagglutination inhibition, and microneutralization assays can be used to confirm influenza infection retrospectively • Post-mortem specimens (the state health department will arrange with CDC if deemed necessary for novel or pandemic strain influenza case); a minimum total of 8 blocks or fixed-tissue specimens representing should be obtained • Radiology: CXR/CT chest with pleural effusion and/or infiltrates

PCR-polymerase chain reaction, IHS-immunohistochemical staining, CXR-Chest X-ray, CT-computed tomography, CSF-cerebrospinal fluid, DIC-disseminated intravascular coagulation, ELISA-enzyme-linked immunosorbent assay, EIA-enzyme immunoassay.

* Table based on references #23–28, 32.

Table 24.3 Infection prevention issues related to biological disaster agents[†]

Organism	Person-to-person spread	Infection control precautions[‡]	Decontamination	Post-mortem care
Anthrax *(Bacillus anthracis)*	No	**Contact precautions***	• Exposed persons: thoroughly wash exposed areas with soap and water • Clean contaminated surfaces with 1:10 dilution of household bleach • Contaminated clothing should be placed in a biohazard bag	• Cremation is preferred • Autopsy instruments should be autoclaved or incinerated
Smallpox (Variola major)	Yes: Droplet and from skin lesions	• Contact precautions • Droplet precautions • Airborne precautions	• Clean contaminated surfaces with manufacturer-recommended concentrations of EPA-registered disinfectants • Use FDA-approved disinfection and sterilization methods for medical instruments and devices • Clothing and bedding should be bagged or contained at the point of use, with minimal agitation to avoid spread of fomites, in accordance with Occupational Safety and Health Administration (OSHA) regulations • Laundry should be autoclaved or laundered in hot water with bleach added	• Cremation whenever possible • Mortuary workers should be vaccinated
Plague *(Yersinia pestis)*	Yes: Droplet spread	• **Droplet precautions:**[§] For 48 hours after treatment and until clinical improvement • Infected patients should wear a mask (a respirator is not necessary) when they are outside their hospital room • Cohorting of plague patients may occur if patient numbers are high • Contact* and Droplet[§] Precautions should be followed if buboes are aspirated	• Environmental decontamination is not generally recommended as *Y. pestis* is only infectious for approximately 1 hour • If cleaning of environmental surfaces is performed, a 1:10 dilution of household bleach is considered adequate for cleaning • Disinfect patient clothing per standard precautions protocols	• Standard precautions are required at autopsy • N-95 masks should be used at autopsy for aerosol generating procedures (bone saw)

Table 24.3 (cont.)

Organism	Person-to-person spread	Infection control precautions‡	Decontamination	Post-mortem care
Tularemia *(Francisella tularensis)*	No	• Standard precautions Microbiology laboratory personnel should be alerted when tularemia is suspected, and diagnostic procedures should be carried out under biological safety level 2 (BSL-2) conditions	• Surface decontamination: spray the suspected contaminant with a 1:10 dilution of household bleach • Persons with direct exposure to powder or liquid aerosols containing *F. tularensis* should wash body surfaces and clothing with soap and water • Disinfect patient clothing per standard precautions protocols	• Standard Precautions are required at autopsy • Aerosolizing procedures (bone sawing) should be avoided
Botulinum Toxin (*Clostridium botulinum)*	No	• Standard precautions	• After exposure to botulinum toxin, clothing and skin should be washed with soap and water • Contaminated objects or surfaces should be cleaned with a 1:10 dilution of household bleach • Botulinum toxin degrades 2 days after aerosolization	• Standard Precautions are required at autopsy
Viral Hemorrhagic Fever (VHF)	Yes: Ebola, Marburg, Lassa Fever can be spread though contact with blood or body fluids. Cadavers can spread disease through fluids.	• Contact precautions* • **Airborne precautions:**†† Although airborne transmission is rare, it has occurred • Healthcare personnel coming into contact with a suspected VHF patient should wear the following PPE: • N-95 respirator or powered air-purifying respirator (PAPR) • Double (leak-proof) gloves • Impermeable gowns • Face shields • Goggles for eye protection	• Environmental surfaces, inanimate contaminated objects, or contaminated equipment: disinfect with a 1:10 dilution of household bleach using standard procedures • Contaminated linens should be incinerated, autoclaved, or placed in double (i.e., leak-proof) bags at the site of use and washed without sorting in a normal hot water cycle with bleach • Hospital housekeeping staff and linen handlers should wear appropriate PPE when	• Standard precautions for autopsy • N95 mask at autopsy • Avoid aerosol generating procedures (bone saw) • Burial o Limit contact to trained personnel o Cremation is preferable

		• Leg and shoe coverings 21-day observation of all persons with high-risk contact including mucous membrane contact, percutaneous injury involving contact with secretions, excretions, or blood from a patient with VHF, or close contact (those who live with, shake hands with, hug, process laboratory specimens from, or care for a patient with VHF).	handling or cleaning potentially contaminated material or surfaces • Decontaminate stool, fluids, and secretions before disposal; such fluids should be autoclaved, processed in a chemical toilet, or treated with several ounces of household bleach for 5 or more minutes before flushing or disposal	
Severe Acute Respiratory Syndrome (SARS) **Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV)**	Yes:Predominantly though close contact or droplets; however, airborne spread has not been excluded and may occur in some cases (e.g., superspreaders)	• Contact precautions • Airborne precautions • Emergency department and ambulatory screening respiratory protocols . Negative pressure room or cohorting for patients who fit case definition . PPE for healthcare personnel entering room of suspected patient . Promote respiratory and hand hygiene • Hospitalized patients . Place patients in negative pressure room if possible or cohort during an epidemic outbreak . PPE should be donned upon entering the room and doffed before exiting room . Limit patient transport. If needed, patient should wear surgical mask and clean gown.	• Designate certain personnel in hospitals to clean and disinfect rooms • Cleaners should wear appropriate PPE • Use any EPA-registered hospital disinfectant • Clean and disinfect SARS patients' rooms at least daily and more often when visible soiling/contamination occurs • Cleaning and disinfection after patient discharge or transfer	• Surgical mask if no aerosols • Use biosafety cabinets for specimens

Table 24.3 (cont.)

Organism	Person-to-person spread	Infection control precautions‡	Decontamination	Post-mortem care

		• Aerosol generating procedures (intubation, bronchoscopy)
		  ◦ Limit use of these
		  ◦ Perform in negative pressure room
		  ◦ PPE during procedure
		• Healthcare personnel who care for SARS or MERS patients should be monitored for fever and respiratory symptoms and should be kept off work if they get sick		

Pandemic influenza The transmission dynamics of pandemic influenza may differ from that of seasonal influenza, or the novel A(H5N1) strain, and will depend upon the characteristics of the pandemic strain	Yes	Contact precautions Droplet precautions Airborne precautions** • For all personnel involved in direct care activities and when performing high-risk aerosol-generating procedures • If negative pressure rooms are not available, put patients in single rooms or cohort patients	• Exposed persons: thoroughly wash exposed areas, especially hands, with soap and water • Use EPA-registered hospital disinfectant • Follow standard facility procedures for cleaning and disinfection of environmental surfaces • Emphasize cleaning and disinfection of frequently touched surfaces	• Follow standard facility practices for care of deceased • Standard precautions for any contact with blood and body fluid

PPE-personal protective equipment (e.g., N-95 mask, gloves gown, face shield).
† Adapted from references 15, 23, 27, 47, 48, 50, 51, 52, 53, 63.
‡ Standard precautions apply to all agents-hand hygiene; use of gown, gloves, mask, face shield, or eye protection depending on exposure; safe injection practices.
* Contact precautions: wear gown and gloves for interactions that involve contact with the patient or contaminated areas around the patient.
§ Droplet precautions: Patient should be in single room. Persons entering the room must wear a mask (a respirator is not necessary) or maintain a distance of >3 feet from the patient.
†† Airborne precautions: place patient in a negative pressure room with an anteroom. N95 mask use by people entering the room.
** Negative pressure isolation is not required for routine patient care of individuals with pandemic influenza. If possible, negative pressure rooms should be used when performing high-risk aerosol-generating procedures.

must, therefore, be in place well ahead of a biological event. Protocols for PPE use must also take into account that shortages will occur during a biological disaster, and provisions must be put in place by the HE to allow for alternate use of PPE. Generally, an N95 mask must be discarded after one use.[16] However, during a biological event such as SARS, MERS, Ebola, or pandemic influenza, N95 masks will become scarce, and protocols that allow for reuse of masks will need to be activated. During the Ebola epidemic of 2014, it became clear that current PPE guidelines provided inadequate protection, particularly after 2 healthcare workers in Dallas became infected while caring for an Ebola patient from Liberia.[17] HEs throughout the US were responsible for implementing constantly changing PPE guidelines during the epidemic and communicating these throughout their hospitals.[18]

The HE will need to be involved in developing distribution plans for antimicrobials and vaccines during a biological disaster. Distribution plans must be established for both patients and staff with input from employee health, infectious diseases, pharmacy and the hospital leadership. Although priority lists have been established for the distribution of vaccines and antivirals during an influenza pandemic,[19] they do not currently exist for other biological disasters (e.g., plague attack). The HE must be involved in prioritizing these valuable resources as they become scarce.

Treatment, immunization and prophylaxis protocols have been developed for most biological agents (Table 24.4). However, as a biological event progresses and resources become scarce, these protocols might change. As an example, guidelines for using antivirals for the 2009 H1N1 influenza pandemic recommended that, if enough medication was available, high-risk healthcare personnel should receive outbreak (or pre-exposure) prophylaxis to prevent disease.[19] However, if antivirals became scarce, this strategy would have to change, and the HE will have to work with infectious diseases, occupational health, pharmacy, and the hospital leadership to modify antiviral use protocols. Mechanisms for modifying the distribution of scarce resources must be worked out before a biological disaster occurs.

Risk Communication: One of the most important tasks for the HE during a biological disaster will be communication of risk to healthcare personnel and patients. Pre-event preparation includes maintaining contact with local, state, and federal public health entities. Involvement with local, regional, and state biopreparedness groups is an excellent way for the HE to stay familiar with key public health, emergency management, law enforcement, and healthcare personnel. Also, participating in local, regional, and state tabletop or functional exercises is an important way to understand how public health, emergency management, law enforcement, and hospitals will work together during a biological disaster.[20,21] The HE will also be part of educating healthcare personnel on biopreparedness plans within the hospital. Certain biological disasters, particularly pandemic influenza, will alter the standards of medical care and staffing ratios within a hospital.[12,22] It is crucial that healthcare personnel be aware of their roles and the role of the hospital in responding to a biological disaster. The HE will be called upon to explain the risks and possible consequences of a biological disaster.

During a biological disaster, the HE will be a key advisor to the incident commander (see NIMS above), but he/she must also be available to healthcare personnel to answer questions and contribute to changes in pre-established protocols. As such, the HE must closely monitor how the biological event is evolving internationally, nationally and at the community level.

Early Identification of a Biological Disaster

The Category A agents of bioterrorism[1] and most of the recently identified emerging infections like SARS, MERS, Ebola, H5N1 avian influenza, and West Nile fever[23–36] present with nonspecific symptoms, especially early in the disease course. Thus, clues to a specific illness may not be evident and may not raise concern. Attention to syndrome complexes may be a better way to quickly identify unusual diseases. While much work has been done on syndromic surveillance of populations (e.g., emergency department visits),[37] there has been little training of clinicians in syndrome complex surveillance for bioterrorism or other biological disaster agents. In addressing biological disaster agents, four syndrome complexes emerge: 1) febrile pulmonary syndromes, 2) febrile rash syndromes, 3) febrile and nonfebrile neurologic syndromes, and 4) viral hemorrhagic fever syndromes.

Febrile Pulmonary Syndromes (FPS): Febrile pulmonary syndromes (FPS) are any constellation of acute symptoms including fevers AND shortness of breath, cough, or dyspnea. Examples of FPS in bioterrorism include anthrax,[23] plague,[26] and tularemia.[27] Biological disaster agents that present as FPS include SARS,[31,32] H5N1 avian influenza,[35] and Ebola.[34] At initial presentation, FPS may not raise much concern, however, several red flags warrant further testing and precautions. These include:

- Rapid progression of symptoms in a previously healthy young patient
- Widened mediastinum on chest x-ray (anthrax)[23]
- Gram positive rods growing in blood cultures within 24 hours of being drawn (anthrax)[23]
- FPS with meningeal signs and symptoms (anthrax, plague)[23,26]
- Recent travel overseas (SARS, H5N1 influenza, anthrax, plague, Ebola)[23,26,31,32,34,35]
- Patient is a healthcare worker
- Recent exposure to a person hospitalized for a FPS

If the initial workup of FPS does not lead to suspicion of a biological disaster agent, subsequent red flags might include:

- No or minimal response to empiric antimicrobial therapy (anthrax, plague, Ebola)[23,26,34]
- Enlarged mediastinal lymph nodes on chest computed tomography scan (anthrax)[23]
- More patients, especially contacts of the initial patient, presenting with a similar FPS over a brief period

Table 24.4 Treatment, prophylaxis, and vaccination of biological agents[ψ]

Organism	Treatment	Prophylaxis	Duration	Vaccination
Anthrax *(Bacillus anthracis)*	**Cutaneous** • Adults (including pregnant women[§]): Ciprofloxacin, 500 mg PO bid **or** Doxycycline, 100 mg PO bid • Children:[§] Ciprofloxacin, 10–15 mg/kg every 12 h (not to exceed 1 g/d) **or** Doxycycline for those aged >8 y and weight >45 kg: 100 mg q 12 h; >8 y and weight <45 kg: 2.2 mg/kg q 12 h; <8 y: 2.2 mg/kg q 12 h **Inhalational, Gastrointestinal[#]** • Adults (including pregnant women[§]): Ciprofloxacin, 400 mg q 12 h **or** Doxycycline, 100 mg 12 h PLUS 1 or 2 additional antimicrobials[*] • Children:[§] Ciprofloxacin, 10–15 mg/kg q 12 h **or** Doxycycline for those aged >8 y and weight >45 kg: 100 mg q 12 h; >8 y and weight <45 kg: 2.2 mg/kg q 12 h; <8 y: 2.2 mg/kg q 12 h PLUS 1 or 2 additional antimicrobials[*] **Meningitis** • Should be suspected and treated in all systemic cases of anthrax • Same treatment as for inhalational, gastrointestinal	**Postexposure prophylaxis (PEP)** Antibiotics • Adults-**Initial PEP** Ciprofloxacin, 500 mg PO bid **Alternative PEP**: Doxycycline, 100 mg PO bid or Amoxicillin, 500 mg PO tid • Children: **Initial PEP** Ciprofloxacin, 20–30 mg/kg per d PO taken in 2 daily doses, not to exceed 1 g/d. – **Alternative PEP**: Weight >20 kg: amoxicillin, 500 mg PO q 8 h Weight <20 kg: amoxicillin, 40 mg/kg taken PO in 3 doses q 8 h • Pregnant women: **Initial PEP:** Ciprofloxacin, 500 mg po q 12 h, **Alternative PEP**: Amoxicillin, 500 mg PO q 8 h Vaccine (see vaccination)	**Treatment and PEP** **cutaneous:** 60 days – disease has occurred in humans up to 58 days after exposure through inhalation **Inhalational, gastrointestinal, meningitis**: 60 days; IV treatment initially and oral therapy when clinically appropriate	Anthrax vaccine adsorbed (AVA) • FDA licensed for 6 dose pre-exposure vaccination but not for postexposure vaccination • Pre-exposure vaccination: 6 doses; 0.5 mL SQ at 0, 4 weeks and 6, 12, and 18 months; annual booster to maintain immunity • Postexposure vaccination: 3 doses 0.5 mL SQ of (day 0,14, 28) with 60 d of PEP

	• Include 1 or more antibiotics that penetrate the central nervous system (ampicillin or penicillin, meropenem, rifampin, or vancomycin) • Consider steroid therapy as an adjunct to antibiotics **Immunotherapeutics:** human-derived anthrax immune globulin (AIG) has been successfully used but studies are lacking; this drug must be obtained from the CDC under an emergency investigational new drug application			

Smallpox (Variola major and minor)	• Currently, there is no proven treatment for smallpox
	• Supportive care
	  ◦ Isolation of the patient to prevent transmission of variola virus to nonimmune persons
	  ◦ Monitoring and maintaining fluid and electrolyte balance
	  ◦ Monitoring for and treatment of complications
	  ◦ Skin care
		Vaccine (see vaccination),
		
		ACAM2000™ Smallpox Vaccine
			Not applicable	Vaccine, postevent
				
				ACAM2000™ Smallpox Vaccine
				
				Pre-exposure prophylaxis:
				• Civilian laboratory personnel
				• Military
				• State public health preparedness programs
				
				PEP:
				• Vaccination within 3 days of exposure to prevent or significantly modify smallpox diseaseVaccination within 4 to 7 days may offer some protection from disease, or modify disease severityVaccine adverse effects
				• Live vaccine can cause excyma vaccinatum, generalized vaccinia, immune reactions, particularly in immunocompromised and people with eczema
				• Mortality 1–2/million

Table 24.4 (cont.)

Organism	Treatment	Prophylaxis	Duration	Vaccination
Plague *(Yersinia pestis)*	All Forms • Adults (preferred):† Streptomycin, 1 gm IM twice daily or Gentamicin, 5 mg/kg IM or IV once daily or 2 mg/kg loading dose followed by 1.7 mg/kg IM or IV 3 times daily • Adults (alternative choices):§ Doxycycline, 100 mg IV twice daily or 200 mg IV once daily or Ciprofloxacin, 400 mg IV twice daily or Chloramphenicol, 25 mg/kg IV 4 times daily • Children (preferred):† Streptomycin, 15 mg/kg IM twice daily (maximum daily dose, 2 gm) or Gentamicin 2.5 mg/kg IM or IV 3 times daily • Children (alternative choices): § Doxycycline: > 45 kg, give adult dosage,<45 kg, give 2.2 mg/kg IV twice daily (maximum, 200 mg/day) or Ciprofloxacin, 15 mg/kg IV twice daily (maximum daily dose, 1 gm or Chloramphenicol‡, 25 mg/kg IV 4 times daily (maximum daily dose, 4 gm) • Pregnant women:†,§ same as adults except avoid streptomycin and chloramphenicol because of fetal toxicity	Postexposure prophylaxis • Adults (preferred)§ Doxycycline, 100 mg PO twice daily or Ciprofloxacin, 500 mg PO twice daily • Adults (alternative choices): Chloramphenicol, 25 mg/kg PO 4 times daily • Children (preferred):§ Doxycycline: if >45 kg, give adult dosage; if <45 kg, give 2.2 mg/kg PO twice daily or Ciprofloxacin, 20 mg/kg PO twice daily(maximum daily dose, 1 gm) • Children (alternative choices):‡ Chloramphenicol, 25 mg/kg PO 4 times daily (maximum daily dose, 4 gm) • Pregnant women: same as adults except avoid chloramphenicol because of fetal toxicity	**Treatment for All forms:** 10–14 days (IV initially followed by oral therapy) **Postexposure Prophylaxis:** 7 days	**No current FDA approved vaccine-**Killed whole-cell plague vaccines effective vs. bubonic plague in animal models but do not appear effective in combating pneumonic plague
Tularemia *(Franciella tularensis)*	All Forms • Adults (preferred):† Streptomycin, 1 gm IM twice daily or Gentamicin, 5 mg/kg IM or IV once daily or 2 mg/kg loading dose followed by	Postexposure prophylaxis • Adults (preferred):§ Doxycycline, 100 mg PO twice daily or Ciprofloxacin, 500 mg PO twice daily • Children (preferred):§ Doxycycline: if >45 kg, give	**Treatment:** 10–14 days (IV initially followed by oral therapy) **Postexposure prophylaxis:** 14 days	**No current FDA-approved vaccine**

	1.7 mg/kg IM or IV 3 times daily • Adults (alternative choices):[§] Doxycycline, 100 mg IV twice daily or 200 mg IV once daily or Ciprofloxacin, 400 mg IV twice daily or Chloramphenicol, 25 mg/kg IV 4 times daily • Children (preferred):[†] Streptomycin, 15 mg/kg IM twice daily (maximum daily dose, 2 gm)or Gentamicin 2.5 mg/kg IM or IV 3 times daily • Children (alternative choices):[§] Doxycycline: >45 kg, give adult dosage,<45 kg, give 2.2 mg/kg IV twice daily (maximum, 200 mg/day) or Ciprofloxacin, 15 mg/kg IV twice daily (maximum daily dose, 1 gm or Chloramphenicol,[‡] 25 mg/kg IV 4 times daily (maximum daily dose, 4 gm) • Pregnant women:[†,§] same as adults except avoid streptomycin and chloramphenicol because of fetal toxicity	adult dosage; if <45 kg, give 2.2 mg/kg PO twice daily or Ciprofloxacin, 20 mg/kg PO twice daily(maximum daily dose, 1 gm) • Pregnant women:[§] same as adults		
Botulinum toxin *(Clostridium botulinum)*	Supportive care • Mechanical ventilation, intensive care unit stay • Nutrition: parenteral or through enteral tube • Treatment of secondary infections (pulmonary) • Trenedelenburg position (20° tilt) for optimal breathing Antitoxin • Heptavalent Botulism Antitoxin (HBAT): Administer all BAT doses (differ by	**Antitoxin:** can be given as postexposure prophylaxis but supply is limited – consultation with state health department and CDC necessary; it may be best to monitor potentially exposed persons carefully and treat if symptoms appear	**Duration of illness:** weeks to months **Duration of treatment with antitoxin:** 1 dose	**No FDA-approved vaccine**

Table 24.4 (cont.)

Organism	Treatment	Prophylaxis	Duration	Vaccination
	patient age after dilution 1:10 in normal saline by slow intravenous dosage and rate per BAT Dosing Guide and Intravenous Infusion Rate information supplied with HBAT; obtain from Centers for Disease Control and Prevention (CDC): (404) 639–2206; (404) 639–2888 [after hours].			
Viral hemorrhagic fever (VHF)	Supportive Care • Blood pressure, fluids, electrolytes • Mechanical ventilation • Renal Dialysis Ribavirin:[††] has activity against Lassa Fever virus, other arenaviruses and Rift Valley fever; no FDA approval but may be used in mass casualty scenario for VHF. • Adults . Contained casualty setting-loading dose of 30 mg/kg (maximum dose, 2 gm) IV once, then 16 mg/kg (maximum dose, 1 gm) IV every 6 hr for 4 days, then 8 mg/kg (maximum dose, 500 mg) IV every 8 hr for 6 days . Mass casualty setting: Loading dose of 2,000 mg PO once, then: Weight >75 kg: 1,200 mg/day PO in 2 divided doses for 10 days; Weight <75 kg: 1,000 mg/day PO in divided doses (400	**None**	**Treatment:** 10 days	**The only VHF agent vaccine is for Yellow Fever:** administered to people traveling to endemic areas; not useful for postexposure yellow fever because incubation period for yellow fever is 3–6 day and vaccine takes 10 days to work Clinical trials are being conducted for Ebola disease as of 2015 **No vaccines for other VHF agents**

	mg in am and 600 mg in pm) for 10 days
	• Children
	  ◦ Contained casualty setting: Loading dose of 30 mg/kg (maximum dose, 2 gm) IV once, then 16 mg/kg (maximum dose, 1 gm) IV every 6 hr for 4 days, then 8 mg/kg (maximum dose, 500 mg IV) every 8 hr for 6 days
	  ◦ Mass casualty setting: Loading dose of 30 mg/kg PO once, then 15 mg/kg/d PO in 2 divided doses for 10 days			

Severe Acute Respiratory Syndrome (SARS) and Middle Eastern Respiratory Syndrome (MERS) Coronoviruses	**Supportive care** • Mechanical ventilation • Antibiotics for secondary pneumonia • Anti-inflammatory agents-corticosteroids (high dose) [SARS] **Antivirals:** none shown to be effective although studies are limited	**None**	**Not applicable**	**No currently approved vaccine:** although there are ongoing trials of candidate vaccines there is currently no FDA approved SARS or MERS vaccine
Pandemic influenza	**Oseltamivir**** (treatment for patients 1 year and older) • Adults and children >13 yrs: 75 mg PO bid • Children: weight <15 kg: 30 mg twice a day. Weight >15 to 23 kg, 45 mg twice a day.	**Oseltamivir** (prophylaxis for patients 1 year and older) • Adults and children >13: 75 mg PO qd • Children: weight <15 kg:30 mg once daily. Weight >15 to 23 kg, 45 mg once daily. For	**Oseltamivir** • Treatment: 5 days • PEP: 10 days **Zanamivir** • Treatment: 5 days	**Prepandemic vaccine** • The US government is currently stockpiling vaccine for highly pathogenic A (H5N1) in the event that this strain mutates into a human pandemic influenza strain

Table 24.4 (cont.)

Organism	Treatment	Prophylaxis	Duration	Vaccination
	For weight >23 to 40 kg, the dose is 60 mg twice a day. For children who weigh >40 kg, the dose is 75 mg twice a day **Zanamivir**** (treatment of persons aged 7 years and older) • Adults and children > 7 years: 10 mg (2 inhalations) twice daily **Amantadine** (consult package insert for persons with creatinine clearance less than or equal to 50 mL/min/1.73 m^2) • Adults and children > 13 years: 100 mg twice daily (> 65 years, less than or equal to 100 mg/day) • Children: 5 mg/kg body weight/day up to 150 mg in 2 divided doses • Children aged 10 years and older who weigh less than 40 kg should be administered amantadine at a dosage of 5 mg/kg body weight/day **Rimantidine** Note: A reduction in dosage to 100 mg/day of rimantadine is recommended for persons who have severe hepatic dysfunction or those with creatinine clearance less than 10 mL/min; other persons with less severe hepatic or renal dysfunction taking 100 mg/day of rimantadine should be observed closely, and the dosage should be reduced or the drug discontinued, if necessary	weight >23 to 40 kg, the dose is 60 mg once daily; for children who weigh >40 kg, the dose is 75 mg once daily **Zanamivir** (prophylaxis of persons aged 5 years) Adults and children > 5 years: 10 mg (2 inhalations) once daily **Amantadine** (consult package insert for persons with creatinine clearance less than or equal to 50 mL/ min/1.73 m2) • Adults: 100 mg twice daily (> 65 years, less than or equal to 100 mg/day) • Children: 5 mg/kg body weight/day up to 150 mg in 2 divided doses • Children aged 10 years and older who weigh less than 40 kg should be administered amantadine at a dosage of 5 mg/kg body weight/day **Rimantidine** • Adults: Adults and children > 13 years: 100 mg twice daily (>65 years, dosage should be 100 mg/day) • Children: 5 mg/kg body weight/day up to 150 mg in 2 divided doses	• PEP: 10 days **Amantadine** • Treatment: 7 days • PEP: 10 days **Rimantidine** Treatment: 7 days **PEP**: 10 days	**Pandemic vaccine** • Pandemic vaccine production will begin immediately upon identification of the pandemic influenza virus strain. • Pandemic vaccine: may be 4–6 months before available for use

	• Adults and children > 13 years: 100 mg twice daily (> 65 years, dosage should be 100 mg/day) • Children: Not FDA-approved for treatment in children Rimantadine is approved by FDA for treatment among adults.; however, certain specialists in the management of influenza consider rimantadine appropriate for treatment among children; studies evaluating the efficacy of amantadine and rimantadine in children are limited, but they indicate that treatment with either drug diminishes the severity of influenza A infection when administered within 48 hours of illness onset	

[Ψ] Adapted from references 15, 23, 27, 47, 48, 50, 51, 52, 53, 64.

[§] The use of ciprofloxacin and doxycycline in pregnant women and children is justified for-life threatening illness as the risk of death outweighs the potential risk of medication-related adverse events. Ciprofloxacin dose should not exceed 1 gram per day in children.

[#] Inhalational, gastrointestinal, and meningeal anthrax should be initially treated with IV antibiotics until the patient improves, and then therapy can be completed with 1 or 2 oral agents.

[*] Additional antimicrobials with activity against *B. anthracis* include rifampin, vancomycin, penicillin, ampicillin, chloramphenicol, imipenem, clindamycin, and clarithromycin. *B. anthracis* resistance to beta-lactam antibiotics has been described, and these medications should not be used alone to treat inhalational, gastrointestinal or meningeal anthrax. Antimicrobial susceptibility testing should be performed.

[†] Aminoglycosides must be adjusted according to renal function, and aminoglycoside levels should be monitored during therapy.

[‡] Children younger than 2 years of age should not receive chloramphenicol.

[††] Ribavirin is teratogenic in animal models and should not be used in pregnant women unless the risk to the patient outweighs the risk to the fetus.

The presence of any FPS and the above red flags should prompt immediate action including efforts to protect healthcare personnel and other patients if a contagious agent is suspected and reporting of the case to other clinicians and, especially, the health department. In addition, aggressive efforts to diagnose and treat should obviously continue.

Febrile Rash Syndrome (FRS): Febrile rash syndrome (FRS) is defined as a constellation of acute symptoms that include fever AND a bodily rash. Biological disaster agents that can produce FRS include smallpox, viral hemorrhagic fevers (Ebola), and anthrax.[23,25,29,34] Recent emerging infections presenting in this fashion include monkeypox and West Nile fever.[36,38] Although the presence of fever and a rash is not uncommon and can be seen with common infections, cancers, drug reactions and rheumatologic conditions, the following features warrant increased suspicion for a biological attack or emerging infection:

- Vesicular/pustular rash in the same stage of development on the face and extremities more than the trunk (smallpox, monkeypox)[25,38]
- Rash presenting several days after fever (smallpox, monkeypox)[25,38]
- Diffuse rash in a toxic-appearing patient (smallpox, monkeypox, viral hemorrhagic fevers, West Nile fever)[25,29,36,38]
- Fever and rash and recent foreign travel (anthrax, smallpox, monkeypox, viral hemorrhagic fevers)[23,25,29,38]
- Fever and rash and recent contact with patient with FRS (smallpox, monkeypox, viral hemorrhagic fevers)[25,29,38]
- Painless, edematous lesion with an eschar in a febrile patient (anthrax)[23]

The presence of any FRS and the above red flags should prompt immediate action including efforts to protect healthcare personnel and other patients if a contagious agent is suspected and reporting of the case to other clinicians and, especially, the health department. In addition, aggressive efforts to diagnose and treat should continue.

Neurological Syndromes (NS): Neurological syndromes (NS) are any constellation of acute symptoms involving diffuse or focal weakness and/or symptoms of meningitis (nuchal ridgidity, headache, photophobia, lethargy) or encephalitis (altered mental status, motor and sensory deficits, speech disorder). Neurological syndromes occur with several bioterrorism-related agents including anthrax, botulinum toxin, and plague. Also, like West Nile fever, emerging infections may present with an encephalitic picture. Clinicians are familiar with neurological complaints among their patients. Strokes occur 500,000 times per year in the US,[39] and there are thousands of cases of viral and bacterial meningitis per year.[40] However, there are some presentations of neurological syndromes that should raise suspicion for a biological agent or an emerging infection. If a patient presents with a NS consisting of no fever with a descending, symmetric, flaccid paralysis that begins in the bulbar muscles, botulism should be considered.[28] If the patient has no history of a recent wound or obvious food exposure, then the possibility of bioterrorism should be entertained.[28] If a patient presents with a febrile NS, the following features should provoke suspicion:

- Encephalitis in a young previously healthy adult (West Nile virusf, St. Louis encephalitis virus, Venezuelan equine encephalitis virus, eastern equine encephalitis virus)[36]
- Meningitis with gram positive rods on gram stain in an immunocompetent host (anthrax)[23]
- Meningoencephalitis with diffuse weakness, blindness or other focal deficits (West Nile virus)[36]

Viral Hemorrhagic Fever Syndrome (VHFS). Viral hemorrhagic fever syndrome (VHFS) results from infection with several viruses including filoviruses (Ebola, Marburg), arenaviruses (Lassa fever), bunyaviruses (Rift Valley Fever), and flaviviruses (Yellow Fever).[29,34] In the early stages of illness, VHFS is nonspecific, and patients present with fever, headache, myalgias, nausea, and nonbloody diarrhea.[29,34] Patients may also have conjunctivitis, pharyngitis and a nonspecific rash. As the disease progresses, a hemorrhagic diathesis ensues and may include petechiae, mucous membrane and conjunctival hemorrhage, hematuria, hematemesis, and melena.[29,34] VHFS in any patient warrants increased suspicion for bioterrorism or an emerging infection especially if the patient has not recently traveled. Some hemorrhagic fever viruses (e.g., yellow fever and dengue fever) are common in parts of Africa, Southeast Asia and Central and South America, and travelers to these areas may present with VHFS.[29,34] However, hemorrhagic fever viruses are uncommon in North America and Europe. Because certain hemorrhagic fever viruses (Ebola, Marburg, Lassa fever and New World arenaviruses) are transmissible from person to person,[29,34] immediate measures should be undertaken to protect others from any patient thought to have VHFS. Also, such cases should be reported to the health department as soon as possible. Rarely, smallpox can present in a hemorrhagic form that is rapidly fatal and highly contagious.[25]

Other Clues to a Biological Disaster: The following are clues early clues to a biological disaster that may not fit into the above four categories:[41,42]

- Animals and humans ill at the same time (e.g., bioterrorism agents, West Nile virus)
- >2 previously healthy young patients presenting with rapid onset of sepsis
- Clusters of patients presenting with a similar presentation (e.g., SARS, H5N1 influenza, bioterrorism agents)
- Unusual temporal or geographic clustering of illness (e.g., severe influenza outbreak in the summer, Ebola in non-endemic region such as the US)
- Unusual presentation of an illness (inhalational anthrax vs. cutaneous anthrax)
- Higher morbidity and mortality than expected with a common disease or syndrome
- Multiple unusual or unexplained disease entities coexisting in the same patient without other explanation
- Unusual, atypical, genetically engineered, or antiquated strain of agent

- Simultaneous clusters of similar illness in noncontiguous areas, domestic or foreign
- Multiple atypical presentations of disease agents

Public Health Surveillance Systems: Since the terrorist attacks on September 11, 2001, the public health sector has accelerated the development of surveillance systems for improved detection of infectious disease outbreaks, including bioterrorism events. Traditional surveillance relies upon the clinician, infection preventionist, HE, or laboratory to report any disease of public health significance to the local public health department, whether laboratory-diagnosed or clinically suspected.[43] At this point, all state public health departments have incorporated electronic disease reporting systems, many of which are accessible by hospital-based providers. This traditional "passive" disease reporting system can alert public health authorities at any point in time that the patient has already entered the healthcare system with clinical signs and systems, which, unfortunately, may be long after the possibly undetected exposure event.

The purpose of a syndromic surveillance system is to attempt to provide an earlier warning of an infectious disease outbreak than traditional systems.[37,43] Many of these systems utilize hospital-based information, such as the surveillance of emergency department patient chief complaints. Numerous states have implemented syndromic surveillance systems, and there are several national initiatives, which are described below.

- **BioSense.** BioSense is a CDC Internet-based syndromic surveillance application, in operation in the United States since November 2003, for the early detection of both intentional and natural infectious disease outbreaks.[45] BioSense receives International Classification of Diseases (ICD) diagnosis and procedure codes from Department of Defense (DOD) and Department of Veterans Affairs ambulatory care visits. The system also receives pharmacy over-the-counter sales information from various retail outlets, and the Laboratory Centers of America provides information on laboratory tests ordered. These data are analyzed daily at the CDC.[46]
- **Real-Time Outbreak and Disease Surveillance:** Software has been developed by the Real-Time Outbreak and Disease Surveillance (RODS) Laboratory, a collaboration of the University of Pittsburgh and Carnegie Mellon University. This software can collect and analyze many types of clinical data, such as emergency department chief complaints or particular laboratory test orders, and is used by a number of state public health departments for early detection of infectious disease or bioterrorism events.[45]
- **ESSENCE:** The Electronic Surveillance System for the Early Notification of Community-Based Epidemics (ESSENCE) is a DOD syndromic surveillance system that automatically collects ICD codes at participating military treatment facilities. Analysis is done of the frequency and distribution of seven syndrome types: respiratory, gastrointestinal, fever, neurologic, dermatologic (infectious), dermatologic (hemorrhagic), and coma or sudden death.[45,47]

Disease Reporting Requirements: Hospitals and their emergency departments may be where a victim of a bioterrorism event may be suspected and subsequently identified. HEs, along with healthcare personnel, infection preventionists, and laboratorians must immediately report *any suspect* case to their local or state public health department.[43] In many states this important reporting is encoded in legal statute, yet the list of diseases required for reporting can vary between states and territories.[43] Due to the public health importance of early and rapid reporting of diseases of public health importance, especially of those that may indicate natural or intentional release of potential bioterror agents, healthcare personnel are integral to public health efforts at the local, state, and federal levels.[43] This early reporting, even of suspect cases allows the immediate public health investigation and response that may be required, and *reporting should not be deferred for confirmatory tests*.

In fact, confirmatory testing of any biologic agent should be performed under specific biosafety conditions within the state public health laboratory. At the time of reporting, public health workers will provide information to the provider regarding specific and safe specimen collection and transportation to the closest diagnostic public health laboratory. The HE will need to ensure the hospital laboratory's capabilities for securely obtaining, packaging, and transporting any suspect bioterror agent samples to the directed public health laboratory so that diagnostic testing can be performed. Again, involvement by the HE with local and state public health departments as well as local, regional, and state biopreparedness groups will allow familiarity with the response plans of public health, emergency management, law enforcement, and surrounding hospitals.

Biological Disaster Agents

Many agents are capable of causing a widespread biological disaster, and the CDC has identified more than 60 agents that might be used as a biological weapon.[44] This chapter will focus on the six CDC Category A bioterrorism agents (anthrax, smallpox, tularemia, plague, botulinum toxin, and viral hemorrhagic fevers), SARS, MERS, and H5N1 influenza. These agents represent a wide range of presentations and modes of spread; thus, they provide an excellent framework for preparedness activities and education.

Agents of Bioterrorism

Bioterrorism is the malevolent use of bacteria, viruses, or toxins against humans, animals or plants in an attempt to cause harm and to create fear. Although concern about bioterrorism has always existed, the 2001 anthrax attack in the US that killed 5 people and prompted pre-emptive treatment of more than 10,000 others has focused attention on this form of terrorism as an imminent threat to national security.[48,49] To understand this concern, one must be familiar with the pathogens that are most likely to be used in any future attack and be aware of the available methods for detecting and responding to such an event.

The use of biological agents for warfare has a centuries-old history, predating even the concept of germ theory.[50] The first documented case was in 1346, when the Tartars, frustrated after years of laying siege to the Black Sea city of Kaffa, catapulted plague victims over the unassailable city walls.[50] The Black Plague epidemic that followed and eventually spread from Kaffa wiped out almost half of Europe. In 1763, Sir Jeffrey Amherst, the commander of British troops in America, sanctioned the use of smallpox-infected blankets as germ warfare implements against the American Indians, who were highly susceptible to this deadly virus.[50]

In World War I, the Germans infected cattle destined for consumption by Allied forces with anthrax and glanders. This act resulted in the 1925 Geneva Protocol that prohibited the use of biological weapons.[50] However, in spite of this agreement and the 1972 Biological and Chemical Weapons Convention, several nations continued to produce biological weapons. Biopreparat, the Russian biological weapons program, was the largest in the world with 10,000 scientists working in 50 production facilities. In 1979, an accidental release of weaponized anthrax from a production plant in Sverdlovsk resulted in 66 deaths downwind of the facility. The program was dismantled in 1992 after Russian president Boris Yeltsin finally admitted that it existed.[50]

Aum Shinrikyo, a Japanese cult, attempted several unsuccessful biological attacks with anthrax and botulinum toxin before releasing sarin gas in the Tokyo subway in 1995.[51] The most successful biological attack in the US was perpetrated by a religious cult, the Rajneeshees. In 1984, in an attempt to affect elections in a small Oregon town, the cult poisoned 10 restaurant salad bars with *Salmonella typhimurium* and sickened more than 700 people.[50]

Biological weapons, unlike other weapons of mass destruction (WMDs), are inexpensive to make. Nuclear and chemical weapons programs are 800 times and 600 times more costly, respectively, than a comparable bioweapons program. The pathogens are relatively easily available, and the materials and equipment for producing biological weapons are the same as those used for peaceful purposes. For example, the organism that causes anthrax is present in the soil in many countries, and the organism can be grown in standard laboratory culture medium. The *Salmonella* used in the Oregon attack was easily obtained by a member of the Rajneeshee cult. The necessary culture media, incubators, and milling equipment are available for purchase, and information on cultivating the organisms and on generating antibiotic-resistant strains is available in the scientific literature and from the Internet.

Biological weapons produce fear and panic as was apparent in the 2001 anthrax attack in the US.[49] The weapon can be released covertly, and its effects only become apparent days later when the terrorist is gone. Unlike chemical and nuclear events, the point of release of a biological agent may not be apparent. If it is a contagious agent, the uncertainty about who has been exposed could lead to widespread panic. Finally, the lethality of a biological attack could exceed that of other WMDs. By one governmental estimate, 50 kilograms of powdered anthrax similar to that used in the 2001 attack released over a city of 500,000 people would cause death in 95,000 and incapacity in 125,000.[52]

The characteristics of an ideal agent for bioterrorism include accessibility, durability, infectiousness and communicability. Although hundreds of agents and toxins may qualify, the CDC has developed a list of about 60 agents based on the perceived threat.[44,45] The most likely agents, designated Category A agents, pose the greatest threat; these agents are discussed individually in this chapter.[1]

Category A agents can be released by aerosolization, contamination of food, contamination of water, person-to-person transmission of a contagious agent, or release of infected insect vectors. Aerosolization, the dispersion of organisms into the environment, is the most feared and potentially lethal method of releasing biological agents. As mentioned above, a very small amount of weaponized anthrax (50 kg) could result in very high casualties (95,000 dead).[52] The Russian bioweapons program spent considerable resources developing effective methods of aerosolizing biological agents, especially anthrax, tularemia and smallpox. Both the 1979 Sverdlovsk outbreak of anthrax and the 2001 anthrax attack in the US involved the release of finely powdered anthrax into the environment. Means of aerosolizing an agent include spraying devices (crop dusters), air handling systems in buildings, incendiary devices (bombs), and the postal system (infected mail).[23] However, aerosolization of a biological agent is not easy. Infectious particles must be precisely the right size (0.5–5 microns) to enter and to infect the lungs.[23] Furthermore, radiation from sunlight, shear forces from sprayers, or explosions from incendiary devices would likely destroy most of the released organism.

Contamination of the food or water supply with biological agents is another method of dissemination. The contamination of salad bars with *S. typhimurium* in Oregon (see above) is an example of a successful attack. The most likely agents to be disseminated in this fashion include botulinum toxin, anthrax, and diarrheal agents including *S. typhimurium*. However, contamination of food and water would be difficult given inspection criteria, water purification and filtering systems, and increased security at water reservoirs and food distribution centers.

Dissemination through person-to-person transmission is a likely means of dispersing a contagious agent such as smallpox. As few as 100 smallpox-infected people could start an epidemic in a nonimmune population. The fear, panic, and quarantine measures that would result from such an epidemic could rapidly overwhelm healthcare resources and destabilize affected countries.

Finally, zoonotic delivery, or the use of insect vectors to disperse a biological agent, is an unlikely method of bioterrorism. It is inefficient and unpredictable. The most likely agents to be delivered in this way include *Yersinia pestis* (plague) or viral hemorrhagic fevers (Ebola, Lassa fever).

Most likely Bioterrorism Agents

The CDC has designated *Bacillus anthracis, Clostridium botulinum* toxin, *Y. pestis*, variola virus, *Francisella tularensis* and

hemorrhagic fever viruses as the six most likely agents to be used in a bioterrorism attack.[1] The clinical presentation and diagnosis of the Category A agents are summarized in Table 24.2. Infection prevention and treatment, prophylaxis and vaccination strategies are summarized in Tables 24.3 and 24.4.

Anthrax: *B. anthracis* is an ideal bioterrorism agent because the organism 1) forms a hardy spore that can exist in the environment for years and can survive aerosolization, 2) is readily available in the soil in many countries, 3) produces a severe inhalational form with a high mortality, and 4) can be manipulated to create antibiotic- resistant strains.[23] Several countries have developed *B. anthracis* into a biological weapon, and in 2001, this agent was used in a biological attack in the US that created widespread panic and five deaths.[23,49]

B. anthracis causes three distinct diseases; cutaneous anthrax, gastrointestinal anthrax, and inhalational anthrax (see Table 24.2).[23] Anthrax meningitis occurs in 50 percent of people with inhalational anthrax (18 percent). While a bioterrorism attack could manifest as any of these forms, a case of inhalational anthrax should immediately raise suspicion of a biological attack. Aerosolized forms of anthrax have been developed by several countries, and a finely milled form (Ames strain) was used in the 2001 attack in the US.[23] Anthrax is not transmissible from person to person and therefore requires no isolation of infected patients (Table 24.3).[23]

Cutaneous anthrax is quite common in endemic areas around the world, and the mortality rate is very low (<1 percent) if treated promptly.[23] Gastrointestinal, meningeal, and inhalational anthrax have much higher mortality rates, but the 2001 anthrax attacks revealed that prompt therapy with a multidrug antibiotic regimen reduced the mortality rate from 90 percent seen previously to less than 50 percent.[23]

Treatment and prophylactic regimens for anthrax are detailed in Table 24.4. Generally, inhalational, gastrointestinal, and meningeal anthrax require multiple antibiotics to achieve cure, while cutaneous anthrax can be treated with one antibiotic.[23] Prophylaxis is administered to exposed and potentially exposed persons. Anthrax vaccine is available and is administered both pre-exposure (researchers, military personnel) and postexposure to aerosolized anthrax (Table 24.4).[23,24]

Smallpox: Smallpox, or variola, virus is an effective biological weapon because it is highly contagious, has a high mortality rate, and there is no treatment for the disease. Furthermore, because vaccination efforts against smallpox ceased in 1982, few people are adequately protected against infection.[25,53] Currently, the smallpox virus is only held in two laboratories in the world, which include the CDC in Atlanta, Georgia, and the Institute of Virus Preparations in Moscow, Russia. However, there is concern that stocks of smallpox virus may exist in other countries.[25,53]

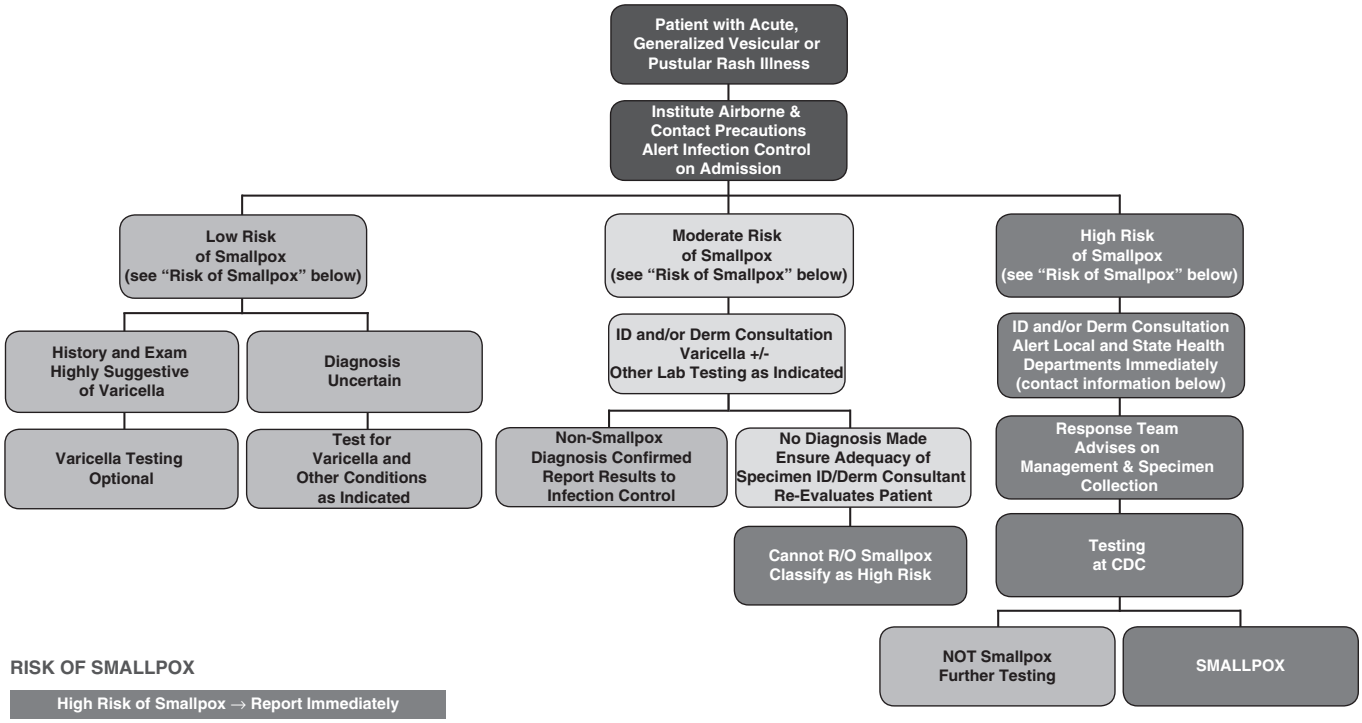
Smallpox could be used as a biological weapon either by aerosolizing virus or by direct person-to-person spread from an infected bioterrorist or unsuspecting infected individual.[28,45] One case of smallpox anywhere in the world would be considered a bioterrorist event given that smallpox has been eradicated;[25,53] thus, one case anywhere would be considered a global public health emergency. A suspected case of smallpox *must* be reported immediately to local public health authorities.[53]

> There are two clinical forms of smallpox, variola major and variola minor. Variola major is the most common form of smallpox, and also the most severe, and cases present with a more extensive rash and with high fevers (Table 24.2). There are four types of variola major smallpox: ordinary, which accounts for 90% or more of cases; modified, which is milder and occurs in previously vaccinated persons; flat; and hemorrhagic. The flat and hemorrhagic forms of smallpox include a malignant smallpox characterized by severe toxemia and flat, confluent lesions that do not progress to pustules and a hemorrhagic-type smallpox characterized by a severe prodrome, toxemia, and a hemorrhagic rash. These two less common forms of smallpox have mortality rates greater than 95%.[25,53] Variola minor is much less common and presents with less severe disease with death rates of 1% or less.[53]

Smallpox is transmitted from person to person through respiratory droplets or contact with infected skin lesions.[25,53] Symptoms begin approximately 12–14 days after exposure; the clinical presentation and diagnosis is outlined in Table 24.2. Smallpox patients are most infectious during the first week of the rash when the oral mucosa lesions ulcerate and release large amounts of virus into the saliva.[53] The patient is no longer infectious once all scabs have separated from the skin, which usually occurs three to four weeks after onset of the rash.[25,53]

The CDC case definition for smallpox identifies it as an illness with acute onset of fever >101°F (38.3°C) followed by a rash characterized by firm, deep-seated vesicles or pustules in the same stage of development without other apparent cause.[53] The laboratory criteria for confirmation require a polymerase chain reaction (PCR) identification of variola virus in a clinical specimen, or isolation of the smallpox virus from a clinical specimen with variola PCR confirmation in a WHO Smallpox Reference Laboratory or a laboratory with appropriate reference capabilities.[54] The HE must be aware that the laboratory diagnostic testing for variola virus should be conducted *only* in a WHO Reference Laboratory or a CDC Laboratory Response Network (LRN) laboratory, such as the state public health department's laboratory, utilizing LRN-approved PCR tests and protocols.[53] Initial confirmation of a smallpox outbreak requires additional testing at CDC. Because few physicians have seen smallpox, the CDC has developed a vesicular/pustular rash protocol which helps differentiate smallpox from other common diseases, particularly chickenpox[54] (Figure 24.3). When the HE is faced with a patient with a FRS, he/she and other clinical staff should be familiar with this information and be able to access this diagnostic aid quickly.

There is currently no treatment for smallpox, although cidofovir, an antiviral, has shown some effect *in vitro*[25] and may be useful as a treatment for severe smallpox vaccine (vaccinia) reactions (EW1). The smallpox vaccine is a live vaccinia virus vaccine produced by Sanofi Pasteur.[55] It can be



RISK OF SMALLPOX

High Risk of Smallpox → Report Immediately

1. Febrile prodrome (defined below) **AND**
2. Classic smallpox lesion (defined below & photo at top right) **AND**
3. Lesions in same stage of development (defined below)

Moderate Risk of Smallpox → Urgent Evaluation

1. Febrile prodrome (defined below) **AND**
2. One other **MAJOR** smallpox criterion (defined below)

OR

1. Febrile prodrome (defined below) **AND**
2. ≥4 **MINOR** smallpox criteria (defined below)

Low Risk of Smallpox → Manage as Clinically Indicated

1. No febrile prodrome

OR

1. Febrile prodrome **AND**
2. <4 **MINOR** smallpox criteria (defined below)

There have been no naturally occurring cases of smallpox anywhere in the world since 1977. A high risk case of smallpox is a public health and medical emergency.

Report all HIGH RISK CASES immediately (without waiting for lab results) to:

1. Hospital Infection Control _____ ( ) _____ - _____
   _____ ( ) _____ - _____
2. _____ health department ( ) _____ - _____
   ( ) _____ - _____
3. _____ health department ( ) _____ - _____
   ( ) _____ - _____

MAJOR SMALLPOX CRITERIA

- **FEBRILE PRODROME:** occurring 1–4 days before rash onset: fever ≥101°F **and** at least one of the following: prostration, headache, backache, chills, vomiting or severe abdominal pain
- **CLASSIC SMALLPOX LESIONS:** deep-seated, firm/hard, round well-circumscribed vesicles or pustules; as they evolve, lesions may become umbilicated or confluent
- **LESIONS IN SAME STAGE OF DEVELOPMENT:** on any one part of the body (e.g., the face, or arm) all the lesions are in the same stage of development (i.e., all are vesicles, or all are pustules)

MINOR SMALLPOX CRITERIA

- Centrifugal distribution: greatest concentration of lesions on face and distal extremities
- First lesions on the oral mucosa/palate, face, or forearms
- Patient appears toxic or moribund
- Slow evolution: lesions evolve from macules to papules → pustules over days (each stage lasts 1–2 days)
- Lesions on the palms and soles

Figure 24.3 Evaluating Patients for Smallpox: ACUTE, GENERALIZED VESICULAR OR PUSTULAR RASH ILLNESS PROTOCOL. From Reference (54).

administered pre-exposure as was done in 2003 in 40,000 healthcare workers and approximately 500,000 military personnel.[55] The vaccine can also be given postexposure and prevents disease if given within 4 days and death if given within 8 days.[25,55] Smallpox vaccine, being live, is contraindicated in immunocompromised patients and those with certain skin conditions, including eczema (Table 24.3).[25,53,55] Smallpox vaccine can only be procured from the CDC or, possibly, state health departments.[25,55]

In the event of a suspected case of smallpox, the HE will need to implement appropriate isolation and disease control measures within the facility (Table 24.3). If a patient with an

acute generalized vesicular or pustular rash illness presents to an emergency department or clinic, actions should be taken to decrease the risk of disease transmission. The patient should not be left in any common waiting areas and should be immediately triaged into a private room where he or she can be assessed quickly to determine the actual risk of smallpox, using the "Evaluating Patients for Smallpox: Acute, Generalized Vesicular or Pustular Rash Illness Protocol" algorithm[53] (Figure 24.3). If in a clinic, the door to the exam room must remain closed until the risk for smallpox is determined. If within a healthcare facility, airborne and contact precautions should be undertaken immediately, and the HE and/or infection control department should be immediately alerted, if not done so already. The HE should ensure that the patient is placed in a private, negative airflow room. The door should be kept closed at all times, except when staff or the patient must enter or exit. Staff and visitors should wear properly fitted respirators, gloves, and gowns, and the patient should wear a surgical mask whenever he or she must be outside of a negative pressure isolation room. The patient's rash should be fully covered with a gown and/or sheet if he or she is transported out of the isolation room.[53] Treatment for the smallpox patient is supportive only (Table 24.4).

Plague: *Y. pestis* is the gram-negative bacterium that causes plague and, historically, has been transmitted to humans through a flea bite.[26] Although it is reported that the Japanese attempted to disseminate plague-infected fleas in China during World War II, the most likely method of release in a biological attack would be in an aerosolized form.[26] Plague has been developed as a biological weapon in the Soviet Union and is considered an attractive agent because of its high mortality, human-to-human transmission, high infectivity (100–500 organisms), and high panic factor.[26]

Naturally occurring plague has three main forms, including bubonic, pneumonic, and septicemic. Bubonic plague presenting as painful lymph nodes and fever after a flea bite is the most common form and occurs frequently throughout the world.[26] A bioterrorist release of aerosolized *Y. pestis* would most likely present as pneumonic or septicemic plague (Table 24.2). Pneumonic plague can be transmitted from person to person, and infected patients must be isolated (Table 24.3).[26]

Bubonic plague is relatively easy to identify, and prompt treatment in the antibiotic era has decreased mortality to 5–14 percent.[26] Pneumonic and septicemic plague, however, present with nonspecific signs and symptoms (Table 24.2), and delayed diagnosis leads to mortality rates of >50 percent if antibiotics are not started within 24 hours of symptoms.[26] Initial treatment of pneumonic and septicemic plague requires intravenous aminoglycosides (Table 24.4), antibiotics not typically given as empiric treatment for pneumonia. Therefore, a high level of suspicion must exist for appropriate therapy to be initiated.[26] Prophylactic therapy should be given to close contacts of pneumonic plague patients and those exposed to aerosolized plague (Table 24.3).[26] There is currently no vaccine available for plague (Table 24.4).[26]

Tularemia: *F. tularensis*, a gram-negative bacterium, is the causative agent of tularemia.[27] Humans are naturally infected with tularemia through arthropod bites (ticks), contact with infected animal tissue (rabbits), ingestion of contaminated food or water, and, rarely, through aerosol inhalation (laboratory accident).[27] Tularemia has been developed as a biological agent because of its high infectivity; 1–2 organisms can cause infection.[27] Japan, the Soviet Union and the US have all developed tularemia as a biological weapon in the past.[27]

There are six naturally occurring forms of tularemia; ulceroglandular, glandular, oculoglandular, oropharyngeal, pneumonic, typhoidal, and septic.[27] The most likely form of tularemia from a biological attack would be pneumonic disease, but typhoidal, septic and oropharyngeal infection might also occur (Table 24.2).[27] Tularemia is not transmitted from person to person and thus the patient need not be isolated (Table 24.4).[27]

Pneumonic tularemia would present as a nonspecific pneumonia and might be difficult to diagnose (Table 24.2).[27] The organism is fastidious and does not grow well in standard cultures. Furthermore, as *F. tularensis* is highly infectious, it must be handled very carefully in the laboratory.[27]

Without antibiotics, the mortality rate is 30–60 percent for pneumonic tularemia and 5–15 percent for other forms.[27] Prompt administration of antibiotics including aminoglycosides (gentamicin, streptomycin), doxycycline, fluoroquinolones or chloramphenicol decreases mortality to less than 2 percent (Table 24.4). Prophylactic antibiotic therapy should be given those exposed to aerosolized F. tularensis after a biological attack (Table 24.4).[27] There is no Food and Drug Administration (FDA)-approved vaccine for tularemia, but a live attenuated vaccine is currently undergoing clinical trials.[56]

Botulism: Botulism is a disease caused by botulinum toxin, one of the most lethal toxins known to man.[28] An inhaled dose of 0.70 micrograms is enough to kill a 70 kg human. Botulinum toxin is produced by *C. botulinum*, an anaerobic bacterium. The disease occurs naturally in three forms: foodborne, wound, and intestinal botulism.[27] Botulinum toxin has been used as a biological weapon by Aum Shinrikyo in Japan in the early 1990s, and it was produced as a biological weapon in the US during World War II.[28] It is also believed that the Soviet Union and Iraq developed botulinum toxin as a weapon.[28]

A biological attack with botulinum toxin would most likely involve an aerosol release or poisoning of the food or water supply.[28] Although there is some concern about terrorists using commercial formulations of botulinum toxin, these aliquots do not contain enough toxin to be lethal (0.005 percent to 0.3 percent of the estimated lethal dose).[28] Botulinum toxin blocks acetylcholine release and thereby prevents normal muscle contraction.[28] Patients affected by botulinum toxin have a classic triad of 1) symmetric, descending flaccid paralysis with bulbar signs; 2) absence of fever; and 3) clear sensorium (Table 24.2).[28]

Diagnosis of botulism is difficult if it is not clinically suspected, and laboratory testing can be delayed and difficult (Table 24.2).[28] The mortality rate is 25 percent or more without

treatment and ventilatory support.[28] Care of a botulism victim is generally supportive (e.g., ventilatory care); however, antitoxin is available through the CDC via the local or state health department.[28] Heptavalent Botulism Antitoxin (HBAT) contains equine-derived antibody to the seven known botulinum toxin types and is available on an emergency basis for the treatment of persons thought to be suffering from botulism. It is supplied only by the CDC.[57]

Viral Hemorrhagic Fever (VHF): VHF agents include a variety of viruses in four families: Filoviridae, Arenaviridae, Bunyaviridae, and Flaviviridae. Specific viruses of concern in include, Ebola, Marburg, Lassa fever, yellow fever, and Rift Valley fever viruses.[29] Several countries including the US, Soviet Union, Russia have developed VHF viruses as biological weapons in the past.[29] Aum Shinrikyo, a Japnese cult, unsuccessfully attempted to acquire Ebola virus and develop this agent as a biological weapon.[29]

As a biological weapon, VHF viruses would most likely be released as an aerosol.29 After an incubation period of 2–21 days, illness would most likely manifest as a nonspecific viral syndrome including myalgias, headache, fever, nausea, vomiting (Table 24.2).[29] As the disease progresses, the patient might develop hemorrhagic manifestations including conjunctival petechiae or hemorrhages, gastrointestinal bleeding, hemoptysis, hematemesis, and petechiae or purpura of the skin.[29] Patients with yellow fever may develop jaundice and/or scleral icterus.[29] Laboratory diagnosis of these organisms is difficult, and a high level of suspicion is warranted in patients presenting with nonspecific viral symptoms with hemorrhagic complications.[29] The mortality rate for VHF varies between <1 percent for Rift Valley fever to 50–90 percent for Ebola.[29]

Treatment is generally supportive and includes intravenous fluid/blood product administration, mechanical ventilation, and nonsteroidal anti-inflammatory drugs[28] (Table 24.4). Ribavirin, an antiviral medication, has activity against arenaviruses bunyaviruses and should be used against these viruses or when the identity of the virus in a case of VHF is not known.[29] Postexposure prophylaxis is not recommended, and only yellow fever virus has an FDA-approved vaccine.[29]

Ebola

The 2014 Ebola outbreak in West Africa was the largest ever recorded.[58] The epidemic was localized to 3 countries (Liberia, Sierra Leone, and Guinea), but a small number of patients were also diagnosed in the US, Nigeria, Senegal, Mali, Italy, Spain, and the United Kingdom. In total, there were close to 29,000 cases (confirmed, probable, or possible) with a case-fatality rate of approximately 40 percent (as of November 4, 2015).[58]

The animal reservoir for Ebola is unclear, although bats have been suggested in several outbreaks.[59] Human-to-human transmission occurs through contact with bodily fluids including blood, urine, semen, saliva, aqueous humor, and breast milk.[60] Transmission is most likely to occur during severe disease as the viral load increases as high as10^8 copies/mL.[6] Healthcare-associated transmission was common in the West African epidemic, and the transmission of Ebola from an infected Liberian patient to two healthcare personnel in Dallas led to very strict isolation requirements and infection prevention protocols in US hospitals.[62]

Patients with Ebola present with symptoms similar to other VHFs (see above). The incubation period for Ebola is generally between 6 to 12 days but can be delayed up to 21 days.[34] Patients with suspected Ebola infection should be treated in specialized care units, and laboratory testing should be limited to only essential tests. Laboratory testing for Ebola should be coordinated with the state public health department and the CDC and usually involves sending specimens for PCR testing.[63]

Treatment for Ebola is generally supportive and includes fluid and electrolyte replacement and respiratory support.[64] There are currently no approved antiviral therapies or vaccines for Ebola virus disease, although clinical trials for an Ebola vaccine are in progress.[63]

Severe Acute Respiratory Syndrome (SARS)

Severe Acute Respiratory Syndrome (SARS) is caused by a coronavirus, SARS-CoV, first isolated in the pandemic outbreak of 2003.[30–32] Cases of SARS first appeared in south China (Guandong Province) in November 2002. In February 2003, an ill physician from Guandong transmitted the virus to 10 other people at a conference in Hong Kong.[30] These 10 individuals then spread the virus to other countries around the world, and on March 13, 2003, the WHO issued a warning about the worldwide spread of this virus.[30] The global outbreak ended in July 2003 after 8,422 cases had been diagnosed and 916 died.[30] There were only 29 cases of SARS in the US and no deaths.[30] Only 9 other cases of SARS have been diagnosed since July 2003, and these were all related to a researcher becoming infected in a laboratory:[30] no cases have been reported since 2004.[65]

The reservoirs for SARS include bats and palm civets, and humans can be infected through contact with these animals.[30] Person-to-person transmission of SARS-CoV occurs through respiratory droplets or contact with bodily secretions such as stool.[30] Certain persons (super-spreaders) seemed to transmit SARS-CoV at a high rate, particularly when they are very ill and hospitalized. As a result, much of the early transmission of SARS-CoV occurred in the hospital setting.[30] Because of the possibility of airborne spread, SARS patients should be placed in respiratory isolation under negative pressure (Table 24.3).[30]

Persons infected with SARS-CoV present with nonspecific symptoms of fever, chills, myalgias, headache, and diarrhea (Table 24.2) After 2 days, the patient develops a nonproductive cough and dyspnea. Respiratory symptoms progress, and 10–20 percent of patients require mechanical ventilation.30 Patients are often hospitalized for over 2 weeks, and the case-fatality rate approaches 11 percent.[30] The diagnosis of SARS is based on a case definition that depends on exposure history, clinical symptoms, and laboratory confirmation of infection.65 Serologic assays and a PCR assay have been developed for the diagnosis of SARS (Table 24.2).[30]

Treatment for SARS is supportive, and there is no specific antiviral medication that has been demonstrated to be effective

(Table 24.4).[30] Steroid therapy has been used to decrease the immune-mediated lung damage, but no prospective studies have been done.[30] Infection prevention precautions must be taken in order to protect family members, the community, healthcare personnel, and other patients (Table 24.3).[30,31]

Novel and Pandemic Influenza

In 2005, the United States government released its first version of a national pandemic influenza plan, the DHHS Pandemic Influenza Plan.[19] Globally, nations began developing response plans in response to an unprecedented spread of a novel highly pathogenic strain of avian influenza A (H5N1) virus, which raised concerns for an imminent influenza pandemic in 1997.[21,66] Novel strains of influenza in humans are newly emerging subtypes that are different from currently circulating human influenza H1 and H3 viruses. Novel subtypes can include H2, H5, H7, and H9 subtypes, H1 and H3 subtypes originating from a nonhuman species, or subtypes arising from genetic reassortment between animal and human viruses.[67] Many subtypes, such as a 2013 outbreak of avian influenza A (H7N9) virus, may cause sporadic human outbreaks in those exposed to a diseased animal, commonly poultry or swine that may be infected with the novel strain. The public health importance for rapid detection and control of these novel strains is critical, as the human population will not have any pre-existing immunity, and if the novel strain mutates to become able to transmit easily from person to person, a pandemic of influenza can result.[66]

Potential Impact of Influenza Pandemics

Three to four pandemics of influenza occur each century; while they vary in severity, world governments understand the necessity for the development of pandemic influenza response plans. Pandemic planning in US hospitals has now been incorporated into current hospital preparedness programs, again in coordination with local, state, and federal groups.

Pandemic influenza, as with any other pandemic disease, will encompass multiple countries or the whole globe and has the potential to have a significantly larger impact across the healthcare system than a localized bioterror event. A bioterror event could have a devastating impact but may be circumscribed in terms of the geography affected and in the time during which it directly or indirectly impacts the population. Pandemic influenza, however, has the potential to encompass the globe rapidly, perhaps more quickly than in past pandemics given the global nature of air travel and trade. The DHHS Pandemic Plan estimated that approximately 75 million to 105 million US citizens may develop influenza, and 209,000 to 1,903,000 of them may die.[19,21] An average influenza season in the US may be associated with 40,000 deaths.[19]

The 2009 Influenza A (H1N1) Pandemic

In April 2009, a novel influenza strain, now referred to as influenza A (H1N1 pdm09), was detected in California, arising from a respiratory illness outbreak in Mexico.[66] The pandemic rapidly affected the entire globe. Ultimately, its impact was of the severity similar to a mild seasonal influenza epidemic; however, the mortality among children, young adults, and pregnant women was more severe than usual. Influenza-related deaths worldwide were estimated to be in the range of 123,000 to 203,000.[68] Because of the global nature of pandemic influenza, hospital preparedness plans that are adequate to address the release of a biologic agent could be insufficient for a pandemic influenza event. Surge capacity plans that may rely on surrounding hospitals or surrounding communities may not be sufficient as they, too, will need to activate their response plans. Further, while a bioterror event may be localized temporarily, pandemic influenza may require hospitals to address surge capacity issues for a period as long as six to eight weeks.[19,68,69] Surge capacity needs may be compromised by the limited ability to replenish stores of personal protective equipment (PPE), basic medical supplies, pharmaceuticals including antivirals for treatment or prophylaxis, and critical care equipment.[68,69] Due to impacts upon healthcare capacity and provisions, the HE and clinical providers may need to implement altered standards of care, which will lead to difficult decisions with regard to allocation of scarce supplies. The HE's role, as explained earlier in this chapter, will be vital for prioritization of PPE, antivirals, and vaccines, according to national and state public health guidance.[16,19,69,70] Further, the HE can assist the planning team in identifying distributers of vital supplies and ensuring that the hospital's potential needs are part of the distributer's contingency plans for a pandemic of influenza as well.[68]

Hospital Pandemic Preparedness: A pandemic preparedness committee should involve all key responders within the hospital organization and have a dedicated leader, a role that may be best served by the bioterrorism preparedness planner or disaster/emergency coordinator.[69] Anticipated surge capacity needs should be documented, and hospitals should prepare to make 30 percent of their beds available quickly, within a week. CDC's FluSurge tool is a valuable tool the HE can use to assist in estimating potential impacts upon surge capacity based on various pandemic influenza scenarios.[70] Toner and Waldhorn[12] note the potential ability of hospital facilities to quickly make approximately 10–20 percent of bed capacity available within a few hours simply by accelerating discharges and utilizing discharge holding areas, as well as by the conversion of single rooms to double rooms, and the opening of previously closed areas.

As mentioned previously in this chapter, hospital involvement in community and regional preparedness programs is vital. An important feature of influenza pandemics is that they impact all sectors of society and all institutions within the community. Hospitals and their HEs should work together in a regional hospital coordinating group that includes neighboring hospitals, local public health officials, and emergency management personnel to address the surge capacity and scarce resource issues that will arise in a pandemic influenza event.[12,68,69] If faced with an impending influenza pandemic, regional hospital planners should be able to address a potential need to increase licensed bed capacity by 200 percent within the region in a period as short as two weeks.[12]

In the event of an influenza pandemic, the HE will need to limit the transmissibility of the pandemic virus strain within the healthcare facility.[12,69] Respiratory etiquette protocols and guidelines should be implemented, and everyone entering the facility, including staff, patients, and visitors should utilize simple surgical masks. For this capacity, hospitals should stockpile enough of these surgical masks to cover needs for at least a three-week period.[12]

Fit-tested N95 respirators should be used in aerosol-generating procedures, in cardiopulmonary resuscitation, and in situations that call for repeated direct contact with patients with influenza or pneumonia, and it may be prudent to use them for other direct patient care activities. Powered air purifying respirators (PAPRs) should be available for use in high-risk aerosol-generating procedures if the provider is unable to use an N95 respirator. The HE can refer to the Occupational Safety and Health Administrations document, "Guidance on Preparing Workplaces for an Influenza Pandemic," to assess risk for pandemic influenza exposure among all hospital personnel, not just direct-care personnel.[6] Healthcare personnel performing aerosol-generating procedures on known or suspected pandemic patients, such as cough induction procedures, bronchoscopies, some dental procedures, or invasive specimen collection, or laboratory personnel collecting or handling specimens, are within the very highest risk category for exposure as determined by the Occupational Safety and Health Administration (OSHA).[71]

N95 respirators will likely be in short supply, and resupply of these within a pandemic period could be difficult. They should be stockpiled, and monitoring of their use should occur in real time.[12] If no other masks are available, surgical masks, which do provide adequate droplet protection, should be used.[12,72] HEs should be aware of the capability of their suppliers to deliver necessary PPE during a potential influenza pandemic and may need to stockpile even more supplies depending upon their distributer's continuity of business plan and response during this type of disaster.

The HE will need to assist the administration in cohorting of patients, which will limit the number of staff working with patients with influenza. Adjustment of schedules may be needed to limit the number of dedicated direct-care staff. Healthcare personnel who are either vaccinated for the pandemic virus strain or who have recovered from pandemic influenza illness, and are thus considered immune, would be candidates to work with these cohorts. Despite strain upon healthcare resources, infected healthcare personnel, or those potentially infected and requiring quarantine, should be excluded from working with non-influenza-infected patients., The HE and infection prevention and occupational health staff will need to track and monitor healthcare personnel accordingly.[12]

The allocation of scarce resources will be a significant logistical, clinical, and ethical issue. While there are currently national guidelines for the allocation of antivirals and pandemic influenza vaccine,[16,19,72] alterations in normal care routines may need to occur if routine care cannot be delivered despite all efforts. Importantly, legal and ethical templates for this action should be developed prior to a mass casualty event.[10] The HE, in regional collaboration with other hospitals, will be able to assist in criteria and clinical guideline development for the use of resources, such as mechanical ventilation, based on evolving national guidelines.[12,68,69]

Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

In 2012, a novel coronavirus, distinct from SARS, was detected in a Saudi Arabian patient.[73] Subsequently named Middle East Respiratory Syndrome coronavirus (MERS-CoV), the virus has spread to several countries, including the US, in persons with history of travel to countries in and near the Arabian Peninsula.[74] Like SARS, human-to-human transmission has occurred in close contacts of ill patients or travelers to the Arabian Peninsula; in 2015, an outbreak occurred due to a traveler who returned from the area to his home in South Korea.[75] Studies have implicated a potential role of camels in the epidemiology of the novel virus; however, this association is not confirmed.[74]

Symptoms of MERS include fever, cough, and shortness of breath (Table 24.2), and the case fatality rate as of late 2015 was approximately 30–40 percent. Like SARS, transmission has predominantly occurred in the healthcare setting, and healthcare personnel are at higher risk due to exposure to respiratory secretions containing the virus.[74] Standard, contact and airborne precautions are recommended in any suspected case (Table 24.3). Currently, no known treatment or vaccine exists for MERS-CoV (Table 24.4).

References

1. Darling RG, Catlett CL, Huebner KD, Jarrett DG. Threats in bioterrorism. I: CDC category A agents. *Emerg Med Clin North Am*. 2002;**20**:273–309.
2. Department of Homeland Security. National Incident Management System. FEMA Publication P-501, December 2008:1–156.
3. National Incident Management System (NIMS). NIMS Implementation Activities for Hospitals and Healthcare Systems. Available at: www.fema.gov/pdf/emergency/nims/imp_act_hos_hlth.pdf. Accessed November22, 2015.
4. NIMS Implementation for Healthcare Organizations Guidance January 2015. Available at: www.phe.gov/Preparedness/planning/hpp/reports/Documents/nims-implementation-guide-jan2015.pdf. Accessed November 22, 2015.
5. McLaughlin S. Ready for anything. *Health Facilities Management*. 2007; **20**: 39–40, 42.
6. Hospital Incident Command System Guidebook 2014. California Emergency Medical Services Authority (EMSA), 2014. Available at: www.emsa.ca.gov/media/default/HICS/HICS_Guidebook_2014_11.pdf. Accessed November 22, 2015

7. Centers for Disease Control and Prevention (CDC). Revised US surveillance case definition for severe acute respiratory syndrome (SARS) and update on SARS cases – United States and worldwide, December 2003. *MMWR Morb Mortal Wkly Rep*. 2003;**52**: 1202–1206.
8. Nam WW. Role of SARS screening clinic in the ED. *Can J Emerg Med*. 2004;**6**:78–79.
9. McGeer AJ. Diagnostic testing or empirical therapy for patients hospitalized with suspected influenza: what to do? *Clin Infect Dis*. 2009;**48** (Suppl 1):S14–S19.
10. World Health Organization (WHO). Current WHO phase of pandemic alert for Pandemic (H1N1) 2009. Available at: www.who.int/csr/disease/swineflu/phase/en/. Accessed November 22, 2015.
11. Centers for Disease Control and Prevention. Enhanced Ebola Screening to Start at Five U.S. Airports and New Tracking Program for all People Entering U.S. from Ebola-affected Countries. Available at: www.cdc.gov/media/releases/192014/p1008-ebola-screening.html.
12. Toner E, Waldhorn R. What hospitals should do to prepare for an influenza pandemic. *Biosecur Bioterror*. 2006;**4**(4): 397–402.
13. Esbitt D. The Strategic National Stockpile: roles and responsibilities of health care professionals for receiving the stockpile assets. *Disaster Manag Response*. 2003;**1**:68–70
14. Hota S, McGeer A. Antivirals and the control of influenza outbreaks. *Clin Infect Dis*. 2007;**45**:1362–1368.
15. Public Health Guidance for Community-Level Preparedness and Response to Severe Acute Respiratory Syndrome (SARS), Supplement I: Infection Control in Healthcare, Home, and Community Settings, CDC. Available at: www.cdc.gov/ncidod/sars/guidance/I/healthcare.htm. Accessed August 26, 2009.
16. Department of Health and Human Services (HHS). Interim Guidance on Planning for the Use of Surgical Masks and Respirators in Health Care Settings during an Influenza Pandemic. Available at: www.pandemicflu.gov/plan/healthcare/maskguidan-cehc.html. Accessed August 26, 2009.
17. Chevalier MS, Chung W, Smith J, et al. Ebola virus disease cluster in the United States–Dallas County, Texas, 2014. *MMWR Morb Mortal Wkly Rep*. 2014;**63**(46):1087–1088.
18. MacIntyre CR, Chughtai AA, Seale H, et al. Uncertainty, risk analysis and change for Ebola personal protective equipment guidelines. *Int J Nurs Stud*. 2015;**52**(5):899–903.
19. Department of Health and Human Services (HHS). HHS Pandemic Influenza Plan. Available at: www.hhs.gov/pandemicflu/plan/. Accessed August 26, 2009.
20. Bartlett JG, Borio L. The current status of planning for pandemic influenza and implications for health care planning in the United States. *Clin Infect Dis*. 2008; **46**:919–25.
21. Cinti SK, Wilkerson W, Holmes JG, et al. Pandemic influenza and acute care centers: taking care of sick patients in a nonhospital setting. *Biosecur Bioterror*. 2008;**6**:335–348.
22. Barnitz L, Berkwits M. The health care response to pandemic influenza. *Ann Intern Med*. 2006;**145**:135–137.
23. Inglesby TV, O'Toole T, Henderson DA, et al. Anthrax as a biological weapon, 2002: updated recommendations for management. *JAMA*. 2002;**287**:2236–2252.
24. Centers for Disease Control and Prevention. Use of anthrax vaccine in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009. *MMWR Recomm Rep*. 2010; **59**(RR-6):1–36.
25. Henderson DA, Inglesby TV, Bartlett JG, et al. Smallpox as a biological weapon: medical and public health management. Working Group on Civilian Biodefense. *JAMA*. 1999;**281**: 2127–2137.
26. Inglesby TV, Dennis DT, Henderson DA, et al. Plague as a biological weapon: medical and public health management. Working Group on Civilian Biodefense. *JAMA*. 2000;**283**(17): 2281–2290.
27. Dennis DT, Inglesby TV, Henderson DA, et al. Tularemia as a biological weapon: medical and public health management. *JAMA*. 2001;**285**:2763–2773.
28. Arnon SS, Schechter R, Inglesby TV, et al. Botulinum toxin as a biological weapon: medical and public health management. *JAMA*. 2001;**285**:1059–1070.
29. Borio L, Inglesby T, Peters CJ, et al. Hemorrhagic fever viruses as biological weapons: medical and public health management. *JAMA*. 2002;**287**:2391–2405.
30. Christian MD, Poutanen SM, Loutfy MR, et al. Severe acute respiratory syndrome. *Clin Infect Dis*. 2004;**38**:1420.
31. Cheng VCC, Lau SKP, Woo PCY, et al. Severe acute respiratory syndrome coronavirus as an agent of emerging and reemerging infection. *Clin Microbiol Rev*. 2007;**20**:660–694.
32. Hui DS, Chan MC, Wu AK, Ng PC. Severe acute respiratory syndrome (SARS): epidemiology and clinical features. *Postgrad Med J*. 2004;**80**:373–381.
33. Arabi YM, Arifi AA, Balkhy HH, et al. Clinical course and outcomes of critically ill patients with Middle East Respiratory Syndrome coronavirus infection. *Ann Intern Med*. 2014;**160** (6):389.
34. Schieffelin JS, Shaffer JG, Goba A, et al. Clinical illness and outcomes in patients with Ebola in Sierra Leone. *N Engl J Med*. 2014;**371**(22):2092.
35. Hien ND, Ha NH, Van NT, et al. Human infection with highly pathogenic avian influenza virus (H5N1) in northern Vietnam, 2004–2005. *Emerg Infect Dis*. 2009; **15** (1):19–23.
36. Sampathkumar P. West Nile virus: epidemiology, clinical presentation, diagnosis, and prevention. *Mayo Clin Proc*. 2003; **78**:1137–1143.
37. Lewis MD, Pavlin JA, Mansfield JL, et al. Disease outbreak detection system using syndromic data in the greater Washington DC area. *Am J Prev Med*. 2002;**23**:180–186.
38. Sejvar JJ, Chowdary Y, Schomogyi M, et al. Human monkeypox infection: a family cluster in the midwestern United States. *J Infect Dis*. 2004;**190**:1833–1840.
39. State-specific mortality from stroke and distribution of place of death: United States, 1999. *MMWR Morb Mortal Wkly Rep*. 2002;**51**: 429–433.
40. Schlech WF III, Ward JI, Band JD. Bacterial meningitis in the United States, 1978 through 1981. The National Bacterial Meningitis Surveillance Study. *JAMA*. 1985;**253**: 1749–1754.
41. Centers for Disease Control and Prevention. Recognition of illness associated with the intentional release of a biologic agent. *MMWR Morb Mortal Wkly Rep*. 2001;**50**(41):893–897.
42. Buehler JW, Berkelman RL, Hartley DM, Peters CJ. Syndromic surveillance and bioterrorism-related

epidemics. *Emerg Infect Dis*. 2003;**9**:1197–1204.

43. Roush S, Birkhead G, Koo D, Cobb A, Fleming D. Mandatory reporting of diseases and conditions by health care professionals and laboratories. *JAMA*. 1999; **282**(2):164–170.
44. Buehler JW, Berkelman RL, Hartley DM, et al. Syndromic surveillance and bioterrorism related epidemics. *Emerg Infect Dis*. 2003;**9**:1197–1204.
45. Borchardt SM, Ritger KA, Dworkin MS. Categorization, prioritization, and surveillance of potential bioterrorism agents. *Infect Dis Clin North Am*. 2006;**20**:213–225.
46. Sokolow LZ, Grady N, Rolka H, et al. Deciphering data anomalies in BioSense. *MMWR Morb Mortal Wkly Rep*. 2005;**54**(Suppl):133–139.
47. Rotz LD, Hughes JM. Advances in detecting and responding to threats from bioterrorism and emerging infectious disease. *Nat Med*. 2004;**10**: S130–S136.
48. Blank S, Moskin LC, Zucker JR. An ounce of prevention is a ton of work: mass antibiotic prophylaxis for anthrax, New York City, 2001. *Emerg Infect Dis*. 2003;**9**:615–622.
49. Dewan PK, Fry AM, Laserson K, et al. Inhalational anthrax outbreak among postal workers, Washington, D.C., 2001. *Emerg Infect Dis*. 2002;**8:** 1066–1072.
50. Christopher GW, Cieslak TJ, Pavlin JA, et al. Biological warfare: a historical perspective. *JAMA*. 1997;**278**:412–417.
51. Sugishima M. Aum Shinrikyo and the Japanese law on bioterrorism. *Prehosp Disaster Med*. 2003;**18**:179–183.
52. Office of Technology Assessment, US Congress. Proliferation of Weapons of Mass Destruction. Washington, DC: US Government Printing Office; 1993. Publication OTA-ISC–559.
53. Centers for Disease Control and Prevention. Smallpox Response Plan and Guidelines, Version 3.0. 2002. Available at: www.bt.cdc.gov/agent/smallpox/response-plan/. Accessed November 22, 2015.
54. Centers for Disease Control and Prevention.Smallpox Case Definitions. Available at: www.bt.cdc.gov/agent/smallpox/diagnosis/casedefinition.asp. Accessed November 22, 2015.
55. Centers for Disease Control and Prevention. CDC Interim Guidance for Revaccination of Eligible Persons Who Participated in the US Civilian Smallpox Preparedness and Response Program, October 2008. Available at: www.bt.cdc.gov/agent/smallpox/revaxmemo.asp. Accessed November 22, 2015.
56. Pasetti MF, Cuberos L, Horn TL, et al. An improved Francisella tularensis live vaccine strain (LVS) is well tolerated and highly immunogenic when administered to rabbits in escalating doses using various immunization routes. *Vaccine*. 2008;**26**:1773–1785.
57. Centers for Disease Control and Prevention. Botulism Antitoxin Heptavalent (Equine), Types A-G. Available at: www.cdc.gov/laboratory/drugservice/formulary.html#bat. Accessed November 22, 2015.
58. World Health Organization. Ebola virus disease outbreak 2014–2015. Available at: www.who.int/csr/disease/ebola/en/. Accessed November 22, 2015.
59. Leroy EM, Epelboin A, Mondonge V, et al. Human Ebola outbreak resulting from direct exposure to fruit bats in Luebo, Democratic Republic of Congo, 2007. *Vector Borne Zoonotic Dis*. 2009;**9** (6):723–728.
60. Bausch DG, Towner JS, Dowell SF, et al. Assessment of the risk of Ebola virus transmission from bodily fluids and fomites. *J Infect Dis*. 2007;**196** (Suppl 2): S142–S147.
61. Dowell SF, Mukunu R, Ksiazek TG, et al. Transmission of Ebola hemorrhagic fever: a study of risk factors in family members, Kikwit, Democratic Republic of the Congo, 1995. *J Infect Dis*. 1999;**179**(Suppl 1): S87.
62. Centers for Disease Control and Prevention. Infection prevention and control recommendations for hospitalized patients with known or suspected Ebola hemorrhagic fever in U.S. hospitals. Available at: www.cdc.gov/vhf/ebola/hcp/infection-prevention-and-control-recommendations.html. Accessed on November 21, 2015.
63. Centers for Disease Control and Prevention. Ebola virus disease information for clinicians in U.S. healthcare settings. Available at: www.cdc.gov/vhf/ebola/hcp/clinician-information-us-healthcare-settings.html. Accessed November 17, 2015.
64. Fowler RA, Fletcher T, Fischer WA 2nd , et al. Caring for critically ill patients with Ebola virus disease: perspectives from West Africa. *Am J Respir Crit Care Med*. 2014;**190**(7):733.
65. Centers for Disease Control and Prevention. Severe Acute Respiratory Syndrome (SARS). Available at: www.cdc.gov/sars/index.html. Accessed November 22, 2015.
66. FIneburg HV. Pandemic preparedness and response: lessons from the H1N1 Influenza of 2009. *N Engl J Med*. 2014; **370**:1335–1342.
67. Centers for Disease Control and Prevention. Novel influenza A virus infections 2014 Case Definition. Available at: wwwn.cdc.gov/nndss/conditions/novel-influenza-a-virus-infections/case-definition/2014/. Accessed November 22, 2015.
68. Simonsen L, Spreeuwenberg P, Lustig R, et al. Global mortality estimates for the 2009 influenza pandemic from the GLaMOR project: a modeling study. *PLoS Med*. 2013;**10**: e1001558–e1001558.
69. Bartlett JG, Borio L. The current status of planning for pandemic influenza and implications for health care planning in the United States. *Clin Infect Dis*. 2008;**46**:919–925.
70. Centers for Disease Control and Prevention. FluSurge, version 2.0. Available at: www.cdc.gov/flu/tools/flusurge/. Accessed November 22, 2015
71. Occupational Safety and Health Administration (OSHA). Guidance on Preparing Workplaces for an Influenza Pandemic. OSHA publication 3327–02 N 2007. Available at: www.osha.gov/Publications/influenza_pandemic.html. Accessed August 26, 2009.
72. Hick JL, Hanfling D, Burstein JL, et al. Health care facility and community strategies for patient care surge capacity. *Ann Emerg Med*. 2004;**44** (3):253–261.
73. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus ADME, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N Engl J Med*. 2012;**367**:1814–1820
74. Centers for Disease Control and Prevention. Middle Eastern Respiratory Syndrome. Available at: www.cdc.gov/coronavirus/mers/index.html. Accessed November 22, 2015.

Chapter

25 Exposure Workups

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Introduction

Several axioms about exposures in the hospital seem to exist. First, they always come at inconvenient times. There is no good time for an exposure even if it's not Friday. The corollary to this axiom is that exposure workups always interrupt other important infection prevention activities. The second axiom is that exposures usually involve more than one department and that at least one of the affected areas will be a large open room in which many persons – who may be very difficult to identify – congregate. The third axiom is that exposures almost always involve the most vulnerable patients or healthcare personnel. The corollary to this axiom is that exposures are guaranteed to cause great anxiety among patients and staff.

Infection prevention personnel define exposures as events in which persons are exposed to infectious microorganisms or ectoparasites. The goals of an exposure workup are to prevent disease, if possible, in the persons who were exposed to the agent, and to prevent further transmission if exposed persons become ill. To achieve this goal, infection prevention and occupational health personnel must work together to identify all patients, visitors, and staff who might have been exposed and then determine whether these persons are susceptible or immune. If the exposed persons are immune to the etiologic agent, they do not require further investigations or interventions. If exposed persons are not immune to the etiologic agent or do not know their immune status, infection prevention and occupational health personnel may need to obtain further data, prescribe prophylactic treatment, and institute work restrictions. In this chapter, we will describe exposure workups for a number of important pathogens.

Many healthcare-associated exposures do not cause secondary cases of infection, or, if secondary cases occur, they are often mild. However, on occasion, patients, visitors, or healthcare personnel acquire infections that cause serious short- or long-term consequences, including prolonged absence from work, exposure to toxic treatments, incurable chronic illness, irreversible disability, or death.[1] Regardless of the ultimate consequences, exposure workups consume considerable time, money, and other resources.[2–4] Therefore, healthcare facilities should strive to prevent exposures with the following measures:

- Implementing policies that reduce the number of susceptible persons exposed (e.g., requiring all healthcare personnel to be immune to measles, mumps, and rubella or requiring all outpatient areas to screen patients for symptoms consistent with communicable diseases).
- Teaching healthcare personnel to recognize when they should stay home to prevent the spread of infectious agents.
- Teaching healthcare personnel to apply standard and transmission-based precautions properly.
- Implementing respiratory etiquette/cough hygiene (i.e., masks for persons with signs/symptoms of a respiratory infection such as fever and cough) for patients and persons accompanying them in outpatient areas and emergency departments.

Given the serious consequences that can result from exposures, healthcare facilities must manage exposures in a systematic and consistent manner. Many healthcare facilities assign this responsibility to infection prevention personnel. Infection prevention personnel must often work with other departments, such as occupational health and human resources, as well as with affected areas to evaluate the impact of a potential exposure event. In this chapter, we describe the steps in exposure investigations.

We have summarized our recommendations for working up exposures in a table (Table 25.1). When developing the recommendations in this chapter we used the Red Book,[5] *Control of Communicable Diseases Manual*,[6] the guidelines published by the Hospital Infection Control Practices Advisory Committee (HICPAC),[7] and the Advisory Committee on Immunization Practices (ACIP),[8] the websites created by the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO), other published studies, and our own experience. We also consulted *Principles and Practice of Infectious Diseases*.[9] We excluded bloodborne pathogens from this discussion, and we included only the agents that cause most exposures in hospitals. Hospitals vary; thus, some facilities may have numerous exposures to agents that we have not discussed. In addition, newer agents, such as severe acute respiratory syndrome (SARS), Middle East Respiratory Syndrome (MERS), and new influenza viruses can and will continue to afflict hospitals. Therefore, infection prevention personnel need to know what is happening in their communities and around the world. One way infection prevention personnel can keep abreast of what is happening is to join list serves such as the Emerging Infections Network sponsored by the Infectious Diseases Society of America. In addition, some state or local health departments inform infection prevention personnel of important developments through emails or faxes.

Table 25.1 Basic information regarding agents that cause most healthcare-associated exposures[9]

Etiologic agent	Incubation period	Diagnostic criteria	Exposure criteria	Period of communicability	Occupational health	Work restrictions	Prophylaxis

Varicella zoster virus	• Usually 14–16 days
	• Range 10–21 days
	• Up to 28 days in persons who received VZIG
		• Fever and vesicular rash (chickenpox) or grouped vesicular lesions in dermatomal distribution (shingles)
		• May consult Dermatology
			Airborne and contact transmission Chickenpox or disseminated zoster
			• Continuous household contact
			• > 5 minutes face-to-face contact with infected person without wearing a respirator
			• Direct contact with vesicle fluid without wearing gloves
			Shingles
			• Direct contact with vesicle fluid without wearing gloves
				Chickenpox
				• Most contagious 1–2 days before and shortly after rash appears
				• Transmission can occur until all lesions are crusted
				• Immunocom-promised persons may be contagious as long as new lesions are appearing
				Shingles
				• 24 hours before the 1st lesion appears and until all lesions are crusted
					• Assess immunity
					• HCP susceptible unless:
					  ◦ Has serologic evidence of immunity or
					  ◦ Has 2 documented doses of varicella vaccine
					  ◦ Documented diagnosis of varicella or zoster by a healthcare provider
					• If immune status unknown, consider obtaining varicella IgG antibody titer to determine immune status at the time of hire
						Exposed Nonimmune
						• Day 1–7 no restrictions
						• Day 8–21 for a single exposure or day 8 after 1st exposure through day 21 after last exposure
						• HCP must:
						• Not work or
						• Have no direct patient contact and work only with immune persons in non–patient care areas
						• Restrict HCP who received VZIG through day 28
						Exposed Immune
						• None
						• Education and symptom monitoring
						Infected
						• May return to work after all lesions are crusted over
							• Consider giving VZIG to nonimmune, immunocom promised or pregnant persons within 96 hours of exposure
							• Administer varicella virus vaccine to susceptible HCP within 3 days of exposure to prevent or modify infection Giving the vaccine does not change the work restrictions

Rubeola (measles) virus	• Usually 8–12 days • Range 7–21 days	• Prodromal symptoms including conjunctivitis, coryza, and cough • Fever and rash with positive measles IgM antibody titer • May consult Dermatology	• Droplet and airborne transmission • Spent time in a room with an infected person without wearing a respirator • If air is recirculated, spent time in the area supplied by the air-handling system while infected person was present or within one hour	• 4 days before rash to 4 days after rash appears, but maximal communicability from prodrome through first 3–4 days of the rash • Immunocom-promised persons may be contagious for the duration of the illness	• Assess immunity • HCP susceptible unless: • Provides serologic evidence of immunity or • Provides documentation of receipt of 2 doses of live measles virus containing vaccine • Consider vaccination (2 doses of MMR) for HCP born before 1957	Exposed Nonimmune • Day 1–4 no restrictions • Day 5–21 for a single exposure or day 5 of first exposure through day 21 of last exposure exclude HCP from work setting Exposed Immune • None • Education and symptom monitoring	• Give MMR vaccine to non-immune HCP within 72 hours of exposure to modify infection • IG can be given within 6 days to nonimmune exposed HCP at high risk for complications due to pregnancy or immuno-compromise • Vaccine or IG given after exposure does not

			after the person's departure • Contact with nasal or oral secretions from an infected person or items contaminated with these secretions without wearing gloves		without evidence of immunity as described above. • Obtain blood for IgG antibody titers as needed	Infected • May return to work 4 days after developing rash	change work restrictions
Rubella virus	• Usually 14 days • Range 12–23 days	• Mild febrile exanthem and positive rubella IgM antibody titer • Up to 50 percent subclinical • May consult Dermatology	• Respiratory droplet transmission • Within 3 feet of infected person without wearing a droplet precautions mask^ • Contact with nasopharyngeal secretions from an infected person or items contaminated with these secretions without wearing gloves • Contact with nasopharyngeal secretions or urine from infant with congenital rubella without wearing gloves	• 7 days before rash to 7 days after rash appears • Most contagious when rash first appears • Up to 1 year for infants with congenital rubella	• Assess immunity • HCP susceptible unless: • Provides serologic evidence of immunity • Provides documentation of receipt of one dose of live rubella containing vaccine • Consider vaccination (one dose of MMR) for HCP born before 1957 without evidence of immunity as described above. • Obtain blood for IgG antibody titers as needed	Exposed Nonimmune • Day 1–6 no restrictions • Day 7–21 for a single exposure or day 7 after first exposure through day 23 after last exposure • HCP must: • Not work or • Not have direct patient contact and work only with immune persons in non–patient care areas Exposed Immune • None • Education and symptom monitoring Infected • May return to work 8 days after developing rash	• None • Rubella vaccine does not prevent infection after exposure • IG does not prevent infection
Mumps virus	• Usually 16–18 days • Range 12–25 days	• Fever with swelling and tenderness of the salivary glands or testes and positive mumps IgM antibody titer	• Respiratory droplet transmission • Within 3 feet of infected person without wearing a droplet precautions mask^ • Contact with saliva or items contaminated with saliva from an infected person without wearing gloves	• Most communicable 48 hours before onset of illness, but may begin as early as 7 days before onset of overt parotitis and/or orchitis and continue 5–9 days thereafter (average 5 days)	• Assess immunity • HCP susceptible unless: • Provides serologic evidence of immunity • Provides documentation of receipt of 2 doses of live mumps virus containing vaccine. • Consider vaccination (two doses of MMR) for HCP born before 1957 without evidence of	Exposed Nonimmune • Day 1–11 no restrictions • Day 12–25 for a single exposure or day 12 after first exposure through day 25 after last exposure HCP must: • Not work or • Have no direct patient contact and work only with immune persons away from patient-care areas	• None • Mumps vaccine not proven to prevent infection after exposure • IG does not prevent infection

Table 25.1 (cont.)

Etiologic agent	Incubation period	Diagnostic criteria	Exposure criteria	Period of communicability	Occupational health	Work restrictions	Prophylaxis
					immunity as described above. • Obtain blood for IgG antibody titers as needed	Exposed Immune • None • Education and symptom monitoring Infected • May return to work 5 days after onset of parotid gland swelling	
Parvovirus B19	• Usually 4–14 days • Range up to 21 days • Rash and joint symptoms occur 2–3 weeks after infection	• "Slapped cheek" rash and positive serum parvovirus B-19 IgM antibody titer • Can cause aplastic crisis in sickle cell or immunocom-promised patient	• Respiratory droplet transmission • Criteria have not been defined but probably include: • Close person-to-person contact (within 3 feet) with infected person without wearing a droplet precautions mask^ • Contact with respiratory secretions from an infected person or items contaminated with these secretions without wearing gloves	• Persons are unlikely to be infectious after the onset of rash • Immunocompromised persons can have chronic infections and can shed virus for prolonged periods	• Assess immunity • Obtain blood for IgG antibody titers as needed • Refer a pregnant HCP to her obstetrician	• Not necessary	• None
Hepatitis A virus	• Usually 28–30 days • Range 15–50 days	• Positive hepatitis A IgM antibody	• Fecal-oral transmission • Contact with stool of infected person without wearing gloves • Consuming uncooked food prepared by an infected person	• Viral shedding in stool lasts 1–3 weeks • Highest viral titers are found in stool 1–2 weeks before onset of symptoms • Risk of transmission is minimal 1 week after onset of jaundice	• Assess immunity • Obtain blood for IgG antibody titers as needed • Describe signs and symptoms and ask exposed HCP to return to occupational health if these occur	Exposed Nonimmune • None • Education and symptom monitoring Infected • May return to work 7 days after onset of jaundice or other clinical symptoms	• <40 years old: Hepatitis A vaccine within 2 weeks • ≥ 40 years old, immunocom-promised or with chronic liver disease: IG within 2 weeks of exposure
Influenza virus	• Usually 2 (1–4) days	• Influenza-like illness between October – April	• Respiratory droplet transmission • Within 3–6 feet of infected person without wearing a	• Infectious starting 24 hours before onset of symptoms • Viral shedding usually ceases within 5–7 days	• Assess immunization status and vaccine strain match to predominant circulating strain(s)	Exposed Nonimmune • Have not been defined for nonimmune HCP exposed to persons with influenza	• Consider vaccinating exposed nonimmune HCP • Consider chemoprophylaxis for

		• Positive diagnostic test for influenza	droplet precautions mask^ • Direct contact with secretions from respiratory tract of infected person or items contaminated with these secretions without wearing gloves	but can persist longer in children or immunocom-promised	• Discuss risks and benefits of chemoprophylaxis • Describe signs and symptoms and inform HCP that they cannot work if these symptoms occur	Exposed Immune • Usually none • Education and symptom monitoring Infected • Ill HCP should not work	nonimmune HCP based on risk of complications, exposure characteristics: • Oseltamivir 75 mg once daily x 7 days for adults exposed to influenza A or B • Zanamivir 10 mg (2 inhalations) once daily x 7 days for adults exposed to influenza A or B • Chemoprophylaxis may vary by location, season, and viral susceptibility. Check CDC annual recommendations.
Creutzfeldt-Jakob Agent† (Prion protein)	• 15 months to > 30 years	• Progressive dementia • Characteristic findings on brain pathology • Recipient cadaver-derived pituitary hormones • Family history of prion disease	• Criteria have not been defined but probably include the following if source patient is diagnosed with CJD or has risk factors for CJD: ‡ • Puncture or cut with instruments contaminated with high risk tissues (see text) • Splash of high-risk fluid/tissue onto mucous membranes • Routine patient care poses a very low risk to HCP	• Unknown, but probably during symptomatic illness and an undetermined period before symptoms appear	• Educate HCP about CJD and risk of transmission • Counsel HCP using data from the literature indicating that the risk of transmission is very low (see text)	• None	• None
Mycobacterium tuberculosis	• 2–10 weeks from exposure to detection of positive TST • Risk of developing active disease is greatest in first 2 years after infection	• MTB found in respiratory secretions or wound drainage	• Airborne transmission • Spent time in a room with a person who has active pulmonary disease without wearing a respirator • Packing or irrigating wounds infected with *M. tuberculosis* without wearing a respirator	• Infected persons are considered infectious if they: • Are coughing • Are undergoing cough-inducing or aerosol-generating procedures • Have sputum smears that are positive for acid-fast bacilli • Are not receiving therapy	• Obtain baseline TST within 2 weeks of exposure if HCP previously negative or unknown status • Perform postexposure TST at 12 weeks • Prescribe treatment if postexposure TST is positive	Exposed • None for persons whose TST becomes positive Infected • Restrict HCP with active TB until they are on effective antituberculosis chemotherapy, respond to therapy, and	• Isoniazid 300 mg daily for 9 months OR • INH 15 mg/kg (Max dose 900 mg) once weekly AND Rifapentene (> 50 kg) 900 mg once weekly X 12 weeks • Pyridoxine 25–50 mg daily with daily regimen or 50 mg weekly with weekly regimen may be

Table 25.1 (cont.)

Etiologic agent	Incubation period	Diagnostic criteria	Exposure criteria	Period of communicability	Occupational health	Work restrictions	Prophylaxis
				• Have just started therapy • Have poor clinical response to therapy • Persons are considered infectious until they are on effective antituberculosis chemotherapy, respond to therapy, and have 3 consecutive negative sputum smears • Children with primary pulmonary TB are rarely contagious		have 3 consecutive negative sputum smears	added for persons with conditions in which neuropathy is common • Check CDC website for most up to date recommen-dations
Neisseria meningitidis	• Usually < 4 days • Range 1–10 days	• Clinical signs of sepsis, meningitis, or pneumonia, and gram-negative diplococci in blood, CSF, sputum, synovial fluid, pericardial fluid, or skin scraping	• Respiratory droplet transmission • Extensive close contact without wearing a droplet precautions mask^ with respiratory secretions from an infected person before patient has completed 24 hours of effective antibiotics, particularly during: • Suctioning • Resuscitation • Intubation • Extensive oral or pharyngeal exam	• Persons are infectious until they have received 24 hours of effective antimicrobial therapy	• Prescribe prophylaxis • Educate exposed HCP about signs and symptoms of meningitis • Reassure HCP who do not meet the exposure definition	Exposed • None	• Ciprofloxacin 20 mg/kg (maximum 500 mg) single dose (contraindicated in pregnancy), OR • Rifampin 10 mg/kg (Maximum 600 mg) every 12 hours for 2 days (contraindicated in pregnancy), OR • Ceftriaxone 250 mg IM, single dose (safe during pregnancy)
Bordetella pertussis	• Usually 7–10 days • Range 6–20 days	• Paroxysmal cough, inspiratory whoop, or other respiratory symptoms, with positive DFA, culture, PCR, or serology for *Bordetella pertussis*	• Respiratory droplet transmission • Within 3 feet of infected person without wearing a droplet precautions mask^ • Direct contact with respiratory tract secretions from	• Most contagious during the catarrhal state • Communicability diminishes rapidly after onset of cough, but can persist as long as 3 weeks	• Regardless of vaccination status: • If HCP has no symptoms, consider prophylaxis within 21 days of exposure for high risk HCP or HCP caring for high risk patients:	Exposed • No restrictions • Education and symptom monitoring +/- prophylaxis Infected • HCP may return to work after completing at least 5 days of therapy	• If indicated: • Azithromycin 500 mg per day for 5 days • Erythromycin 40 mg/kg/day in 4 divided doses (maximum 2 gm/day) for 14 days (estolate preparation preferred)

			infected persons or items contaminated with these secretions without wearing gloves		• High risk = infants; pregnant women in 3rd trimester; immunocompromised; asthma or lung disease • If HCP symptomatic, begin therapy and relieve from work		• TdaP should be considered in nonimmune HCP
Lice	• Head lice: 7–12 days (from egg to hatch) 9–12 days (adult lice to reproduce egg) • Body lice: 1–2 weeks (from egg to hatch) 9–19 days (adult lice to reproduce egg) • Pubic lice: 6–10 days (from egg to hatch) 2–3 weeks (adult lice to reproduce egg)	• Live lice or nits (eggs) on hair shaft <1 cm from skin • May consult Dermatology	• Direct contact transmission • Head lice: Hair-to-hair contact with infested person; less commonly shared hair brushes, combs or hats • Body lice: Contact with linen or clothes of infested person without wearing gloves • Pubic lice: Sexual contact	• As long as lice or eggs remain alive on infested person, clothing, or personal items • Survival time for lice away from the host • Head lice 1–2 days (adult lice), 7–10 days (egg) • Body lice 5–7 days (adult lice), up to a month (egg) • Pubic lice 2 days (adult) • Nits ≥ 1 cm from scalp have been present ≥ 2 weeks and may not be viable	• Treat HCP only if infested	Exposed • No restrictions Infested • Immediate restriction until 24 hours after treatment	• Not recommended
Scabies	• 4–8 weeks if no previous infestation • 1–4 days if previous infestation	• Burrows or papular lesions in classic body sites and intense itching at night • May consult Dermatology	• Direct contact transmission • Prolonged, close, skin-to-skin contact • Minimal direct contact with crusted scabies (Norwegian) can result in transmission	• Transmission can occur before the onset of symptoms • Person remains contagious until treated	• Prescribe scabicide for all HCP exposed to persons with crusted scabies • For other scabies exposure, treat if infestation acquired • Pregnant women should not use lindane	Exposed • No restriction • Education and symptom monitoring Infested • Immediate restriction until 24 hours after treatment	• Drug of choice: • Topical 5 percent Permethrin cream • Alternative drugs: • Topical Lindane • Topical 10 percent Crotamiton

Abbreviations: VZIG, Varicella-Zoster Immune Globulin; HCP, healthcare personnel; IgG, immunoglobulin G; MMR, measles, mumps, and rubella vaccine; IG, immune globulin; CJD, Creutzfeldt-Jakob disease; TST, tuberculin skin test; AFB, acid-fast bacilli; TB, tuberculosis; IM, intramuscular.

* A small percentage of HCP born before 1957 will not be immune to measles.[49] Infection prevention personnel should determine whether this criterion is appropriate for the staff in their hospital.

^Droplet precautions mask refers to a paper surgical/procedure mask.

† These precautions should be used for persons who have CJD, progressive dementia, or a family history of prion disease, CJD, Gerstmann-Straussler-Scheinker syndrome, or fatal familial insomnia.

‡ Data from a study with mice suggest that prions might be transmitted by contact of infected blood or CSF with mucous membranes.[128] No data are available with humans to support or refute the data from mice.

References: 5,6,12,121.

General Recommendations Regarding Exposure Workups

Obtain Mandate from the Administration

If the hospital administration assigns the responsibility for doing exposure workups to the infection prevention program, the administrators also must define the scope of that responsibility and delegate the authority for the associated activities to staff in the infection prevention program. The hospital administration must define prospectively what tests and prophylactic treatments the hospital will provide. In addition, the hospital administration must specify if exposed healthcare personnel will be granted administrative leave, leave with pay, leave without pay, or if they will be allowed to work in nonpatient care areas during the period in which they might be infectious.[10,11]

Develop Policies and Procedures

Once the infection prevention program has been given the authority to do exposure workups, the staff must develop specific policies that define exposures to various bacterial and viral pathogens and to ectoparasites and describe the investigative and preventive measures that should be undertaken for exposures caused by each agent. The staff also should develop general policies and procedures that define what tasks should be undertaken and who will do them.

Collaborate with Occupational Health

In many institutions, the infection prevention staff initiate the exposure workup and assess the need for prophylaxis and work restrictions for exposed healthcare personnel. However, staff in the occupational health service actually evaluate whether healthcare personnel were exposed and susceptible, examine healthcare personnel, enforce work restrictions, and give permission for healthcare personnel to return to work. Thus, as they develop policies and procedures, infection prevention personnel must collaborate extensively with staff in occupational health and clearly delineate responsibilities.

Develop a Database on the Immune Status of Healthcare Personnel

Infection prevention personnel will save countless hours if they have access to a database with information on the immune status of all healthcare personnel. This type of database is often maintained by the occupational health department. The most important data are healthcare personnel's immune status to chicken pox, measles, mumps, rubella, and hepatitis B. However, some hospitals might find it useful to test healthcare personnel for antibody to parvovirus B19 if they work in ante-partum clinics or with patients who are immunocompromised or have hemolytic anemias. Healthcare personnel's tuberculosis skin-test results and the results of respirator fit testing should be recorded in the database. The database also could store information on healthcare personnel's immunity to diphtheria, tetanus, and hepatitis A. Dates of receipt of pertussis and influenza vaccines should be recorded. Baseline data should be obtained from all new healthcare personnel before they start working in the institution. If the hospital is establishing a new database, the same information should be obtained from all current healthcare personnel.

The database should be computerized; it may be as simple as a spreadsheet format that can be easily managed in smaller hospitals. The persons who develop and maintain the database could be in the hospital's information management group, in the infection prevention program, or in the occupational health service. Regardless of who manages the database, the persons investigating exposures must have unobstructed access to the database so that they can use the data regardless of when the exposure occurs while ensuring healthcare personnel confidentiality. Some programs have found a shared drive that clinicians, infection prevention staff, and occupational health staff can access useful to facilitate data sharing necessary for complete, prompt exposure evaluations.

Develop a Data Collection Form

Infection prevention staff must investigate exposures in a consistent fashion. Therefore, in addition to developing policies and procedures, infection prevention staff should design a form (preferably electronic) with which they can collect the necessary data for each exposure. A list of healthcare personnel who were in the affected areas and, when appropriate, either the immune status of these healthcare personnel or the date of their last tuberculin skin test should be generated. This list can usually be generated from staffing records but may also require additional chart review and confirmation with area managers to capture healthcare personnel who were in the affected area and are not hospital employees (e.g., physicians and students) or assigned to a particular area or unit. However the list is generated and the form it is in (i.e., paper or electronic), it should be shared as soon as possible with occupational health, so they are prepared when exposed healthcare personnel come to them for follow-up.

Educate Healthcare Personnel

Healthcare personnel should know the modes of transmission for common communicable pathogens and basic infection prevention practices that limit the spread of microorganisms. In addition, exposure workups will go more smoothly if infection prevention personnel prospectively educate healthcare personnel about exposure workups in general and about the specific steps taken during common exposure workups. Infection prevention staff also will need to educate and reassure the healthcare personnel while doing an exposure workup. It is not uncommon for healthcare personnel to be anxious regarding an exposure, and they may panic and act irrationally; this is a common response when healthcare personnel think they have been exposed to *N. meningitidis* or to lice, for example.

Collect and Evaluate Data on Exposures

Infection prevention personnel should collect data on all the exposure workups that they conduct. At least once per year infection prevention staff should review the following:

- The number of exposures,
- The etiologic agents,
- The affected locations,
- The number of susceptible healthcare personnel, patients, and visitors exposed,
- The number of secondary cases,
- The number of healthcare personnel who were placed on leave,
- The number of leave days,
- The breaks in infection prevention technique that led to the exposures,
- The prophylactic treatments given,
- The cost in time and dollars.

Infection prevention personnel should report these data to the infection control committee and should use these data to do the following:

- Document their effort to the administration,
- Identify topics for in-service educational programs,
- Identify interventions
- Identify areas for collaboration with other departments (e.g., work with staff in other departments to develop methods for screening and triage of potentially infectious patients),
- Identify areas for improvement,
- document quality improvement efforts required for accreditation.

Disease-Specific Exposure Workups

Viral Diseases

Varicella-zoster Virus

Varicella-zoster virus (VZV) causes a primary infection, chicken pox, and a recrudescent infection, herpes zoster, or shingles. VZV can be transmitted through the air by persons with chicken pox or through direct contact with active chicken pox or herpes zoster lesions. Thus, patients with chicken pox or disseminated zoster should be placed on airborne and contact precautions until all lesions are crusted to prevent exposures within hospitals.[12] Nonimmune patients who have been exposed to chicken pox should be placed on airborne precautions between days 10 and 21 after their exposure (day 28 if the person is immunocompromised or has received varicella-zoster immune globulin [VZIG]). Because VZV rarely is spread through the air from persons with localized herpes zoster, patients, visitors, and healthcare personnel with this entity do not need to be restricted if their lesions can be covered.

The incidence of varicella among adults is estimated to be <0.1/1,000 population.[8] Approximately 2 percent to 5 percent of all healthcare personnel are not immune to VZV, and approximately 15 percent of susceptible healthcare personnel will develop chicken pox each year.[13,14] At-risk exposure is generally defined as nontransient close contact with an infectious individual (e.g., indoor or face to face contact). The duration of close contact necessary for transmission is not well defined and ranges from 5 minutes to 1 hour. Nonimmune healthcare personnel who have been exposed to a person with chicken pox could be incubating the infection. To prevent the spread of VZV, infection prevention personnel must identify those healthcare personnel and restrict their work during the incubation period. Most healthcare facilities do not allow susceptible, exposed healthcare personnel to continue their patient-care duties during the incubation period. Some healthcare facilities place such healthcare personnel on leave,[10, 11] and other facilities reassign exposed susceptible healthcare personnel to non–patient care areas if all the healthcare personnel in that area are immune.[15] Staff members who develop active disease must not work until all lesions are crusted. Exposed visitors who are not immune should not be allowed to enter the hospital during the incubation period. Exposed visitors who do not know their immune status should not enter the hospital during the incubation period until they have obtained sufficient antibody levels and are documented to be immune.

Although all nonimmune healthcare personnel should be offered the chicken pox vaccine when they are hired, some healthcare personnel may remain nonimmune and be exposed. Infection prevention personnel should work with occupational health staff, expert clinicians, pharmacists, and hospital administrators to determine whether exposed persons will be offered the chicken pox vaccine (Varivax, Merck & Co, West Point, PA) or varicella zoster immune globulin (VZIG). This group should decide prospectively which persons will be offered which agent. This decision may not be a simple one for the following reasons:

- Five percent of healthcare personnel who receive the vaccine will develop a varicella-like rash that will require them to miss work. Although transmission of the vaccine virus is rare, it has been documented to occur, mostly outside the healthcare setting.
- Recently vaccinated healthcare personnel do not required any restriction in their work activities unless they develop a rash. Those who develop a varicella-like rash should not have contact with nonimmune individuals at risk for severe varicella (e.g., immunocompromised individuals, nonimmune pregnant women, and newborns of such women) until all lesions have crusted over.
- According to the Varivax package insert, up to 27 percent of vaccinated persons will have subclinical or breakthrough varicella infection after close exposure to a person with chicken pox.

Vaccinated persons who acquire chicken pox often have milder disease than unvaccinated persons.[8,16–19] Some healthcare facilities have experienced substantial transmission of VZV,[2,3,20] and several investigators have found that varicella

vaccine is cost effective given the costs associated with secondary cases.[21–24]

Table 25.1 outlines an approach to managing healthcare personnel who have been exposed to VZV.[5,11,19] Infection prevention personnel who want additional information about VZV exposures should consult the appropriate references.[6,8,9,13–15,25]

Measles Virus

Measles is a febrile illness that is characterized by Koplik's spots on the buccal mucosa and an erythematous rash. The measles rash starts on the face and spreads to the trunk and extremities and also progresses from a maculopapular to confluent rash. Measles virus, which is highly communicable, is spread by airborne transmission. Despite sensitivity to acid, strong light, and drying, the measles virus can remain viable in airborne droplets for hours, especially if the relative humidity is low. Consequently, outbreaks have occurred in healthcare facilities when the index patient was no longer present.[26,27] To prevent the spread of measles virus within healthcare facilities, patients with measles should be placed on airborne precautions.[12]

Before the measles vaccine was licensed in 1963, 500,000 cases of measles occurred in the United States each year. Subsequently, the number of measles cases in the United States declined dramatically, reaching a nadir in 1983. An increase in cases was noted in 2008 as a result of transmission within communities of unvaccinated individuals.[28] Immunization requirements for school age children and the routine use of two doses of the vaccine have decreased the number of measles cases over the past 20 years. However, in 2014 more cases were reported than in any year since 2000 when measles was declared eliminated in the US. In 2014, there were 23 outbreaks in the US with one large outbreak that involved 383 cases in an unvaccinated Amish community. Many of the other cases were associated with importation of measles from the Philippines.[29] Another large outbreak in 2015 was traced to Disney theme parks in Orange County, California.[30] In one study of 22 confirmed cases in the 2015 outbreak, there were 5 secondary cases among healthcare personnel.[31] In four of these cases, the individuals had prior evidence of immunity and continued to work in spite of developing symptoms.

Despite the recommendation that all persons receive two doses of measles vaccine unless they have a medical contraindication, and that all healthcare personnel should be immune to measles, outbreaks and healthcare-associated transmissions continue to occur.[26,27,31–49] Steingart et al reported that 8 of 31 persons in Clark County, Washington, who acquired measles in 1996 were healthcare personnel, and 5 were patients or visitors in healthcare facilities.[48] Compared with adults in Clark County, the relative risk of measles in healthcare personnel was 18.6 (95 percent confidence interval, 7.4–45.8; $p < 0.001$). Only 47 percent of facilities surveyed by these authors had measles immunization policies, and only 21 percent met the ACIP recommendations and enforced their policies. Kelly et al. described several outbreaks of measles in Australian healthcare facilities. They concluded that the outbreaks occurred because published guidelines for preventing healthcare-associated measles were not followed.[50] They suggested that transmission of measles in a healthcare facility could be considered "a sentinel sign of system failure." Five to 10 percent of healthcare personnel are susceptible to measles,[13] including 4.7 percent of those born before 1957, 16 percent of those born in the 1960s, and 34 percent of those born in the 1970s.[45] Younger healthcare personnel (<30 years old) are at higher risk of contracting measles in the healthcare setting, and in some reports of outbreaks healthcare personnel had higher attack rates than patients.[51]

Although measles exposures are infrequent, infection prevention personnel still must develop policies to limit the spread of measles if it is introduced into the hospital. A study conducted by Enguidanos et al. suggests that infection prevention programs may be ignoring measles because the incidence is low.[45] These investigators noted that 74 adults employed in acute-care hospitals acquired measles during a community-wide outbreak in 1987 through 1989. The investigators surveyed all 102 infection prevention professionals in the acute care hospitals in Los Angeles County to determine whether infection prevention policies were adequate. Only 17 percent of the hospitals required healthcare personnel to document immunity to measles, and only 4 percent had policies that covered students or volunteers. The investigators also surveyed the healthcare personnel who became ill. Of these 74 persons, 46 percent worked in hospitals that did not have measles infection prevention policies, 43 percent were born before 1957, and 31 percent were working in jobs that have not been considered to increase the risk of measles exposure.[45]

All healthcare personnel should have presumptive evidence of immunity to measles. Only documentation of 2 doses of measles, mumps, rubella (MMR) vaccination (at least 28 days apart), serologic evidence of immunity, or laboratory confirmation of prior infection should be accepted as evidence of measles immunity.[8] For healthcare personnel born before 1957 without any of the prior evidence of immunity, facilities should consider MMR vaccination.[52] When an exposure occurs, rapid vaccination is required to stop transmission, and serologic screening is not recommended in those circumstances.

As discussed previously, infection prevention personnel should work with occupational health to develop a database of healthcare personnel's measles immune status. If such a database is not available and a person with measles comes to the hospital, the infection prevention staff must identify exposed personnel and then determine whether these persons are immune. Nonimmune patients who have been exposed to measles should be placed on airborne precautions between day 5 and day 21 after their exposure.[12] Nonimmune family members and friends who have been exposed to a person with measles should not come to the hospital during the incubation period. Table 25.1 provides information necessary for managing a measles exposure.

Rubella Virus

Rubella (German measles) is an acute exanthematous viral infection that affects children and adults. Postnatal rubella, which resembles a mild case of measles, is characterized by

rash, fever, and lymphadenopathy. In contrast, rubella acquired in pregnancy can cause fetal death, premature labor, and severe congenital defects. Consequently, it is very important to prevent spread of rubella in healthcare facilities. However, the mild clinical symptoms associated with rubella have, at times, facilitated healthcare-associated spread of rubella virus because healthcare personnel have continued to work while they were ill. The literature documents numerous outbreaks of rubella in medical settings, some of which affected many susceptible pregnant women.[53–61] Furthermore, these institutions had to invest large amounts of time and money to control the outbreaks.[57,59,61]

The epidemiology of rubella has been changing. Data from the CDC indicate that the incidence of rubella has been decreasing among children less than 15 years old but increasing in adults, primarily those born outside the United States.[62,63] After universal vaccination was implemented in the US in 2004, endemic rubella transmission was eliminated. From 2004 to 2012, 79 cases of rubella and 6 cases of congenital rubella syndrome were reported. Rubella virus continues to circulate elsewhere in the world; thus the risk of imported cases of rubella remains.[64]

Rubella virus is spread in droplets that are shed from the respiratory secretions of infected persons. Persons with rubella are most contagious when the rash is erupting. In addition, persons with subclinical illness (up to 50 percent of cases) also may transmit the virus. To prevent healthcare-associated transmission, patients with rubella should be placed on droplet precautions until 7 days after the onset of the rash. Infants with congenital rubella shed large quantities of virus for many months, despite having high titers of neutralizing antibody. Such patients should be placed on droplet precautions each time they are admitted during the first year of life unless nasopharyngeal and urine cultures after 3 months of age are negative.

Nonimmune patients who have been exposed to rubella should be placed on droplet precautions between days 7 and 21 after their exposure.[12] Nonimmune family members and friends who have been exposed to a person with rubella should not come to the hospital during the incubation period.

Despite vaccination campaigns, 10 percent to 20 percent of hospital personnel may be susceptible to rubella.[13] A recent seroprevalence study of 642 healthcare personnel in Spain showed that 97.2 percent had rubella antibodies.[65] Older healthcare personnel (30–44 years old) were significantly more likely to have rubella antibodies than younger (<30 years old) healthcare personnel. The prevalence of rubella antibodies in this study is higher than that found in most other studies. Given the adverse effects of rubella virus on the fetus, many healthcare facilities require healthcare personnel, especially those working in obstetrics, to be immune to rubella.[34,53]

Table 25.1 provides information infection prevention personnel need for evaluating exposures to persons with rubella.

Mumps Virus

Mumps is characterized by fever and parotitis. In postpubertal men, mumps virus also can cause orchitis, which can be the primary manifestation of the infection. The mumps virus is transmitted through direct contact with contaminated respiratory secretions, inhalation of droplet nuclei, or through contact with fomites contaminated by respiratory secretions. Transmission of mumps virus requires more intimate contact with the infected person than does transmission of either measles virus or VZV. To prevent exposures in healthcare facilities, persons with mumps should be placed on droplet precautions until 9 days after parotid (or other glandular) swelling began.[12]

The incidence of mumps decreased substantially in the United States after the vaccine was licensed in 1967.[5,34] In 2006, the US experienced a large epidemic of mumps, which was centered in the Midwest.[66,67] This community-based outbreak caused numerous exposures in healthcare facilities. During this outbreak, the ACIP changed its requirements for evidence of mumps immunity among healthcare personnel. Presumptive evidence of immunity for healthcare personnel includes any of the following: 1) written documentation of vaccination with 2 doses of live mumps or MMR vaccine administered at least 28 days apart; 2) laboratory evidence of immunity; or 3) laboratory confirmation of disease.[8,52] For healthcare personnel born before 1957 without evidence of immunity, facilities should consider MMR vaccination (should receive 2 doses during an outbreak). From 2009 to 2010, there was an outbreak of mumps in a religious community in the northeast US with approximately 3500 cases. In 2011, there was another outbreak on a California university campus where 76 percent of cases occurred among individuals previously vaccinated with 2 doses of MMR vaccine.[68]

Polgreen et al. studied the duration of shedding of the mumps virus during an outbreak and found that the probability of mumps virus shedding decreased rapidly after the onset of symptoms.[69] However, they estimated that 8 percent to 15 percent of patients are still shedding the virus five days after the onset of symptoms and, thus, may still be contagious during this period. They concluded that their statistical model and the absence of positive culture results >9 days after the onset of symptoms may support excluding healthcare personnel from work for up to 9 days after the onset of symptoms, although current recommendations are to exclude infected healthcare personnel for 5 days after onset of parotitis.[8]

Most adults are immune to mumps, and approximately 90 percent of adults who have no history of mumps have antibody to the virus.[5] Thus, only a small proportion of healthcare personnel will be susceptible to mumps. For example, Nichol and Olson found that only 6.7 percent of the medical students they studied were nonimmune.[70] Consequently, it might be cost-beneficial to assess antibody titers of exposed persons who have no history of mumps and who have not received the mumps vaccine. Only those who are seronegative would be excluded from patient care during the incubation period (day 12 from first unprotected exposure through 25 after last day of unprotected exposure). Table 25.1 provides information necessary to evaluate an exposure to a person with mumps. Nonimmune patients who have been exposed to mumps should be placed on droplet precautions between

days 12 and 25 after their exposure.[12] Nonimmune family members and friends who have been exposed to a person with mumps should not come to the hospital during the incubation period.

Parvovirus B19

Erythema infectiosum, or fifth disease, is a common manifestation of acute parvovirus B19 infection. Fifth disease acquired its name because common childhood exanthems were numbered in the late 19th century. The first three illnesses were scarlet fever, rubeola, and rubella, and the fourth was a variation of scarlet fever known as Filatov-Dukes Disease. Erythema infectiosum was the fifth disease, and roseola infantum was the sixth. Erythema infectiosum is characterized by mild systemic symptoms (fever in 15 percent to 30 percent), followed in 1 to 4 days by an erythematous rash on the cheeks, the "slapped cheek" appearance. Subsequently, an asymmetric macular or maculopapular, lace-like erythematous rash can involve the trunk and extremities.

Parvovirus B19 has a predilection for infecting rapidly dividing cells, especially rapidly dividing red blood cells. Thus, persons with sickle cell disease, hereditary spherocytosis, pyruvate kinase deficiency, and other hemolytic anemias can develop transient hemolytic crises when infected. Parvovirus B19 can cause severe chronic anemia associated with red cell aplasia in persons who are on maintenance chemotherapy for acute lymphocytic leukemia, who have congenital immunodeficiencies, or who have acquired immunodeficiency syndrome. Parvovirus B19 also can cause hydrops fetalis. However, most parvovirus B19 infections during pregnancy do not affect the fetus adversely. Several studies indicate that the risk of fetal death is less than 10 percent in infected fetuses.[5,71]

Parvovirus B19 DNA has been found in the respiratory secretions of viremic patients, but most persons are no longer viremic when the rash appears. In general, healthcare personnel with parvovirus B19 infection do not need to be removed from patient care because they are usually not diagnosed until after the rash appears. Some hospitals might choose to restrict healthcare personnel from caring for patients at high risk of complications until the individual's symptoms have resolved. Persons with transient hemolytic crises and babies with hydrops fetalis can remain viremic for prolonged periods. These patients can be the source of infection for susceptible patients or healthcare personnel and thus should be placed on droplet precautions while they are hospitalized to prevent spread of parvovirus B19.[12] Lui et al. documented healthcare-associated patient-to-patient transmission of this virus from a renal transplant patient who apparently transmitted the virus many weeks after the onset of symptoms.[72]

Transmission of parvovirus B19 is common in the community.[73] Outbreaks have occurred in day-care centers and in elementary and junior high schools. Secondary spread to susceptible household contacts also is frequent. Documented transmission within hospitals has been uncommon.[74–79] However, when transmission occurs, a high proportion (13 percent to 50 percent) of susceptible persons may be infected.[75–77,80] Transmission of parvovirus B19 usually requires prolonged, frequent, close contact. Adler and colleagues investigated the rate of seroconversion to parvovirus B19 among persons employed either in schools or hospitals during an endemic period.[81] The investigators found that the risk of seroconversion for persons who had daily contact with school-aged children at home (ages 5–11 years) or at work (ages 5–18 years) was five times higher than that for other study participants. The overall rate of seroconversion was 5.2 percent for primary-school employees, 2.4 percent for other school employees, and 0–0.5 percent for hospital employees.

In general, routine infection prevention precautions should minimize healthcare-associated transmission of this virus.[77] A study by Cartter et al. of risk factors for parvovirus B19 infection in pregnant women demonstrated that the rate of infection was highest among nurses who cared for patients before they were isolated.[82] These results suggest that isolation precautions can prevent healthcare-associated spread of this virus from infected patients. Ray et al. obtained serology for parvovirus B19 infection from 32 nonimmune healthcare personnel who cared for two patients with transient aplastic crisis before they were put in isolation and from 37 nonimmune healthcare personnel who were not exposed.[76] The incidence of serologic evidence of recent parvovirus B19 infection was 3.1 percent among the exposed healthcare personnel and 8.1 percent among the healthcare personnel in the comparison group ($p = 0.06$). On the basis of their data, Ray et al. concluded that the risk of healthcare-associated transmission was low even when isolation precautions are not implemented.

Table 25.1 provides information about how infection prevention personnel could evaluate an exposure to parvovirus B19. In addition, the article by Crowcroft and colleagues reviews relevant literature and provides recommendations for protecting "at-risk seronegative healthcare personnel" and "at-risk patients."[79]

Hepatitis A Virus

Hepatitis A is transmitted primarily by the fecal-oral route, but transfusion-transmitted hepatitis A infection has also been reported. Infected persons excrete the highest concentration of virus in their stools during the 2 weeks before their symptoms begin. Most persons are no longer shedding the virus 1 week after they become jaundiced. However, infants can shed the virus in their stools for months.

Healthcare-associated transmission of hepatitis A is relatively uncommon. Most healthcare-associated outbreaks have occurred after an infant or a young child has received blood from a viremic but asymptomatic donor. The child often has an asymptomatic infection.[83–89] Healthcare-associated outbreaks have occurred when healthcare personnel cared for an older child or an adult who had vomiting, diarrhea, or fecal incontinence.[90–100]

Healthcare personnel who are exposed to the stool of infected patients are at greatest risk for acquiring hepatitis A infection. Occasionally, patients, visitors, and healthcare personnel could be at risk of acquiring hepatitis A if they eat uncooked food prepared by a food handler who is shedding the

virus. Several food-related healthcare-associated epidemics have been reported.[101,102]

To prevent healthcare-associated transmission of hepatitis A virus, healthcare personnel should follow standard precautions (i.e., wear gowns and gloves whenever they might contaminate their hands or clothes with a patient's stool). Healthcare personnel must perform hand hygiene after doing any patient-care activities and after removing their gloves. Adult patients with hepatitis A who are continent do not require private rooms, but diapered or incontinent persons should be placed in private rooms.[12] Healthcare personnel who cared for patients with hepatitis A do not need to be restricted from work unless they develop hepatitis. The risk of acquiring hepatitis from a patient is very low, and the risk of transmission from infected healthcare personnel to patients also is low. Healthcare personnel with hepatitis A infection should not work during the first 7 days of their symptomatic illnesses. Table 25.1 provides information infection prevention personnel need when evaluating an exposure to hepatitis A.

The Guideline for Infection Control in Health Care Personnel, 1998 states that "immunoglobulin given within two weeks of exposure is greater than 85 percent effective in preventing hepatitis A virus infection and may be advisable in some outbreaks."[7] The usual dose of immune globulin is 0.02 mg/kg IM when given as postexposure prophylaxis. The hepatitis A vaccine has helped terminate outbreaks in the community, but its role in hospitals has not been determined. Healthcare personnel are not considered at increased risk for hepatitis A virus infection from occupational exposure.[8]

Influenza Virus

Healthcare personnel tend to think that transmission of influenza virus occurs primarily in the community and not in the hospital. However, Evans et al. identified 17 reports of healthcare-associated influenza transmission that were published between 1959 and 1994.[103] In 5 of these outbreaks, healthcare personnel were implicated in transmitting the virus, and in 12 outbreaks healthcare personnel became infected with influenza virus. There have subsequently been many additional reports of healthcare-associated influenza outbreaks, including reports where healthcare personnel were clearly affected. The affected units included neonatal intensive care units, a pediatric unit, a solid organ transplant unit, an adult bone marrow transplant unit, a cancer unit, and an adult pulmonary unit. Thus, patients, visitors, and healthcare personnel can spread influenza virus in healthcare facilities.[103–119] In the outbreak described by Pachucki et al., 118 workers were affected, including 8 percent of the nurses and 3 percent to 6 percent of the doctors.[105] Everts described two outbreaks of influenza A affecting wards that treated and rehabilitated elderly patients.[119] The attack rate among patients was 48 percent on one ward and 58 percent on the other; 46 percent of the ill patients had lower respiratory tract involvement, and 7 percent died. The attack rate among staff was 69 percent on one ward and 36 percent on the other.

Healthcare-associated influenza probably goes unrecognized in many instances. Clinicians and infection prevention personnel should consider this diagnosis when healthcare personnel or hospitalized patients develop symptoms of influenza during the appropriate season. Table 25.1 describes how infection prevention personnel could manage healthcare personnel who were exposed to influenza. The role of postexposure prophylaxis with oseltamivir or zanamivir has not been defined for healthcare personnel who are exposed to influenza in acute care facilities.[120] Clinical judgment is an important factor in making decisions regarding postexposure prophylaxis. These decisions should take into account the exposed individual's risk for influenza complications and the type and duration of contact. Postexposure prophylaxis is not a substitute for influenza vaccination, and although it lowers the risk for influenza, it does not eliminate it.

Influenza increases absenteeism among healthcare personnel and increases the costs associated with sick leave. The Advisory Committee on Immunization Practices (ACIP) recommends that everyone 6 months and older receive influenza vaccine. Thus, all healthcare personnel should be vaccinated regardless of whether or not they have patient contact.[121] Healthcare facilities are expected by The Joint Commission to offer their all healthcare personnel influenza vaccine free of charge to protect healthcare personnel and to prevent spread of influenza within the healthcare facility.[8] In 2013, the FDA approved a vaccine produced using non-egg-based technology that may be considered for individuals 18 to 49 years old with severe egg allergy. Live attenuated influenza vaccines (LAIV), delivered intranasally, are not commonly used in healthcare facilities. Individuals can shed vaccine virus, but only one case of transmission, occurring in a daycare setting, has been documented. Although no healthcare personnel associated transmission events have been documented, it is recommended that persons vaccinated with LAIV should not have close contact with severely immunocompromised patients who require a protective environment for 7 days after receiving the vaccine. Many institutions use LAIV for non-clinical staff, when recommended, particularly in times of shortage of the injectable form of influenza vaccine, given the stated concerns regarding potential transmission to high risk patients. As of 2016, LAIV is not recommended due to concerns regarding efficacy, though LAIV may be reevaluated in the future.[122,123]

In spite of offering healthcare personnel influenza vaccination at no cost, acceptance remains low. There are many suggested ways to increase participation (e.g., roving vaccination teams, vaccine fairs, financial incentives, and pandemic preparedness drills),[124] but none have been consistently effective in improving acceptance of the vaccine. Thus, there is much discussion about requiring influenza vaccination for healthcare personnel as a condition of employment. Among the benefits of influenza vaccination are the reduction of influenza transmission in healthcare settings and decreases in staff illness and absenteeism.

Creutzfeldt-Jakob Agent

Creutzfeldt-Jakob agent, a prion, has been transmitted in the healthcare setting by brain-to-brain inoculation (e.g., through contaminated instruments) and by contaminated tissues or

tissue extracts. To date, there have been no documented instances of transmission to healthcare personnel, and the incidence of Creutzfeldt-Jakob disease (CJD) is not higher in healthcare personnel than it is in the general population.[127,128] A recent literature review of case reports of healthcare personnel with sporadic CJD from 1979 through 2011 found 66 cases (including 8 physicians).[129] The authors found a wide spectrum of healthcare personnel types and medical specialties represented; specific activities that might put an individual at risk were not documented in most cases.[129]

Criteria for defining exposures to the Creutzfeldt-Jakob agent have not been developed. The World Health Organization (WHO) categorizes the following tissues as having high infectivity: brain, spinal cord, pituitary gland, dura mater and eye (retina, optic nerve).[130] WHO categorizes the following tissues or fluids as having low infectivity: cerebrospinal fluid, peripheral nerves, kidney, liver, lung, lymph nodes, spleen, placenta, and blood (for variant CJD).[131] WHO categorizes the following tissues or fluids as having no detectable infectivity: bone, gingival tissue, heart muscle, intestine, prostate, skeletal muscle, testis, thyroid gland, tears, nasal mucous, saliva, sweat, serous exudates, milk, semen, urine, and feces.[129,131] See the WHO reference[131] for the full list of high, low and no detected infectivity tissues, body fluids, secretions and excretions.

The highest-risk injuries involve high-risk tissues and needlestick injuries with inoculation. Exposures via mucous membranes have the "theoretical risk" of transmitting the CJD prion. WHO recommends the following procedures if an exposure occurs:

- Wash exposed unbroken skin with detergent and abundant quantities of warm water (avoid scrubbing). Then rinse and dry the affected area. Brief (1 minute) exposure to 0.1 N NaOH or a 1:10 bleach solution can be used for maximum safety.
- After a needlestick or laceration, gently encourage bleeding, wash (avoid scrubbing) as described above, rinse, dry, cover with a dressing.
- After splashing an eye or mouth, irrigate the affected area with saline (eye) or water (mouth).
- Report any exposures to the appropriate department.[132]

If an exposure occurs, infection prevention personnel should create a list of all exposed staff, which should be saved indefinitely in case anyone develops the disease. Staff from hospital epidemiology and the occupational health service should counsel exposed healthcare personnel. In addition, infection prevention staff should work with staff from the operating suite and central sterile supply to ensure that, if possible, the reusable surgical instruments used on the index case are recalled and reprocessed properly and that all contaminated equipment in other departments (e.g., Pathology) is properly cleaned and disinfected.

The best exposure management for Creutzfeldt-Jakob agent is to prevent exposures from occurring. Therefore, infection prevention staff should work with persons from the operating suite, the neurosurgery department, the ophthalmology department, the pathology department, the laboratory, central sterile supply, and the morgue to develop policies that prevent exposures. Precautions should be used for all persons who undergo invasive procedures or ophthalmologic exams and who are known to have Creutzfeldt-Jakob disease or a progressive dementia or who have a family history of prion disease, Creutzfeldt-Jakob disease, fatal familial insomnia, or Gerstmann-Sträussler-Scheinker disease.[121,130,133] Precautions also should be used for patients who have received gonadotropin or human growth hormone extracted from cadaveric pituitary glands.[133]

Infection prevention personnel who are developing policies should review recommendations written by Steelman and HICPAC.[133–135] These documents recommend methods for protecting healthcare personnel from exposure to potentially infectious tissues, limiting contamination of equipment and the environment, and effectively eradicating prions from surgical equipment. The guidelines on the care of surgical equipment are extremely important because the Creutzfeldt-Jakob agent is not inactivated/killed by routine chemical and physical means of sterilization, including routine steam sterilization, ethylene oxide sterilization, and dry heat sterilization; processes using peracetic acid, hydrogen peroxide, ultraviolet light, radiation, freezing, drying, or hot bead glass; and any level of cleaning and disinfection with glutaraldehyde, dry heat radiation, detergents, or formaldehyde. Of note, some of the recommendations differ between the documents developed by Steelman and HICPAC.

Variant CJD (vCJD) has become an important issue in the United Kingdom and Europe.[133,134,136,137] vCJD is thought to be transmitted from beef infected with the agent of bovine spongiform encephalopathy (BSE). The United States has not identified BSE as a problem, and thus, many people in this country are not concerned about vCJD. However, given the ease with which people travel, the presence of chronic wasting disease (another spongiform encephalopathy) in cervids in the United States, and the lax regulation of the rendering industry, infection prevention personnel should not ignore vCJD.

Unlike the CJD prion, the vCJD prion infects the lymphoreticular tissues. Thus, a tonsillar biopsy is the preferred diagnostic test, and a wider variety of tissues may be able to transmit this agent. The Department of Health in the United Kingdom has mandated that decontamination facilities be upgraded and that all adenotonsillectomy procedures must be performed using disposable instruments.[137] In addition, decontamination and sterilization of equipment is different for vCJD than for CJD.[138,139] Given that lymphoreticular tissue is affected and that infected persons may not show symptoms or signs of the disease for years, many hospitals in Europe have changed their general decontamination and sterilization such that vCJD will be inactivated/killed.

Bacterial Diseases

Mycobacterium tuberculosis

Mycobacterium tuberculosis is an acid-fast bacillus that is spread through the air. This organism causes a primary infection, which in normal hosts usually is not manifested as clinical disease, and a recrudescent pulmonary or

disseminated disease. Persons who are infected with *M. tuberculosis* typically have positive tuberculin skin tests or blood interferon gamma release assays but are not necessarily contagious. Those who have active pulmonary disease are infectious and are the persons who cause most healthcare-associated exposures. On occasion, patients who have active infections at other sites also can cause exposures. For example, a patient with a large soft-tissue abscess underwent incision, drainage, and irrigation in an operating suite.[140] Because he continued to have copious drainage, the wound was cleaned with a pressurized irrigation system. Subsequently, 59 employees were identified who converted their tuberculin skin tests, and 9 persons acquired active tuberculosis (5 employees, 2 patients, and 2 family members of the index patient). Matlow et al. reported that 111 healthcare personnel were exposed to tuberculosis while caring for an infant with peritoneal tuberculosis.[141] Two (5 percent) of the primary-care nurses but no doctors or housekeepers had skin test conversions.

Persons are considered exposed to *M. tuberculosis* if they shared air space with a patient who had active pulmonary tuberculosis or who had an extrapulmonary site of infection from which *M. tuberculosis* was aerosolized and healthcare personnel were not wearing an N95 or better respirator. During outbreaks a large proportion (3.6 percent to 100 percent) of exposed persons may become tuberculin skin test positive.[140,142–144] In general, approximately 30 percent of persons will become infected when they are exposed to a patient whose sputum contains acid-fast bacilli, whereas only 10 percent of persons will become infected when they are exposed to an infected patient whose sputum does not contain visible acid-fast bacilli.[145]

As with the other airborne infections – measles and chicken pox – it is best to prevent exposures by screening patients in clinics and on admission for symptoms and signs of tuberculosis. However, screening can be difficult because some patients present with atypical signs or symptoms, and others do not answer truthfully to screening questions designed to identify patients who might have tuberculosis so that they can be isolated before they expose persons in the healthcare setting. Moreover, some patients present with tuberculosis at unusual sites, and immunocompromised patients can have atypical signs and symptoms.

Healthcare personnel continue to acquire *M. tuberculosis* through occupational exposures.[146–156] In countries where tuberculosis is common, healthcare personnel may be at considerable risk of acquiring tuberculosis.[153–157] Persons who move from countries with high incidences of tuberculosis to countries with a low incidence can cause substantial exposures in healthcare facilities.[158] In addition, studies done in Canada indicate that delays in diagnosis, inadequate ventilation (<2 air exchanges per hour) in general patient rooms, the type of work (nursing, respiratory therapy, physical therapy, and housekeeping) and the duration of work all increase the risk of transmission.[147,159]

The goal of an exposure workup is to identify all patients, visitors, and healthcare personnel who were exposed so that those who become infected can be treated with antimycobacterial agents. Unfortunately, before being diagnosed, the infectious person may have visited many clinics and diagnostic laboratories or may have been hospitalized in a multipatient room. All persons who meet the criteria for exposure should have baseline tuberculin skin testing if they have not had a recent skin test (within 6 weeks in a high-prevalence area or 1 year in a low-prevalence area). Healthcare personnel should be evaluated by the occupational health service. Exposed patients and visitors should be notified about the exposure and told to contact their own physicians or should be offered the opportunity to have their skin tests done at the medical facility where the exposure occurred. In addition, exposed patients' primary physicians should receive letters informing them of the exposure. Twelve weeks after the exposure, exposed persons should have another skin test. If that skin test is positive, they should be encouraged to take prophylaxis.[143] Interferon gamma release assays may be used as an alternative to tuberculin skin testing for both diagnosis of latent tuberculosis infection and in contact investigations following a potential tuberculosis exposure to identify new infections.[160] These tests offer a higher specificity compared to tuberculin skin testing and comparable sensitivity. Additionally, these tests only require one visit and are less subject to variability in test performance and interpretation.

Neisseria meningitidis

Neisseria meningitidis is a Gram-negative diplococcus that causes meningitis and septicemia. Household contacts of persons with invasive meningococcal disease are at 500 to 800 times greater risk of acquiring meningococcal infection than are members of the general public.[161] Other semiclosed or closed populations, such as persons living in college dormitories, chronic-care hospitals, nursery schools, and military barracks, also are at high risk of infection.[162] Despite caring for patients with meningococcal infection, healthcare personnel are not at higher risk than members of the general population for acquiring this infection.[13]

N. meningitidis is transmitted by respiratory droplets. Thus, patients with suspected or confirmed meningococcal infection should be placed on droplet precautions for the first 24 hours of treatment.[12] Healthcare-associated transmission of *N. meningitidis*, which has occurred rarely, may be more likely to occur from patients who have meningococcal pneumonia than from patients with meningitis or septicemia.[163,164] Persons are considered exposed to *N. meningitidis* if they did not wear a mask and had either prolonged close contact with a person who had meningococcal disease or had contact with the patient's respiratory secretions. Exposed persons should begin prophylactic treatment within 24 hours of their exposure.[5] Thus, immediately upon identifying a patient with meningococcal disease, infection prevention personnel must determine whether any healthcare personnel meet the criteria for exposure. Healthcare personnel who meet criteria for exposure must be sent to the occupational health service at once to receive a prescription for an appropriate antimicrobial agent.

Despite the very low risk of transmission, healthcare personnel often are very anxious when they learn that a patient with meningococcal disease has been admitted to their unit. Healthcare personnel who do not meet the criteria for exposure frequently demand prescriptions for prophylactic antimicrobial agents. If infection prevention personnel refuse to oblige them, these healthcare personnel often have other physicians write prescriptions for them. However, prophylactic treatment is not without complications (e.g., allergic reactions, side effects of the medications, *C. difficile* colitis), and its use should be discouraged when the criteria for exposure are not met.

Bordetella Pertussis

The whole-cell pertussis vaccines dramatically altered the epidemiology of pertussis. Before the vaccines were introduced, most adults were immune to pertussis because they had the disease during childhood, and their immunity was probably boosted by frequent exposures to infected persons. However, most adults are now susceptible to pertussis because vaccine-induced immunity disappears within 12 years after the last vaccination.[165] Consequently, the incidence of pertussis in adults is now increasing,[166–170] and adolescents and adults have become the primary source of infection for susceptible young children.[169] In the United States the proportion of persons with pertussis who are over 10 years of age increased from 7.2 percent during 1992–1994 to over 50 percent during 1997–2000.[171]

Pertussis may be transmitted in the hospital by patients, visitors, and healthcare personnel.[172–181] Recently, a cross-sectional study at a large quaternary care pediatric hospital from 2002 to 2011 revealed the frequency of healthcare personnel exposure to pertussis.[182] In this study, 1,193 healthcare personnel were exposed to pertussis from 219 confirmed case patients. Outbreaks also have occurred in other healthcare settings, including homes for disabled persons[183–185] and a nursing home.[170] During the outbreak in the nursing home, 11 (10 percent) of 107 residents and 17 (14 percent) of 116 employees developed clinical or laboratory-confirmed pertussis infection.[170] The mean age of persons with clinical infection was 75 years for residents and 34 years for employees. Wright et al. reported the results of a study in which they followed 106 resident physicians and 39 emergency room physicians over time to see if their antibody levels to pertussis toxin and filamentous hemagglutinin increased 50 percent (diagnostic of pertussis infection) over a 1 to 3 year follow-up period.[181] Two residents (1.3 percent; 95%, CI 0 percent–3.5 percent) and 3 emergency medicine physicians (3.6 percent; 95% CI 0 percent to 9.6 percent) had serologic evidence of recent pertussis infection. Only 2 of these 5 physicians had symptomatic illnesses.

Most adults with pertussis have persistent and sometimes severe cough. These adults frequently are diagnosed as having bronchitis. Thus, many exposures are not identified. Several studies indicate that erythromycin treatment early in the course of illness decreases the frequency of secondary spread.[184–186] However, physicians rarely see adult patients early in their illness.

Several communities have experienced outbreaks of pertussis in the past five years.[185,187–191] Patients involved in these outbreaks have caused exposures when they were evaluated in clinics or were admitted to a hospital. ACIP recommends a one-time dose of the tetanus-diptheria-acelluar pertussis (Tdap) vaccine, a generally well tolerated vaccine, to boost the immunity of healthcare personnel.[192,193] Table 25.1 illustrates how infection prevention personnel could evaluate an exposure to a person with pertussis.[5,194]

Previously published guidelines have supported the administration of antimicrobial postexposure prophylaxis (PEP) or close symptom monitoring for 21 days postexposure with prompt treatment and work exclusion if symptoms develop.[192] Decisions regarding the administration of PEP should take into consideration the type and intensity of exposure, the potential consequences of infection and the risk of secondary exposure as well as the ability to monitor exposed healthcare personnel. A recently published randomized control trial found that among vaccinated healthcare personnel exposed to pertussis, those who received antimicrobial PEP were at decreased risk of new infection.[195] However, this study was small, and newly infected patients did not display clinical evidence of infection and were unlikely to be implicated in secondary transmission. A macrolide such as azithromycin can be administered as PEP in healthcare personnel identified as close contacts to patients with pertussis provided there are no contraindications.[196]

Group A *Streptococcus*

Although not typically considered a disease warranting postexposure intervention, there have been reports of outbreaks affecting healthcare personnel.[197–199] These outbreaks demonstrate that group A *Streptococcus* can spread quickly to both patients and healthcare personnel. Given that group A *Streptococcus* is on occasion transmitted to healthcare personnel, prophylaxis may be appropriate under some circumstances. Healthcare personnel who are epidemiologically linked to an outbreak of group A *Streptococcus* should be tested for colonization. Colonized healthcare personnel should be suspended from work responsibilities for 24 hours after receiving chemoprophylaxis.[200] If healthcare personnel are colonized with the same strain as the index patient, repeat testing for colonization is recommended 7–10 days after completing chemoprophylaxis.

Ectoparasites

Infection prevention personnel also must investigate exposures to ectoparasites such as lice and scabies.[201] Healthcare personnel often react more irrationally to these exposures than they do to exposures involving infectious agents and expect prophylactic treatment when it is not necessary.

Lice

Pediculus humanus capitis, Pediculus humanus corporis, and *Phthirus pubis* are found not infrequently on patients admitted to healthcare facilities. These ectoparasites are transmitted by direct contact with infested persons or their clothing. Persons infested with lice should be placed on contact precautions until

they have been treated.[12,202] All clothing, bedding, hats, and other personal-care items should be washed in hot water and dried on the hot cycle because lice and their eggs cannot survive temperatures above 53.5°C.[9] Clothes that cannot be washed should be dry cleaned or placed in a plastic bag for 2 weeks.[9] Brushes and combs should be soaked in a pediculicide shampoo.[5] Healthcare personnel who have had direct contact with the patient's head (head lice) or clothes (body lice) should be evaluated by the occupational health service. Because the risk of acquiring lice in a healthcare facility is very low, only staff who become infested should be treated with a pediculicide.

Scabies

In contrast to lice, *Sarcoptes scabiei* can be transmitted easily within healthcare facilities, especially if the index case has crusted (Norwegian) scabies.[203–218] Of note, several outbreaks have occurred because patients with human immunodeficiency syndrome and unrecognized Norwegian (crusted or keratotic) scabies were admitted without the necessary precautions.[207,208,212,215,217]

Exposures to scabies can be quite expensive. For example, an outbreak of scabies occurred in an extended-care unit that was attached to an acute care hospital. To terminate the outbreak, 78 residents and over 100 staff and family members were treated at a cost of more than $20,000.[209] Scabies spread within the unit, in part because the protocol for control of this ectoparasite was inadequate. The policy was based on the assumption that staff had previous experience with scabies exposures and would know what to do. The outbreak described by Obasanjo et al. was enormous (773 healthcare personnel and 204 patients were exposed) and was not terminated until precautions beyond those recommended by CDC were implemented.[213] These precautions included: 1) early identification of infested patients; 2) prophylactic topical treatment of all exposed healthcare personnel; 3) two treatments for patients with Norwegian scabies; 4) barrier isolation precautions until 24 hours after the second treatment; and 5) oral ivermectin treatment for patients who failed conventional therapy. Van Vliet et al. identified six reasons for spread of scabies in healthcare facilities: 1) many patients who have scabies are at risk of developing Norwegian scabies; 2) many people have contact with these patients; 3) diagnosis is often delayed; 4) the epidemiologic evaluation is often inadequate; 5) treatment failures occur; and 6) follow-up is often inadequate.[210]

Persons with scabies should be placed on contact precautions until they are treated.[12] Personnel who have cared for patients with Norwegian scabies or during outbreaks of scabies when transmission continues to occur should be evaluated in the occupational health clinic, and those who had contact with the patient's skin should be treated. In "routine" cases of scabies (i.e., noncrusted scabies and nonoutbreak situation), exposed healthcare personnel should be treated only if they acquire scabies. If two or more persons who live or work in a long-term care facility acquire scabies, all residents and healthcare personnel should be treated to prevent further spread. Persons receiving effective therapy may have pruritus for up to 2 weeks after therapy. Thus, infection prevention personnel should not interpret pruritus occurring during this time period as treatment failure.

The index patient's bedding and clothes that contacted the patient's skin should be washed in hot water and dried on the hot cycle.[9] Clothes that cannot be washed can be stored in a plastic bag for several days to a week because the mite cannot survive more than 3 to 4 days in the environment.

Emerging Pathogens

Just when it seems that we in hospital epidemiology have survived one crisis and are ready to restore some normalcy, a new disease emerges and upsets our fragile equilibrium. We anticipate that more organisms of epidemiologic import within healthcare facilities will emerge as the global population continues to grow and as world travel remains rapid and common. We chose to discuss four viral diseases in this category that infection prevention staff in the US have had to spend considerable time addressing in the past decade.

Smallpox

Smallpox (variola) is a serious, contagious, and sometimes fatal infectious disease. Although smallpox was declared globally eradicated in 1980, there is concern that smallpox virus may be used for bioterrorism. There is no specific treatment for smallpox disease, and the only prevention is vaccination. The smallpox vaccine, which was routinely administered to Americans until 1972, is highly effective in protecting against the disease when given before or shortly after exposure to the virus. Though protection by the live vaccinia virus vaccine is long lived and may prevent death from illness in those who were vaccinated over two decades ago, all children and most adults are now considered susceptible unless they were recently vaccinated.[219] Because of concerns that smallpox could be used as a bioweapon, a program of pre-event vaccination took place in many hospitals in early 2003.[219,220] This would allow for recently vaccinated personnel to care for smallpox patients (or patients with suspected smallpox) and to vaccinate other healthcare personnel.

If smallpox virus was released into the community, one would expect transmission to occur as an infected person's fever peaks and the skin rash starts. Persons with smallpox are occasionally contagious during the prodrome phase, but they become more contagious with the onset of the rash. Fever usually begins 10–14 days after the initial infection (range 7–19 days), and the rash typically occurs about 2–4 days later.[219] Infectious particles are released when oropharyngeal lesions are sloughed (approximately one week duration). Transmission via contact with material from the smallpox pustules or crusted scabs can also occur; however, scabs are much less infectious than respiratory secretions. Generally, direct and fairly prolonged face-to-face contact is required to spread smallpox virus from one person to another. Smallpox also can be spread through direct contact with infected bodily fluids or contaminated objects such as bedding or clothing.

Rarely, smallpox has been spread by the airborne route in enclosed settings such as buildings, buses, and trains.

Healthcare personnel would be considered exposed to smallpox if they had unprotected contact with an infected patient (no N95 respirator worn within 7 feet of patient and/or no gloves for contact with skin lesions). Follow-up would include monitoring healthcare personnel's temperature twice daily for 17 days following the last exposure date (including vaccination days). It is likely that healthcare personnel exposed to a case of smallpox would be quarantined and that infection prevention guidelines created by public health officials at the time would direct management of smallpox exposures. At present, infection prevention and public health recommend that healthcare personnel who have had the smallpox vaccine recently should not be restricted from patient care.[219]

Severe Acute Respiratory Syndrome (SARS)

Worldwide, numerous healthcare personnel and patients acquired severe acute respiratory syndrome (SARS) in healthcare facilities in 2003.[221] According to WHO statistics, 1,707 healthcare workers were infected with SARS, accounting for 21 percent of all cases.[222] In fact, healthcare facilities amplified transmission beyond that seen in the community. In general, transmission appears to have occurred after close contact with symptomatic individuals before infection prevention measures were implemented or if breaches in infection prevention practices occurred. Studies indicate that appropriate use of masks or respirators, gloves and gowns, and hand hygiene significantly decreased the risk of acquiring SARS while caring for patients with SARS.[223] However, some healthcare personnel did acquire SARS despite wearing appropriate personal protective equipment (gown, mask, goggles or face shield, and gloves) while helping intubate patients with SARS.[224]

The incubation period for SARS ranges from 2 to 10 days, but most patients develop symptoms around day 4 or 5.[225] To manage SARS exposures, infection prevention staff need mechanisms for monitoring healthcare personnel for fever and respiratory symptoms, managing asymptomatic exposed healthcare personnel, symptomatic exposed healthcare personnel, and symptomatic exposed visitors.[226] During the first SARS outbreak in 2003, CDC did not recommend work restrictions for asymptomatic exposed persons unless they had unprotected high-risk exposures. CDC did recommend that exposed healthcare personnel be monitored for respiratory symptoms and fever (i.e., check temperature twice daily) for 10 days following their last exposure. If fever or respiratory symptoms develop, healthcare personnel should notify their healthcare provider, restrict their movements outside their home, and reassess the situation in 72 hours. However, a number of hospitals took a more restrictive approach, such as placing healthcare personnel who had unprotected exposure to patients with SARS on leave for 10 days from the last date of exposure.

CDC recommended that healthcare personnel who have unprotected high-risk exposures should be excluded from duty for 10 days following the exposure. An unprotected high-risk exposure is defined as being present in the room when a probable or confirmed SARS patient underwent an aerosol-generating procedure without complying with the recommended infection prevention precautions. Symptomatic exposed healthcare personnel who develop either fever or respiratory symptoms within 10 days following exposure should be excluded from duty and should be evaluated in a manner that does not expose other persons to the SARS virus. If symptoms improve or resolve in 72 hours after onset of symptoms, the person may be allowed to return to duty after consultation with infection prevention, occupational health, and local public health staff. For persons who progress to meet the case definition of SARS, infection prevention precautions should be continued until 10 days after fever and respiratory symptoms have resolved.

To prevent exposures within healthcare facilities, infection prevention staff should consider designing a process for screening healthcare personnel who have traveled to areas where the SARS virus is being transmitted. In addition, symptomatic exposed visitors should not be allowed to visit their family member or friend but should be evaluated to determine whether they may have SARS. Thus, infection prevention personnel must design a way to identify visitors who might have been exposed and to screen them for symptoms and signs of SARS. To prevent transmission within the homes of exposed healthcare personnel, infection prevention personnel should counsel exposed persons to avoid contact with members of their household (i.e., avoid physical contact, stay in a separate part of the house, avoid eating together, and use separate bathrooms) or to find alternative living arrangements for household members during the 10 days following exposure.

Many of the lessons learned from the 2003 SARS experience, including the use of respiratory hygiene/cough etiquette, are being applied to pandemic influenza planning and were use in managing the 2009 novel influenza (H1N1) pandemic.

Middle East Respiratory Syndrome Coronavirus

First reported in 2012, Middle East Respiratory Syndrome (MERS) is a potentially fatal disease caused by MERS coronavirus (MERS-CoV).[227] Initially identified in Saudi Arabia, epidemiological data has identified spread to over 30 countries, including the United States. Symptomatic patients develop an initial period of fevers, chills, cough and myalgias which can progress to pneumonia, and in severe cases, respiratory failure and circulatory shock. The incubation period ranges from 5–14 days,[228] though a large percentage of individuals are believed to have asymptomatic infection and may be potential reservoirs for spreading the virus.

In the healthcare setting, preventing transmission of MERS-CoV requires rapid identification of potential cases, initiation of engineering and administrative controls, and the use of personal protective equipment among healthcare personnel who may have contact with infected patients. Recommended personal protective equipment that should be used in the care of patients with MERS includes gown, gloves, eye protection and a respirator, and care for these patients should be in an airborne infection isolation room (similar precautions as used for SARS). The CDC has issued interim

guidance for the monitoring and management of exposed healthcare personnel.[229] Healthcare personnel who care for patients with MERS-CoV should be closely monitored for any symptoms for a period of 14 days after exposure, regardless of their use of personal protective equipment. During this time period, asymptomatic healthcare providers who have an unprotected exposure should be excluded from work responsibilities. Should symptoms develop during this 14 day period, healthcare personnel, even those who had been using appropriate personal protective equipment, should be excluded from any work responsibilities.

Ebola virus disease

In 2013 an epidemic of Ebola virus disease began in Western Africa which resulted in over 10,000 deaths, including a large number of healthcare personnel. The virus is predominantly transmitted from person to person through direct contact with blood and body fluids of infected individuals, though contact with contaminated surfaces and objects is another important means of transmission. As with the other infections described in this chapter, early detection of infected patients and the initiation of appropriate infection prevention strategies are critical to preventing transmission within the healthcare setting. Symptoms of Ebola virus disease typically begin within 6–12 days of exposure but may occur up to 21 days after exposure.[230]

The CDC has issued guidance for the evaluation and management of healthcare personnel who are exposed to patients with Ebola virus infection.[231] Healthcare personnel who provide care for infected patients using appropriate personal protective equipment without breaches should be actively monitored (i.e., fever and symptom monitoring), and if they remain asymptomatic, they may continue with their routine responsibilities. Individuals caring for a patient at a facility in which a healthcare-associated Ebola transmission occurred or those involved in a situation where a breach of infection prevention procedures has occurred should be restricted from patient care for 21 days after the unprotected exposure. Additionally, any healthcare personnel who develop fever or other symptoms suggestive of Ebola infection following any Ebola exposure should be restricted from work responsibilities.

Conclusion

Exposure workups are an important responsibility for infection prevention personnel. If they evaluate exposures promptly and effectively, infection prevention staff can prevent transmission of infectious agents or ectoparasites to healthcare personnel, patients, and visitors. Exposure workups consume resources, such as time and money, which could be used for other infection prevention activities. In addition, many exposures could be averted if healthcare personnel are immune to vaccine-preventable infections, if staff use isolation precautions and personal protective equipment appropriately and consistently, and if healthcare personnel do not come to work when they have communicable illnesses. Thus, wise infection prevention staff learn from their own experience and develop policies and procedures to limit the number of exposures in their institutions.

References

1. Weltman AC, DiFerdinando GT. Jr, Washko R, Lipsky WM. A death associated with therapy for nosocomially acquired multidrug-resistant tuberculosis. *Chest*. 1996; **110**(1):279–281.
2. Weber DJ, Rutala WA, Parham C. Impact and costs of varicella prevention in a university hospital. *Am J Public Health*. 1988; **78**(1):19–23.
3. Faoagali, JL, Darcy, D. Chickenpox outbreak among the staff of a large, urban adult hospital: costs of monitoring and control. *Am J Infect Control*. 1995; **23** (4):247–250.
4. Christie CD, Glover AM, Willke MJ, et al. Containment of pertussis in the regional pediatric hospital during the Greater Cincinnati epidemic of 1993. *Infect Control Hosp Epidemiol*. 1995; **16** (10):556–563.
5. Committee on Infectious Diseases, A.A. o.P. *2015 Red Book: Report of the Committee on Infectious Diseases*. 30th ed. 2015, Elk Grove Village, Ill: American Academy of Pediatrics.
6. Heymann DL. *Control of Communicable Diseases Manual*. 19th ed. 2008. Washington, D.C.: American Public Health Association.
7. Bolyard EA, Tablan OC, Williams WW, et al. Guideline for infection control in healthcare personnel, 1998. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol*. 1998; **19**(6):407–63.
8. Advisory Committee on Immunization Practices, Centers for Disease Control, and Prevention. Immunization of healthcare personnel: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2011; **60**(RR-7):1–45.
9. Mandell GL, Bennett JE, Dolin R, eds. *Principles and Practice of Infectious Diseases*. 6th ed. New York, NY: Churchill Livingstone, 2010.
10. Valenti WM. Employee work restrictions for infection control. *Infect Control*. 1984; **5**(12):583–584.
11. Myers MG, Rasley DA, Hierholzer WJ. Hospital infection control for varicella zoster virus infection. *Pediatrics*. 1982; **70**(2):199–202.
12. Siegel JD, Rhinehart E, Jackson M, et al. 2007 Guideline for isolation precautions: preventing transmission of infectious agents in health care settings. *Am J Infect Control*. 2007; **35** (10 Suppl 2):S65–S164.
13. Sepkowitz KA. Occupationally acquired infections in health care workers. Part I. *Ann Intern Med*. 1996; **125**(10):826–834.
14. McKinney WP, Horowitz MM, Battiola RJ. Susceptibility of hospital-based health care personnel to varicella-zoster virus infections. *Am J Infect Control*. 1989; **17**(1):26–30.
15. Hayden GF, Meyers JD, Dixon RE. Nosocomial varicella. **Part II**: suggested guidelines for management. *West J Med*. 1979; **130**(4):300–303.
16. Galil K, Lee B, Strine T, et al. Outbreak of varicella at a day-care center despite vaccination. *N Engl J Med*. 2002; **347** (24):1909–1915.
17. Galil K, Fair E, Mountcastle N, et al. Younger age at vaccination may increase risk of varicella vaccine failure. *J Infect Dis*. 2002; **186**(1):102–105.
18. Saiman L, LaRussa, P, Steinberg SP, et al., Persistence of immunity to varicella-zoster virus after vaccination

of healthcare workers. *Infect Control Hosp Epidemiol*. 2001; **22**(5):279–283.

19. Wurtz R, Check IJ. Breakthrough varicella infection in a healthcare worker despite immunity after varicella vaccination. *Infect Control Hosp Epidemiol*. 1999; **20**(8):561–562.
20. Richard VS, John TJ, Kenneth J, et al. Should health care workers in the tropics be immunized against varicella? *J Hosp Infect*. 2001; **47**(3):243–245.
21. Weinstock DM, Rogers M, Eagan J, et al. Seroconversion rates in healthcare workers using a latex agglutination assay after varicella virus vaccination. *Infect Control Hosp Epidemiol*. 1999; **20**(7):504–507.
22. Nettleman MD, Schmid M. Controlling varicella in the healthcare setting: the cost effectiveness of using varicella vaccine in healthcare workers. *Infect Control Hosp Epidemiol*. 1997; **18**(7):504–508.
23. Tennenberg AM, Brassard JE, Van Lieu J, et al. Varicella vaccination for healthcare workers at a university hospital: an analysis of costs and benefits. *Infect Control Hosp Epidemiol*. 1997; **18**(6):405–411.
24. Baracco GJ, Eisert S, Saavedra S, et al. Clinical and economic impact of various strategies for varicella immunity screening and vaccination of health care personnel. *Am J Infect Control*. 2015; **43**(10):1053–1060.
25. Weitekamp Schan MR, Aber RC. An algorithm for the control of nosocomial varicella-zoster virus infection. *Am J Infect Control*. 1985; **13**(5):193–198.
26. Bloch AB, Orenstein WA, Ewing WM, et al. Measles outbreak in a pediatric practice: airborne transmission in an office setting. *Pediatrics*. 1985; **75**(4):676–683.
27. Remington PL, Hall WN, Davis IH, et al. Airborne transmission of measles in a physician's office. *JAMA*. 1985; **253**(11):1574–1577.
28. Centers for Disease Control and Prevention. Update: measles – United States. January-July 2008. *MMWR Morb Mortal Wkly Rep*. 2008; **57**(33):893–896.
29. World Health Organization. Country profile for measles elimination: Philippines. WHO Western Pacific Region. October 26, 2015. Available at: www.wpro.who.int/immunization/documents/measles_country_profile_mar2015_phl.pdf?ua=1.
30. Zipprich J, Winter K, Hacker J, et al. Measles outbreak – California, December 2014-February 2015. *MMWR Morb Mortal Wkly Rep*. 2015; **64**(6):153–154.
31. Gohil SK, Okubo S, Klish S, et al. Healthcare workers and post-elimination era measles: lessons on acquisition and exposure prevention. *Clin Infect Dis.* 2015; 62(2):166-172.
32. Davis RM, Orenstein WA, Frank JA, et al. Transmission of measles in medical settings. 1980 through 1984. *JAMA*. 1986; **255**(10):1295–1298.
33. Istre GR, Mckee PA, West GR, et al. Measles spread in medical settings: an important focus of disease transmission? *Pediatrics*. 1987; **79**(3):356–358.
34. Papania M, Reef S, Jumaan A, Lingappa JR, Williams WW, Nosocomial measles, mumps, rubella, and other viral infections. In: *Hospital Epidemiology and Infection Control*, Mayhall G.G., ed. Philadelphia, PA: Lippincott, Williams & Wilkins: 2004, 829–849.
35. Edmonson MB, Addiss DG, McPherson JT, et al. Mild measles and secondary vaccine failure during a sustained outbreak in a highly vaccinated population. *JAMA*. 1990; **263**(18):2467–2671.
36. Atkinson WL, Markowitz LE, Adams NC, Seastrom GR. Transmission of measles in medical settings: United States. 1985–1989; *Am J Med*. 1991; **91**(3B):320S–324S.
37. Raad II, Sherertz RJ, Rains CS, et al. The importance of nosocomial transmission of measles in the propagation of a community outbreak. *Infect Control Hosp Epidemiol*. 1989; **10**(4):161–166.
38. Sienko DG, Friedman C, McGee HB, et al. A measles outbreak at university medical settings involving health care providers. *Am J Public Health*. 1987; **77**(9):1222–1224.
39. Rivera ME, Mason WH, Ross LA, Wright HT Jr. Nosocomial measles infection in a pediatric hospital during a community-wide epidemic. *J Pediatr*. 1991; **119**(2):183–186.
40. Rank EL, Brettman L, Katz-Pollack H, DeHertogh D, Neville D. Chronology of a hospital-wide measles outbreak: lessons learned and shared from an extraordinary week in late March 1989. *Am J Infect Control*. 1992; **20**(6):315–318.
41. Farizo KM, Stehr-Green PA, Simpson DM, Markowitz LE. Pediatric emergency room visits: a risk factor for acquiring measles. *Pediatrics*. 1991; **87**(1):74–79.
42. Weber DJ., Rutala WA, Orenstein WA. Prevention of mumps measles, and rubella among hospital personnel. *J Pediatr*. 1991; **119**(2):322–326.
43. Subbarao EK, Andrews-Mann L, Amin S, Greenberg J, Kumar ML. Postexposure prophylaxis for measles in a neonatal intensive care unit. *J Pediatr*. 1990; **117**(5):782–785.
44. Ammari LK, Bell IM, Hodinka RL. Secondary measles vaccine failure in healthcare workers exposed to infected patients. *Infect Control Hosp Epidemiol*. 1993; **14**(2):81–86.
45. Enguidanos R, Mascola L, Frederick P. A survey of hospital infection control policies and employee measles cases during Los Angeles County's measles epidemic, 1987 to 1989. *Am J Infect Control*. 1992; **20**(6):301–304.
46. Wright LJ, Carlquist JF. Measles immunity in employees of a multihospital healthcare provider. *Infect Control Hosp Epidemiol*. 1994; **15**(1):8–11.
47. de Swart RL, Wertheim-van Dillen PM, van Binnendijk RS, et al. Measles in a Dutch hospital introduced by an immuno-compromised infant from Indonesia infected with a new virus genotype. *Lancet*. 2000; **355**(9199):201–202.
48. Steingart KR, Thomas AR, Dykewicz CA, Redd SC. Transmission of measles virus in healthcare settings during a communitywide outbreak. *Infect Control Hosp Epidemiol*. 1999; **20**(2):115–119.
49. Marshall TM, Hlatswayo D, Schoub B. Nosocomial outbreaks –a potential threat to the elimination of measles? *J Infect Dis*. 2003; **187**(Suppl 1):S97–S101.
50. Kelly HA, Riddell MA, Andrews RM. Measles transmission in healthcare settings in Australia. *Med J Aust*. 2002; **176**(2):50–51.
51. Botelho-Nevers E, Gautret P, Biellik R, Brouqui P. Nosocomial transmission of measles: an updated review. *Vaccine*. 2012; **30**(27):3996–4001.
52. McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2013; **62**(RR-04):1–34.
53. Greaves WL, Orenstein WA, Stetler HC, et al. Prevention of rubella transmission in medical facilities. *JAMA*. 1982; **248**(7):861–864.

54. Polk BF, White JA, DeGirolami PC, Modlin JF. An outbreak of rubella among hospital personnel. *N Engl J Med*. 1980; **303**(10):541–545.
55. Centers for Disease Control and Prevention. Rubella in hospitals – California. *MMWR Morb Mortal Wkly Rep*. 1983; **32**(3):37–39.
56. Poland GA, Nichol KL. Medical students as sources of rubella and measles outbreaks. *Arch Intern Med*. 1990; **150**(1):44–46.
57. Storch GA, Gruber C, Benz B, Beaudoin J, Hayes J. A rubella outbreak among dental students: description of the outbreak and analysis of control measures. *Infect Control*. 1985; **6** (4):150–156.
58. Strassburg MA, Stephenson TG, Habel LA, Fannin SL. Rubella in hospital employees. *Infect Control*. 1984; **5** (3):123–126.
59. Fliegel PE, Weinstein WM. Rubella outbreak in a prenatal clinic: management and prevention. *Am J Infect Control*. 1982; **10**(1):29–33.
60. Strassburg MA, Imagawa DT, Fannin SL, et al. Rubella outbreak among hospital employees. *Obstet Gynecol*. 1981; **57**(3):283–288.
61. Gladstone JL, Millian SJ. Rubella exposure in an obstetric clinic. *Obstet Gynecol*. 1981; **57**(2):182–186.
62. Reef SE, Frey TK, Theall K, et al. The changing epidemiology of rubella in the 1990s: on the verge of elimination and new challenges for control and prevention. *JAMA*. 2002; **287**(4):464–472.
63. Centers for Disease Control and Prevention. Control and prevention of rubella: evaluation and management of suspected outbreaks, rubella in pregnant women, and surveillance for congenital rubella syndrome. *MMWR Recomm Rep*. 2001; **50**(RR-12):1–23.
64. Centers for Disease Control and Prevention, Three cases of congenital rubella syndrome in the postelimination era – Maryland, Alabama, and Illinois, 2012. *MMWR Morb Mortal Wkly Rep*. 2013; **62** (12):226–229.
65. Borras E, Campins M, Esteve M, et al. Are healthcare workers immune to rubella? *Hum Vaccin Immunother*. 2014; **10**(3):686–691.
66. Centers for Disease Control and Prevention. Mumps epidemic – Iowa, 2006. *MMWR Morb Mortal Wkly Rep*. 2006; **55** (13):366–368.
67. Dayan GH, Quinlisk MP, Paker AA, et al. Recent resurgence of mumps in the United States. *N Engl J Med*. 2008; **358** (15):1580–1589.
68. Centers for Disease Control and Prevention. Mumps outbreak on a university campus – California, 2011. *MMWR Morb Mortal Wkly Rep*. 2012; **61**(48):986–989.
69. Polgreen PM, Bohnett LC, Cavanaugh JE, et al. The duration of mumps virus shedding after the onset of symptoms. *Clin Infect Dis*. 2008; **46**(9):1447–1449.
70. Nichol KL, Olson R. Medical students' exposure and immunity to vaccine-preventable diseases. *Arch Intern Med*. 1993; **153**(16):1913–1916.
71. Watt AP, Brown M, Pathiraja M, Anbazhagan A, Coyle PV. The lack of routine surveillance of parvovirus B19 infection in pregnancy prevents an accurate understanding of this regular cause of fetal loss and the risks posed by occupational exposure. *J Med Microbiol*. 2013; **62**(Pt 1):86–92.
72. Lui SL, Luk WK, Cheung CY, et al. Nosocomial outbreak of parvovirus B19 infection in a renal transplant unit. *Transplantation*. 2001; **71**(1):59–64.
73. Dowell SF, Torok TJ, Thorp JA, et al. Parvovirus B19 infection in hospital workers: community or hospital acquisition? *J Infect Dis*. 1995; **172** (4):1076–1079.
74. Bell LM, Naides SJ, Stoffman P, Hodinka RL, Plotkin SA. Human parvovirus B19 infection among hospital staff members after contact with infected patients. *N Engl J Med*. 1989; **321**(8):485–491.
75. Seng C, Watkins P, Morse D, et al. Parvovirus B19 outbreak on an adult ward. *Epidemiol Infect*. 1994; **113** (2):345–353.
76. Ray SM, Erdman DD, Berschling JD, et al. Nosocomial exposure to parvovirus B19: low risk of transmission to healthcare workers. *Infect Control Hosp Epidemiol*. 1997; **18**(2):109–114.
77. Shishiba T, Matsunaga Y. An outbreak of erythema infectiosum among hospital staff members including a patient with pleural fluid and pericardial effusion. *J Am Acad Dermatol*. 1993; **29**(2 Pt 1):265–267.
78. Miyamoto K, Ogami M, Takahashi Y, et al. Outbreak of human parvovirus B19 in hospital workers. *J Hosp Infect*. 2000; **45**(3):238–241.
79. Crowcroft NS, Roth CE, Cohen BJ, Miller E. Guidance for control of parvovirus B19 infection in healthcare settings and the community. *J Public Health Med*. 1999; **21**(4):439–446.
80. Lohiya GS, Stewart K, Perot K, Widman R. Parvovirus B19 outbreak in a developmental center. *Am J Infect Control*. 1995; **23**(6):373–376.
81. Adler SP, Manganello AM, Koch WC, Hempfling SH, Best AM. Risk of human parvovirus B19 infections among school and hospital employees during endemic periods. *J Infect Dis*. 1993; **168**(2):361–368.
82. Cartter ML, Farley TA, Rosengren S, et al. Occupational risk factors for infection with parvovirus B19 among pregnant women. *J Infect Dis*. 1991; **163** (2):282–285.
83. Noble RC, Kane MA, Reeves SA, Roeckel I. Posttransfusion hepatitis A in a neonatal intensive care unit. *JAMA*. 1984; **252**(19):2711–2715.
84. Azimi PH, Roberto RR, Guralnik J, et al. Transfusion-acquired hepatitis A in a premature infant with secondary nosocomial spread in an intensive care nursery. *Am J Dis Child*. 1986; **140** (1):23–27.
85. Giacoia GP, Kasprisin DO. Transfusion-acquired hepatitis A. *South Med J*. 1989; **82**(11):1357–1360.
86. Seeberg S, Brandberg A, Hermodsson S, Larsson P, Lundgren S. Hospital outbreak of hepatitis A secondary to blood exchange in a baby. *Lancet*. 1981; **1**(8230):1155–1156.
87. Klein BS, Michaels JA, Rytel MW, Berg KG, Davis JP. Nosocomial hepatitis A. A multinursery outbreak in Wisconsin. *JAMA*. 1984; **252**(19):2716–2721.
88. Rosenblum LS, Villarino ME, Nainan OV, et al. Hepatitis A outbreak in a neonatal intensive care unit: risk factors for transmission and evidence of prolonged viral excretion among preterm infants. *J Infect Dis*. 1991; **164** (3):476–482.
89. Burkholder B., Coronado VG, Brown J, et al. Nosocomial transmission of hepatitis A in a pediatric hospital traced to an anti-hepatitis A virus-negative patient with immunodeficiency. *Pediatr Infect Dis J*. 1995; **14**(4):261–266.
90. Drusin LM, Sohmer M, Groshen SL, et al. Nosocomial hepatitis A infection in a paediatric intensive care unit. *Arch Dis Child*. 1987; **62**(7):690–695.
91. Reed CM, Gustafson TL, Siegel J, Duer P. Nosocomial transmission of hepatitis A from a hospital-acquired case. *Pediatr Infect Dis*. 1984; **3**(4):300–303.
92. Krober MS, Bass JW, Brown JD, Lemon SM, Rupert KJ. Hospital outbreak of

hepatitis A: risk factors for spread. *Pediatr Infect Dis*. 1984; **3**(4):296–299.

93. Orenstein WA, Wu E, Wilkins J, et al. Hospital-acquired hepatitis A: report of an outbreak. *Pediatrics*. 1981; **67** (4):494–497.
94. Edgar WM, Campbell AD. Nosocomial infection with hepatitis A. *J Infect*. 1985; **10**(1):43–7.
95. Goodman RA, Carder CC, Allen JR, Orenstein WA, Finton RJ. Nosocomial hepatitis A transmission by an adult patient with diarrhea. *Am J Med*. 1982; **73**(2):220–6.
96. Petrosillo N, Raffaele B Martini L, et al. A nosocomial and occupational cluster of hepatitis A virus infection in a pediatric ward. *Infect Control Hosp Epidemiol*. 2002; **23**(6):343–5.
97. Jensenius M, Ringertz SH, Berild D, et al. Prolonged nosocomial outbreak of hepatitis A arising from an alcoholic with pneumonia. *Scand J Infect Dis*. 1998; **30**(2):119–23.
98. Hanna JN, Loewenthal MR, Negel P, Wenck DJ. An outbreak of hepatitis A in an intensive care unit. *Anaesth Intensive Care*. 1996; **24**(4):440–4.
99. Doebbeling BN, Li N, Wenzel RP. An outbreak of hepatitis A among health care workers: risk factors for transmission. *Am J Public Health*. 1993; **83**(12):1679–84.
100. Guet L, Desbois D, Roque-Afonso AM, Germain JM, Merle V. Investigation of a severe nosocomial outbreak of hepatitis A among healthcare workers and adult patients. *J Hosp Infect*. 2011; **78**(1):70–1.
101. Eisenstein AB, Aach RD, Jacobsohn W, Goldman A. An epidemic of infectious hepatitis in a general hospital. Probable transmission by contaminated orange juice. *JAMA*. 1963; **185**:171–4.
102. Meyers JD, Romm FJ, Tihen WS, Bryan JA. Food-borne hepatitis A in a general hospital. Epidemiologic study of an outbreak attributed to sandwiches. *JAMA*. 1975; **231** (10):1049–53.
103. Evans ME, Hall KL, and Berry SE. Influenza control in acute care hospitals. *Am J Infect Control*. 1997; **25** (4):357–62.
104. Weingarten S, Friedlander M, Rascon D. Influenza surveillance in an acute-care hospital. *Arch Intern Med*. 1988; **148**(1):113–6.
105. Pachucki CT, Pappas SA, Fuller GF, et al. Influenza A among hospital personnel and patients. Implications for recognition, prevention, and control. *Arch Intern Med*. 1989; **149** (1):77–80.
106. Berlinberg CD, Weingarten SR, Bolton LB, Waterman SH. Occupational exposure to influenza–introduction of an index case to a hospital. *Infect Control Hosp Epidemiol*. 1989; **10**(2):70–3.
107. Centers for Disease Control and Prevention. Suspected nosocomial influenza cases in an intensive care unit. *MMWR Morb Mortal Wkly Rep*. 1988; **37**(1):3–4, 9.
108. Adal KA, Flowers RH, Anglim AM, et al. Prevention of nosocomial influenza. *Infect Control Hosp Epidemiol*. 1996; **17**(10):641–8.
109. Horcajada JP, Pumarola T, Martinez JA, et al. A nosocomial outbreak of influenza during a period without influenza epidemic activity. *Eur Respir J*. 2003; **21**(2):303–7.
110. Berg HF, Van Gendt J, Rimmelzwaan GF, Peeters MF, Van Keulen P. Nosocomial influenza infection among post-influenza-vaccinated patients with severe pulmonary diseases. *J Infect*. 2003; **46**(2):129–32.
111. Slinger R, Dennis P. Nosocomial influenza at a Canadian pediatric hospital from 1995 to 1999: opportunities for prevention. *Infect Control Hosp Epidemiol*. 2002; **23** (10):627–9.
112. Hirji Z, O'Grady S, Bonham J, et al. Utility of zanamivir for chemoprophylaxis of concomitant influenza A and B in a complex continuing care population. *Infect Control Hosp Epidemiol*. 2002; **23** (10):604–8.
113. Sagrera X, Ginovart G, Raspall F, et al. Outbreaks of influenza A virus infection in neonatal intensive care units. *Pediatr Infect Dis J*. 2002; **21** (3):196–200.
114. Malavaud S, Malavaud B, Sandres K, et al. Nosocomial outbreak of influenza virus A (H3N2) infection in a solid organ transplant department. *Transplantation*. 2001; **72** (3):535–7.
115. Weinstock DM, Eagan J, Malak SA, et al. Control of influenza A on a bone marrow transplant unit. *Infect Control Hosp Epidemiol*. 2000; **21**(11):730–2.
116. Cunney RJ, Bialachowski A, Thornley D, Smaill FM, Pennie RA. An outbreak of influenza A in a neonatal intensive care unit. *Infect Control Hosp Epidemiol*. 2000; **21**(7):449–54.
117. Munoz FM, Campbell JR, Atmar RL, et al. Influenza A virus outbreak in a neonatal intensive care unit. *Pediatr Infect Dis J*. 1999; **18**(9):811–5.
118. Schepetiuk S, Papanaoum K, Qiao M. Spread of influenza A virus infection in hospitalised patients with cancer. *Aust N Z J Med*. 1998; **28**(4):475–6.
119. Everts RJ, Hanger HC, Jennings LC, Hawkins A, Sainsbury R. Outbreaks of influenza A among elderly hospital inpatients. *N Z Med J*. 1996; **109** (1026):272–4.
120. Fiore AE, Fry A, Shay D, et al. Antiviral agents for the treatment and chemoprophylaxis of influenza – recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2011; **60**(1):1–24.
121. Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines. Recommendations of the Advisory Committee on Immunization Practices–United States, 2013–2014. *MMWR Recomm Rep*. 2013; **62**(RR-07):1–43.
122. Grohskopf LA, Sokolow LA, Olsen SJ, et al. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices, United States, 2015–16 Influenza Season. *MMWR Morb Mortal Wkly Rep*. 2015; **64** (30):818–25.
123. Talbot TR, Babcock H, Cotton D, et al. The use of live attenuated influenza vaccine (LAIV) in healthcare personnel (HCP): guidance from the Society for Healthcare Epidemiology of America (SHEA). *Infect Control Hosp Epidemiol*. 2012; **33**(10):981–3.
124. Kuntz JL, Holley S, Helms CM, et al. Use of a pandemic preparedness drill to increase rates of influenza vaccination among healthcare workers. *Infect Control Hosp Epidemiol*. 2008; **29**(2):111–5.
125. Anikeeva O, Braunack-Mayer A, Rogers W. Requiring influenza vaccination for health care workers. *Am J Public Health*. 2009; **99**(1):24–9.
126. Pitts SI, Maruthar NM, Millar KR, Perl TM, Segal J. A systematic review of mandatory influenza vaccination in healthcare personnel. *Am J Prev Med*. 2014; **47**(3):330–40.
127. Will RG. Epidemiology of Creutzfeldt-Jakob disease. *Br Med Bull*. 1993; **49** (4):960–70.

128. Harries-Jones R, Knight R, Will RG, et al. Creutzfeldt-Jakob disease in England and Wales, 1980–1984: a case-control study of potential risk factors. *J Neurol Neurosurg Psychiatry*. 1988; **51**(9):1113–9.

129. Alcalde-Cabero E, Almazan-Isla J, Brandel JP, et al. Health professions and risk of sporadic Creutzfeldt-Jakob disease, 1965 to 2010. *Euro Surveill*. 2012; **17**(15).

130. World Health Organization. WHO infection control guidelines for transmissible spongiform encephalopathies. Report of a WHO consultation Geneva, Switzerland, 23–26 March 1999 and WHO guidelines on transmissible spongiform encephalopathies in relation to biological and pharmaceutical products. 2003 October 15, 2015]; Available from: www.who.int/emc.

131. World Health Organization. WHO guidelines on tissue infectivity distribution in transmissible spongiform encephalopathies. [2010 October 20, 2015]; Available from: w ww.who.int/bloodproducts/tablestis sueinfectivity.pdf.

132. Berger JR, David NJ. Creutzfeldt-Jakob disease in a physician: a review of the disorder in health care workers. *Neurology*. 1993; **43**(1):205–6.

133. Steelman VM. Creutzfeld-Jakob disease: recommendations for infection control. *Am J Infect Control*. 1994; **22**(5):312–8.

134. Steelman VM. Creutzfeldt-Jakob disease: decontamination issues. *Infection Control and Sterilization Technology* 1996; **2**:32–39.

135. Centers for Disease Control and Prevention. Healthcare Infection Control Practices Advisory Committee (HICPAC): guideline for disinfection and sterilization in healthcare facilities. 2008 October 15, 2015]; Available from: www.cdc.gov/hicpac/Disinfection_Sterilization/acknowledg.html.

136. Centers for Disease Control and Prevention, Probable variant Creutzfeldt-Jakob disease in a U.S. resident–Florida, 2002. *MMWR Morb Mortal Wkly Rep*. 2002; **51**(41):927–9.

137. Frosh A, Joyce R, Johnson A. Iatrogenic vCJD from surgical instruments. *BMJ*. 2001; **322**(7302):1558–9.

138. Spencer RC, Ridgway GL,. on behalf of the vCJD Consensus Group., Sterilization issues in vCJD–towards a consensus: meeting between the Central Sterilizing Club and Hospital Infection Society. 12th September 2000. *J Hosp Infect.* 2002; **51**(3):168–74.

139. Axon AT, Beilenhoff U, Bramble MG, et al. Variant Creutzfeldt-Jakob disease (vCJD) and gastrointestinal endoscopy. *Endoscopy*. 2001; **33**(12):1070–80.

140. Hutton MD, Stead WW, Cauthen GM, Bloch JB, Ewing WM. Nosocomial transmission of tuberculosis associated with a draining abscess. *J Infect Dis*. 1990; **161**(2):286–95.

141. Matlow AG, Harrison A, Monteath A, Roach P, Balfe JW. Nosocomial transmission of tuberculosis (TB) associated with care of an infant with peritoneal TB. *Infect Control Hosp Epidemiol*. 2000; **21**(3):222–3.

142. Bowden KM, McDiarmid MA. Occupationally acquired tuberculosis: what's known. *J Occup Med*. 1994; **36**(3):320–5.

143. Stead WW. Management of health care workers after inadvertent exposure to tuberculosis: a guide for the use of preventive therapy. *Ann Intern Med*. 1995; **122**(12):906–12.

144. Templeton GL, Illing LA, Young L, et al. The risk for transmission of Mycobacterium tuberculosis at the bedside and during autopsy. *Ann Intern Med*. 1995; **122**(12):922–5.

145. Sepkowitz KA, Raffalli J, Riley L, Kiehn TE, Armstrong D. Tuberculosis in the AIDS era. *Clin Microbiol Rev*. 1995; **8**(2):180–99.

146. Conover C, Ridzon R, Valway S, et al. Outbreak of multidrug-resistant tuberculosis at a methadone treatment program. *Int J Tuberc Lung Dis*. 2001; **5**(1):59–64.

147. Menzies D, Fanning A, Yuan L, FitzGerald AM. Hospital ventilation and risk for tuberculous infection in canadian health care workers. Canadian Collaborative Group in Nosocomial Transmission of TB. *Ann Intern Med*. 2000; **133**(10):779–89.

148. Suzuki K, Onozaki I, Shimura A. [Tuberculosis infection control practice in hospitals from the viewpoint of occupational health]. *Kekkaku*. 1999; **74**(4):413–20.

149. Nakasone T, [Tuberculosis among health care workers in Okinawa Prefecture]. *Kekkaku*. 1999; **74**(4):389–95.

150. Schoch OD, Graf-Deuel E, Knoblauch A. [Tuberculin testing of hospital personnel: large investment with little impact]. *Schweiz Med Wochenschr*. 1999; **129**(6):217–24.

151. Ridzon R, Kenyon T, Luskin-Hawk R, et al. Nosocomial transmission of human immunodeficiency virus and subsequent transmission of multidrug-resistant tuberculosis in a healthcare worker. *Infect Control Hosp Epidemiol*. 1997; **18**(6):422–3.

152. Centers for Disease Control and Prevention. Multidrug-resistant tuberculosis outbreak on an HIV ward–Madrid, Spain, 1991–1995. *MMWR Morb Mortal Wkly Rep*. 1996; **45**(16):330–3.

153. Yanai H, Limpakarnjanarat K, Uthaivoravit W, et al. Risk of *Mycobacterium tuberculosis* infection and disease among health care workers, Chiang Rai, Thailand. *Int J Tuberc Lung Dis*. 2003; **7**(1):36–45.

154. Uyamadu N, Ahkee S, Carrico R, et al. Reduction in tuberculin skin-test conversion rate after improved adherence to tuberculosis isolation. *Infect Control Hosp Epidemiol*. 1997; **18**(8):575–9.

155. Silva VM, Cunha AJ, Oliveria JR, et al. Medical students at risk of nosocomial transmission of Mycobacterium tuberculosis. *Int J Tuberc Lung Dis*. 2000; **4**(5):420–6.

156. Kilinc O, Ucan ES, Cakan MD, et al. Risk of tuberculosis among healthcare workers: can tuberculosis be considered as an occupational disease? *Respir Med*. 2002; **96**(7):506–10.

157. Eyob G, Gebeyhu M, Goshu S, et al. Increase in tuberculosis incidence among the staff working at the Tuberculosis Demonstration and Training Centre in Addis Ababa, Ethiopia: a retrospective cohort study (1989–1998). *Int J Tuberc Lung Dis*. 2002; **6**(1):85–8.

158. Moore DAJ, Lightstone L, Javid B, Friedland JS. High rates of tuberculosis in end-stage renal failure: the impact of international migration. *Emerg Infect Dis*. 2002; **8**(1):77–8.

159. Greenaway C, Menzies D, Fanning A, et al. Delay in diagnosis among hospitalized patients with active tuberculosis–predictors and outcomes. *Am J Respir Crit Care Med*. 2002; **165**(7):927–33.

160. Mazurek GH, Jereb J, Vernon A, et al. Updated guidelines for using interferon gamma release assays to detect *Mycobacterium tuberculosis* infection – United States, 2010. *MMWR Recomm Rep*. 2010; **59**(RR-5):1–25.

161. [No authors listed]. Analysis of endemic meningococcal disease by serogroup and evaluation of chemoprophylaxis. *J Infect Dis*. 1976; **134**(2):201–4.
162. Apicella MA. *Neisseria meningitidis*, in *Principles and Practice of Infectious Diseases*, Mandell GL, Bennett JE, Dolin R, eds. 2005; Churchill Livingstone: New York, NY. 2498–2513.
163. Rose HD, Lenz IE, Sheth NK. Meningococcal pneumonia. A source of nosocomial infection. *Arch Intern Med*. 1981; **141**(5):575–7.
164. Cohen MS, Steere AC, Baltimore R, et al. Possible nosocomial transmission of group Y *Neisseria meningitidis* among oncology patients. *Ann Intern Med*. 1979; **91**(1):7–12.
165. Lambert HJ. Epidemiology of a small pertussis outbreak in Kent County, Michigan. *Public Health Rep*. 1965; **80**:365–9.
166. Bass JW, Stephenson SR. The return of pertussis. *Pediatr Infect Dis J*. 1987; **6** (2):141–4.
167. Mortimer EA Jr. Pertussis and its prevention: a family affair. *J Infect Dis*. 1990; **161**(3):473–9.
168. Mink CM, Cherry JD, Christenson P, et al. A search for *Bordetella pertussis* infection in university students. *Clin Infect Dis*. 1992; **14**(2):464–71.
169. Nelson JD. The changing epidemiology of pertussis in young infants. The role of adults as reservoirs of infection. *Am J Dis Child*. 1978' **132** (4):371–3.
170. Addiss DG, Davis JP, Meade BP, et al. A pertussis outbreak in a Wisconsin nursing home. *J Infect Dis*. 1991; **164** (4):704–10.
171. Robbins JB. Pertussis in adults: introduction. *Clin Infect Dis*. 1999; **28 Suppl** 2:S91–3.
172. Linnemann CC Jr, Nasenbeny J. Pertussis in the adult. *Annu Rev Med*. 1977; **28**:179–85.
173. Kurt TL, Yeager AS, Guenette S, et al. Spread of pertussis by hospital staff. *JAMA*. 1972; **221**(3):264–7.
174. Linnemann CC Jr, Ramundo N, Perlstein PH, Minton SD, EnglenderGS. Use of pertussis vaccine in an epidemic involving hospital staff. *Lancet*. 1975; **2**(7934):540–3.
175. Valenti WM, Pincus PH, Messner MK. Nosocomial pertussis: possible spread by a hospital visitor. *Am J Dis Child*. 1980; **134**(5):520–1.
176. Martinez SM, Kemper CA, Haiduven D, Cody SH, Deresinski SC. Azithromycin prophylaxis during a hospitalwide outbreak of a pertussis-like illness. *Infect Control Hosp Epidemiol*. 2001; **22**(12):781–3.
177. Spearing NM, Horvath RL, McCormack JG, Pertussis: adults as a source in healthcare settings. *Med J Aust*. 2002; **177**(10):568–9.
178. Karino T, Osaki K, Nakano N, Okimoto N. [A pertussis outbreak in a ward for severely retarded]. *Kansenshogaku Zasshi*. 2001; **75** (11):916–22.
179. Gehanno JF, Pestel-Caron M, Neuvellon M, Caillard JF. Nosocomial pertussis in healthcare workers from a pediatric emergency unit in France. *Infect Control Hosp Epidemiol*. 1999; **20**(8):549–52.
180. Matlow AG, Nelson S, Wray R, Cox P. Nosocomial acquisition of pertussis diagnosed by polymerase chain reaction. *Infect Control Hosp Epidemiol*. 1997; **18**(10):715–6.
181. Wright SW, Decker MD, Edwards KM. Incidence of pertussis infection in healthcare workers. *Infect Control Hosp Epidemiol*. 1999; **20**(2):120–3.
182. Kuncio DE, Middleton M, Cooney MG, et al. Health care worker exposures to pertussis: missed opportunities for prevention. *Pediatrics*. 2014; **133**(1):15–21.
183. Steketee RW, Burstyn DG, Wassilak SG, et al. A comparison of laboratory and clinical methods for diagnosing pertussis in an outbreak in a facility for the developmentally disabled. *J Infect Dis*. 1988; **157**(3):441–9.
184. Steketee RW, Wassilak SG, Adkins WM Jr, et al. Evidence for a high attack rate and efficacy of erythromycin prophylaxis in a pertussis outbreak in a facility for the developmentally disabled. *J Infect Dis*. 1988; **157**(3):434–40.
185. Fisher MC, Long SS, McGowan KL, Kaselis E, Smith DG. Outbreak of pertussis in a residential facility for handicapped people. *J Pediatr*. 1989; **114**(6):934–9.
186. Biellik RJ, Patriarca PA, Mullen JR, et al. Risk factors for community- and household-acquired pertussis during a large-scale outbreak in central Wisconsin. *J Infect Dis*. 1988; **157** (6):1134–41.
187. Christie CD, Marx ML, Marchant CD, Reising SF. The 1993 epidemic of pertussis in Cincinnati. Resurgence of disease in a highly immunized population of children. *N Engl J Med*. 1994; **331**(1):16–21.
188. Winter K, Glaser C, Watt J, Harriman K. Pertussis epidemic–California, 2014. *MMWR Morb Mortal Wkly Rep*. 2014; **63**(48):1129–32.
189. Centers for Disease Control and Prevention. Pertussis epidemic–Washington, 2012. *MMWR Morb Mortal Wkly Rep*. 2012; **61**(28):517–22.
190. Matthias J, Dusek C, Pritchard PS, et al. Notes from the field: outbreak of pertussis in a school and religious community averse to health care and vaccinations–Columbia County, Florida, 2013. *MMWR Morb Mortal Wkly Rep*. 2014; **63**(30):655.
191. Rodgers L, Martin SW, Cohn A, et al. Epidemiologic and laboratory features of a large outbreak of pertussis-like illnesses associated with cocirculating *Bordetella holmesii* and *Bordetella pertussis*–Ohio, 2010–2011. *Clin Infect Dis*. 2013; **56**(3):322–31.
192. Kretsinger K, Broder KR, Cortese MM, et al. Preventing tetanus, diphtheria, and pertussis among adults: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine recommendations of the Advisory Committee on Immunization Practices (ACIP) and recommendation of ACIP, supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC), for use of Tdap among health-care personnel. *MMWR Recomm Rep*. 2006; **55**(RR-17):1–37.
193. Sandora TJ, Pfoh E, Lee GM. Adverse events after administration of tetanus-diphtheria-acellular pertussis vaccine to healthcare workers. *Infect Control Hosp Epidemiol*. 2009; **30**(4):389–91.
194. Weber DJ. Rutala WA. Management of healthcare workers exposed to pertussis. *Infect Control Hosp Epidemiol*. 1994; **15**(6):411–5.
195. Goins WP, Edwards KM, Vnencak-Jones CL, et al. A comparison of 2 strategies to prevent infection following pertussis exposure in vaccinated healthcare personnel. *Clin Infect Dis*. 2012; **54**(7):938–45.
196. Tiwari T, Murphy TM, Moran J. Recommended antimicrobial agents for the treatment and postexposure prophylaxis of pertussis: 2005 CDC guidelines. *MMWR Recomm Rep*. 2005; **54**(RR-14):1–16.
197. Kakis A, Gibbs L, Eguia J, et al. An outbreak of group A streptococcal

infection among health care workers. *Clin Infect Dis*. 2002; **35**(11):1353–9.

198. Ramage L, Green K, Pyskir D, Simor AE. An outbreak of fatal nosocomial infections due to group A streptococcus on a medical ward. *Infect Control Hosp Epidemiol*. 1996; **17**(7):429–31.
199. Hagberg C, Radulescu A, Rex JH. Necrotizing fasciitis due to group A streptococcus after an accidental needle-stick injury. *N Engl J Med*. 1997; **337**(23):1699.
200. Prevention of Invasive Group A Streptococcal Infections Workshop Participants. Prevention of invasive group A streptococcal disease among household contacts of case patients and among postpartum and postsurgical patients: recommendations from the Centers for Disease Control and Prevention. *Clin Infect Dis*. 2002; **35**(8):950–9.
201. Lettau LA. Nosocomial transmission and infection control aspects of parasitic and ectoparasitic diseases. Part III. Ectoparasites/summary and conclusions. *Infect Control Hosp Epidemiol*. 1991; **12**(3):179–85.
202. Meinking TL, Entzel P, Villar ME, et al. Comparative efficacy of treatments for Pediculosis capitis infestations. *Arch Dermatol*. 1986; **122**(3):267–71.
203. Degelau J. Scabies in long-term care facilities. *Infect Control Hosp Epidemiol*. 1992; **13**(7):421–5.
204. Pasternak J, Richtmann R, Ganme AP, et al. Scabies epidemic: price and prejudice. *Infect Control Hosp Epidemiol*. 1994; **15**(8):540–2.
205. Yonkosky D, Ladia L, Gackenheimer L, Schultz MW. Scabies in nursing homes: an eradication program with permethrin 5% cream. *J Am Acad Dermatol*. 1990; **23**(6 Pt 1):1133–6.
206. Clark J, Friesen DL, Williams WA. Management of an outbreak of Norwegian scabies. *Am J Infect Control*. 1992; **20**(4):217–20.
207. Corbett EL, Crossley I, Holton J, et al. Crusted ("Norwegian") scabies in a specialist HIV unit: successful use of ivermectin and failure to prevent nosocomial transmission. *Genitourin Med*. 1996; **72**(2):115–7.
208. Sirera G, Rius F, Romeu J, et al. Hospital outbreak of scabies stemming from two AIDS patients with Norwegian scabies. *Lancet*. 1990; **335**(8699):1227.
209. Jack M. Scabies outbreak in an extended care unit–a positive outcome. *Can J Infect Control*. 1993; **8**(1):11–3.
210. van Vliet J.A, Samsom M, van Steenbergen JE. [Causes of spread and return of scabies in health care institutes; literature analysis of 44 epidemics]. *Ned Tijdschr Geneeskd*. 1998; **142**(7):354–7.
211. Meltzer E. [Ivermectin and the treatment of outbreaks of scabies in medical facilities]. *Harefuah*. 2002; **141**(11):948–52, 1011.
212. Portu JJ, Santamaria JM, Zubero Z, et al. Atypical scabies in HIV-positive patients. *J Am Acad Dermatol*. 1996; **34**(5 Pt 2):915–7.
213. Obasanjo OO, Wu P, Conlon M, et al. An outbreak of scabies in a teaching hospital: lessons learned. *Infect Control Hosp Epidemiol*. 2001; **22**(1):13–8.
214. Deabate MC, Calitri V, Licata C, et al. [Scabies in a dalysis unit. Mystery and prejudice]. *Minerva Urol Nefrol*. 2001; **53**(2):69–73.
215. Zafar AB, Beidas SO, Sylvester LK. Control of transmission of Norwegian scabies. *Infect Control Hosp Epidemiol*. 2002; **23**(5):278–9.
216. Robles Garcia M, de la Lama Lopez-Areal J, Avellaneda Martinez C, et al. [Nosocomial scabies outbreak]. *Rev Clin Esp*. 2000; **200**(10):538–42.
217. Boix V, Sanchez-Paya J, Portilla J, Merino E. Nosocomial outbreak of scabies clinically resistant to lindane. *Infect Control Hosp Epidemiol*. 1997; **18**(10):677.
218. Nandwani R, Crossley I, Holton J, et al. Crusted ("Norwegian") scabies in a specialist HIV unit. *Genitourin Med*. 1996' **72**(6):453.
219. Petersen BW, Damon JK, Pertowski CA, et al. Clinical guidance for smallpox vaccine use in a postevent vaccination program. *MMWR Recomm Rep*. 2015; **64**(RR-02):1–26.
220. Centers for Disease Control and Prevention. Update: adverse events following civilian smallpox vaccination–United States, 2003. *MMWR Morb Mortal Wkly Rep*. 2004; **53**(5):106–7.
221. Centers for Disease Control and Prevention. Update: severe acute respiratory syndrome–worldwide and United States, 2003. *MMWR Morb Mortal Wkly Rep*. 2003; **52**(28):664–5.
222. World Health Organization. Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003. 2003 October 16, 2015]; Available from: www.who.int/csr/sars/country/table2003_09_23/en/.
223. Seto WH, Tsang D, Yung RW, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet*. 2003; **361**(9368):1519–20.
224. Centers for Disease Control and Prevention. Cluster of severe acute respiratory syndrome cases among protected health-care workers–Toronto, Canada, April 2003. *MMWR Morb Mortal Wkly Rep*. 2003; **52**(19):433–6.
225. Lessler J, Reich NG, Broomeyer R, et al. Incubation periods of acute respiratory viral infections: a systematic review. *Lancet Infect Dis*. 2009; **9**(5):291–300.
226. Centers for Disease Control and Prevention, Use of quarantine to prevent transmission of severe acute respiratory syndrome–Taiwan, 2003. *MMWR Morb Mortal Wkly Rep*. 2003; **52**(29):680–3.
227. Zaki AM, van Boheemen S, Bestebroer TM, et al. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N Engl J Med*. 2012; **367**(19):1814–20.
228. Assiri A, McGeer A, Perl TM, et al. Hospital outbreak of Middle East Respiratory Syndrome coronavirus. *N Engl J Med*. 2013; **369**(5):407–16.
229. Centers for Disease Control and Prevention. Interim infection prevention and control recommendations for hospitalized patients with Middle East Respiratory Syndrome Coronavirus (MERS-CoV). 2014 October 15, 2015]; Available from: www.cdc.gov/coronavirus/mers/downloads/MERS-Infection-Control-Guidance-051414.pdf.
230. Schieffelin JS, Shaffer JG, Goba A, et al. Clinical illness and outcomes in patients with Ebola in Sierra Leone. *N Engl J Med*. 2014; **371**(22):2092–100.
231. Centers for Disease Control and Prevention. Interim U.S. guidance for monitoring and movement of persons with potential Ebola virus exposure. 2015 October 9, 2015 October 16, 2015]; Available from: www.cdc.gov/vhf/ebola/exposure/monitoring-and-movement-of-persons-with-exposure.html.

Chapter

26 Employee Health and Infection Control

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A healthcare facility's occupational medicine program is one of three vital services that provide occupational medical and safety support for its healthcare personnel. The other two programs are the institution's biosafety division and its hospital epidemiology service. These three departments work in concert to ensure the health and safety of workers and patients in healthcare institutions. This chapter reviews the intersection of these three programs in screening staff for infectious diseases, providing pre-exposure education and immunoprophylaxis, and in ensuring an adequate infrastructure for the safe provision of care.

Serologic Screening and Immunization

Preplacement Examination

Prior to entry into the workplace, hospital personnel who may have patient contact or work in patient care areas should be evaluated by the occupational medicine service to ensure their fitness for duty. The most important aspect of this evaluation is the employee's medical history. From the perspective of the hospital epidemiologist, the critical aspects of the employee's medical history are his or her communicable disease history (including immunization history) and the presence of underlying medical conditions that place the employee at elevated risk for occupational infection in the healthcare workplace. Whereas an employee's report of past infection used to be considered sufficiently reliable evidence of immunity to some infections (e.g., varicella), healthcare provider documentation of disease is now requisite in most settings. Substance abuse screening is often part of this pre-employment evaluation. A focused "entry-into-duty" physical examination is performed by some occupational medical services; others require that the employee's personal physician provide the findings from a recent examination.

Laboratory Evaluation

Routine, unfocused laboratory testing is of limited value in screening potential employees who will have patient contact or work in patient areas. Screening should be limited to diseases that healthcare personnel are at high risk of acquiring or transmitting in the occupational setting. Hepatitis B, measles, mumps, rubella, pertussis, and varicella are vaccine-preventable infections that are prioritized for healthcare personnel screening and immunization.[1] Healthcare personnel should also be screened for tuberculosis (TB) (see below).

Hepatitis B: Routine serologic screening for hepatitis B virus (HBV) is generally not cost-effective, unless healthcare personnel have high personal risk of hepatitis B infection, such as birth in a region with high HBV prevalence, human immunodeficiency virus (HIV) infection or other immunosuppressive conditions, past high-risk substance abuse, and hemodialysis.[1]

Measles, mumps, rubella: Personnel born in 1957 or after should be screened for antibody titers if they lack documentation of past infection, previous laboratory evidence of immunity, and full immunization series.

Varicella: Personnel should be screened for antibody titers if they lack documentation of past infection, previous laboratory evidence of immunity, and full immunization series.[1] Although commercially available varicella ELISAs are less sensitive than the labor-intensive gold standard, the fluorescent antibody to membrane assay (FAMA), they have acceptable specificity and are considered adequate for screening healthcare personnel. Routine postvaccination serologic testing is not recommended.[2]

Pertussis: Personnel should provide documentation of immunization, but no screening serology is recommended.[1]

Screening for Prior Tuberculosis Infection

The occupational medicine, hospital epidemiology, and institutional biosafety programs should work together to establish an effective ongoing TB prevention program, including a TB surveillance system. The scope of this program should be based on a detailed risk assessment, taking into account the annual TB case load, size of the hospital, history of TB transmission in the institution, and the prevalence of TB in the hospital's community.[3]

Each new employee should receive pre-employment two-step TB skin testing, unless the employee has a previous positive skin test result or documentation of previously treated TB. Staff who have a history of latent TB must receive a chest X-ray or submit documentation of prior evaluation for active TB or treatment of latent TB. Experienced occupational medicine staff should evaluate TB skin test results using stringent, consistent criteria. Staff who have received the Bacille Calmette-Guerin (BCG) vaccine should generally be tested via interferon gamma release assay (IGRA), such as T Spot TB or Quantiferon Gold. The IGRAs do not cross-react with BCG, but they do cross-react with *Mycobacterium marinum, M. szulgai*, and *M. kansasii*, making false positives uncommon but still possible.[4] Discordance between TB skin test and IGRA results occurs frequently, and reproducibility of low

positive IGRA results is poor. Healthcare personnel who have positive skin test or IGRA results should be managed according to existing guidelines.[3,4]

Pre-Exposure Immunoprophylaxis

As noted above, healthcare personnel should have immunity against certain key infectious diseases. Table 26.1 provides a summary list of immunizations recommended for healthcare personnel. Any healthcare worker whose job entails potential exposure to blood, mucous membranes, or blood-containing body fluids should have demonstrable immunity against HBV. The occupational medicine and hospital epidemiology services should work together to ensure that an efficient program is in place to educate staff about the occupational risks of bloodborne pathogen infection and to provide HBV immunization. Immunization against measles, mumps, and rubella and varicella is essential for all susceptible healthcare personnel. Since adult immunity to pertussis has been demonstrated to be waning, pertussis vaccine is strongly recommended as a one-time immunization for healthcare personnel – and for all adults.[1,5]

Influenza immunization deserves special emphasis as a critical patient safety intervention. Healthcare facilities should require annual influenza immunization of all staff who have patient contact or work in patient areas,[1] including ancillary staff such as housekeepers, clerks, and escort personnel. Annual immunization of healthcare personnel is the single most efficacious strategy for reducing the risk for influenza transmission to patients. Voluntary influenza immunization has only produced low immunization rates,[6] which have been associated with nosocomial outbreaks of influenza.[7] By contrast, higher immunization rates have been associated with both a reduced incidence of influenza-like illness and reduced mortality among patients.[8–12] Additional beneficial effects of a successful influenza immunization program include a decrease in worker absenteeism during influenza epidemics and a decrease in healthcare costs.

In 2007 the Infectious Diseases Society of America (IDSA) called for mandatory annual influenza immunization of healthcare personnel, and in 2013 the IDSA, joined by the Society for Healthcare Epidemiology of America (SHEA) and the Pediatric Infectious Diseases Society, strengthened that message with a recommendation that mandatory immunization of personnel who have patient contact be a condition of continued employment in healthcare facilities.[13] In our own institution, a mandatory influenza immunization program yields 97 percent immunization rates among staff who have face-to-face contact with patients. Staff who have serious medical contraindication, such as a history of Guillain-Barre syndrome or severe allergic reaction to the vaccine, must present documentation from a licensed provider in order to be exempt from immunization. Those who have religious reasons for declining immunization must complete a form to that effect.

Infectious Disease Surveillance for Employees

The one infectious disease for which active surveillance is almost uniformly recommended for healthcare personnel is TB. In addition to ensuring that the TB control program is tailored to the unique aspects of risk in their own environments, institutions should develop programs that address the variable risks for exposure of individuals in differing job categories. At a minimum, healthcare personnel who have prior negative TB skin test or IGRA results should be retested at appropriate intervals, on the basis of the institutional risk assessment, as recommended by the most recent guidelines from the Centers for Disease Control and Prevention (CDC) and the US Public Health Service.[3] Staff members who, on the basis of their job categories, are at higher risk for occupational exposure to TB (e.g., critical care physicians and nurses, pulmonologists, anesthesiologists, and respiratory therapists) should be tested more frequently. Employees who have underlying immunodeficiencies that place them at high risk of developing active TB may be discouraged from caring for patients who have TB and may undergo more frequent surveillance than others in their job category.

TB control programs are generally collaborative efforts that include participation by the hospital epidemiology service, the biosafety officer, and the occupational medicine service. The roles of the occupational medicine service include preemployment testing, as described above, Occupational Safety and Health Administration (OSHA)-mandated medical evaluations for N95 respirator fit testing, ongoing surveillance, and exposure management.

Additional details can be found in Chapter 27, on control of TB.

Postexposure Prophylaxis for Occupational Exposures to Bloodborne Pathogens

The occupational medical service is the first stop for any employee who sustains a potential blood or body fluid exposure. Assisted by published guidelines, occupational medicine specialists evaluate the nature of the exposure, the clinical status of the source patient (if known), and the underlying health of the employee to determine the risk of pathogen transmission and the need for postexposure prophylaxis. For HBV and influenza, postexposure prophylaxis is simple and effective. For varicella zoster virus, postexposure prophylaxis is more complex but still highly effective. Hepatitis C treatment has changed dramatically since the last edition of this book, though efficacy in the postexposure prophylaxis setting has not yet been demonstrated with the new directly acting antiviral agents. Occupational medicine providers work closely with infectious diseases specialists to administer antiretroviral drugs as postexposure prophylaxis to healthcare personnel who have an exposure at high risk of transmitting HIV. Postexposure management strategies for occupational exposures to the major bloodborne pathogens (HBV, HCV, and HIV) are discussed below. The management of other occupational exposures and the issues relating to their postexposure management are discussed in Chapter 25, on exposure workups.

Table 26.1 Vaccinations recommended for hospital employees

Disease or pathogen	Indication	Vaccine and dosage	Cautions
Diphtheria	In an outbreak or following documented exposures for employees who have not been vaccinated in the past 10 years or who lack serological evidence of immunity.	Td, 0.5 mL intramuscularly (or Tdap if not boosted previously for pertussis; see below).	Known hypersensitivity to thimerosal or any component of the vaccine.
Hepatitis A	Staff who have chronic liver disease, travel internationally, work with sewage, or work in high-risk areas (e.g., dietary service, cafeteria, or hepatitis ward) who do not have serologic evidence of previous hepatitis A virus infection.	Hepatitis A vaccine, 1.0 mL intra muscularly at months 0 and 6–12.	Known hypersensitivity to any component of the vaccine.
Hepatitis B	Pre-exposure for all staff at risk for occupational exposure to blood or body fluids; postexposure for those with potential needlestick or mucous membrane exposure to hepatitis B if not immune.	Hepatitis B recombinant vaccine, 1.0 mL intramuscularly (in the deltoid muscle) at months 0, 1, and 6.	History of anaphylaxis to baker's yeast.
Influenza	All hospital staff	Inactivated trivalent or quadrivalent influenza vaccine, 0.5 mL intramuscularly annually; immunization with live attenuated intranasal vaccine is allowed in some healthcare facilities.	History of severe hypersensitivity to eggs or severe allergic reaction to prior doses of influenza vaccine. Theoretical risk of transmitting live attenuated vaccine strain to immunocompromised patients.
Measles	All HCP who lack presumptive evidence of immunity (never received two live vaccines on or after their first birthday or do not have serological proof of immunity); consider immunizing those born before 1957.	Two doses trivalent MMR, 0.5 mL subcutaneously, at least 28 days apart.	Live vaccine. Pregnancy, immunosuppression, history of anaphylactic reaction to gelatin or neomycin, recent receipt of immune globulin.
Mumps	All HCP who lack presumptive evidence of immunity (never received two live vaccines on or after their first birthday or do not have serological proof of immunity); consider immunizing those born before 1957.	Two doses trivalent MMR, 0.5 mL subcutaneously, at least 28 days apart.	Live vaccine. Pregnancy, immunosuppression, history of anaphylactic reaction to gelatin or neomycin, recent receipt of immune globulin.
Meningococcus	Researchers or clinical microbiologists who might be exposed to *Neisseria meningitidis* isolates; institutional outbreak.	One dose of meningococcus quadrivalent conjugate vaccine (MenACWY), 0.5 mL intramuscularly, every five years while at increased risk.	Safety in pregnancy uncertain; sensitivity to thimerosal or any other component of the vaccine
Pertussis	All HCP who have patient contact.	Tdap 0.5 mL intramuscularly every 10 years.	Known hypersensitivity to any component of the vaccine, prior encephalop- athy associated with primary immunization.
Rubella	All HCP who lack presumptive evidence of immunity (never received two live vaccines on or after their first birthday or do not have serological proof of immunity).	One dose trivalent MMR, 0.5 mL subcutaneously.	Live vaccine. Pregnancy, immunosuppression, history of anaphylactic reaction to gelatin or neomycin, recent receipt of immune globulin. Risk for rubella vaccine-associated fetal malformations is low.

Table 26.1 (cont.)

Disease or pathogen	Indication	Vaccine and dosage	Cautions
Tetanus	Staff who sustain tetanus-prone wounds, those who never completed the initial vaccination series, and those who have not received a booster dose.	Tdap 0.5 mL intramuscularly if no Tdap in past 10 years or if uncertain about timing of Tdap; one 0.5 mL dose Td intramuscularly if received Tdap in past 10 years but no tetanus toxoid-containing vaccine in past five years.	History of neurological or hypersensitivity reaction following a previous dose.
Varicella	HCP with patient contact who lack evidence of immunity: no diagnosis or history of chickenpox or herpes zoster documented by a healthcare provider, have not received two doses of varicella vaccine, and a negative varicella titer.	Varicella vaccine, 0.5 mL subcutaneously at weeks 0 and 4–8.	Live vaccine. Pregnancy, immunosuppression, Hypersensitivity to vaccine, gelatin, or neomycin. No salicylates for six weeks after receipt of vaccine.

NOTE: HCP, healthcare personnel; MMR, measles, mumps, and rubella vaccine; Td, tetanus and diphtheria toxoids; Tdap, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine.

HBV Exposure

Historically, prior to the development of the HBV vaccine, hepatitis B represented one of the most significant occupational risks for healthcare providers (particularly those who had occupational exposure to blood). As a result of exposures to HBV in the workplace, healthcare personnel, and particularly those whose workplace tasks involved frequent exposure to blood, were at significantly increased risk for HBV infection when compared with the population at large.

Transmission

HBV is transmitted parenterally, with percutaneous exposure to infected blood the most important mode of occupational transmission. Exposure to mucous membranes or nonintact skin also may result in infection. HBV also can be transmitted sexually and perinatally. Both acutely and chronically infected individuals transmit infection; infected individuals who have high viral loads and high levels of circulating hepatitis B e antigen (HBeAg) represent the greatest risk for transmission. The risk for serologic evidence of transmission following parenteral exposure to blood from a hepatitis B surface antigen (HBsAg)-positive, HBeAg-positive patient is 37 percent to 62 percent per exposure, with a 22–31 percent risk of developing clinical hepatitis. In contrast, the risk of seroconversion following exposure to blood from a patient who tests positive for HBsAg but negative for HBeAg is approximately 23–37 percent, with a 1–6 percent risk of developing clinical hepatitis.[14,15]

Criteria for Exposure

Any worker who sustains a percutaneous, mucous membrane, or nonintact skin exposure to blood or body fluids that may contain blood from an HBsAg-positive patient (or a patient whose HBV serologic status cannot be determined) should be considered exposed. Source patients with unknown serologic status should be tested as soon as possible after the exposure.

Postexposure Prophylaxis

Unimmunized or Incompletely Immunized Healthcare Personnel: If a healthcare worker who has not been immunized with the HBV vaccine sustains an occupational exposure to HBV, the worker should be given 0.06 mL/kg of hepatitis B immune globulin intramuscularly. Ideally, this first dose should be administered within 24 hours after the exposure, and definitely within 7 days. The first dose of the HBV vaccine series should be administered at the same time, followed by additional doses 1 month later and 6 months later.[16] The CDC does not recommend measuring anti-HBs in unimmunized or incompletely immunized personnel until at least one month after the vaccine series has been completed.[16] For personnel who, for some reason, cannot be immunized, a second dose of hepatitis B immune globulin should be administered 1 month after the first dose (unless the source patient is found to be HBsAg negative).

Immunized Healthcare Personnel: For previously immunized healthcare personnel, the anti-HBs level should be measured as soon as possible; those whose anti-HBs levels are greater than 10 mIU/mL are considered protected. Personnel who have anti-HBs levels below 10 mIU/mL and who were never demonstrated to have had an adequate vaccine response should be treated as if they are unprotected and given two doses of hepatitis B immune globulin a month apart and should repeat the vaccine series if they previously received only one three-dose vaccine series. For staff who are known to have had protective antibody levels but whose levels have fallen below 10 mIU/mL, a booster dose of vaccine is given, and titers checked one to two months later.[16]

More details on HBV pre-exposure and post-exposure management are available in the CDC guidelines by Schillie et al. that were published in 2013.[16]

Control Measures

Universal immunization of healthcare personnel against HBV should be a primary goal of the occupational medicine service, and education and vaccination campaigns should focus on achieving that goal. Receipt of the full vaccine series provides immunity in more than 93 percent of recipients, and should mitigate the risk of HBV transmission from patients to healthcare personnel.

Whereas patient-to-healthcare worker transmission occurs far more frequently than does healthcare worker-to-patient transmission, the latter type of transmission does occur, particularly when the healthcare worker is HBeAg positive and conducts invasive procedures.[17,18] SHEA guidelines for the management of providers who are infected with hepatitis B, hepatitis C, and/or HIV published in 2011 recommended that providers who have circulating HBe antigen or a viral burden greater than or equal to 10^4 genome equivalents (GE) per mL use double gloves for procedures and mucous membrane contact, and avoid performing highly invasive, exposure-prone procedures.[19] The 2012 CDC guidelines recommended a more conservative threshold of 10^3 GE/mL.[20] Both guidelines recommend regular viral monitoring by occupational medicine services[19,20] and the involvement of an expert review panel to advise on the healthcare provider's participation in procedures.[21]

In the United Kingdom, HBV-infected providers who are negative for HBeAg but have HBV DNA levels between 10^3 and 10^5 GE/mL may conduct exposure-prone invasive procedures if their viral burden can be suppressed below 10^3 GE/mL on continuous antiviral therapy, and must be retested every year to ensure that the viral load remains below 10^3 GE/mL.[22] The major challenge associated with this latter recommendation is the development of an effective monitoring strategy to make certain the circulating viral burden remains less than 10^3 GE/mL. The variability of various testing systems further complicates monitoring.[22]

A European consortium developed a set of guidelines that do not permit HBV-infected healthcare personnel who are HBeAg positive to conduct exposure-prone procedures but that do permit those who are HBeAg negative but have HBV DNA levels of less than 10^4 GE/mL to perform such procedures.[23] According to these guidelines, such individuals must be retested at least annually to make certain that the circulating viral burden remains below 10^4 GE/mL.[23] These guidelines also do not allow healthcare personnel who are identified as having transmitted HBV to perform exposure-prone procedures and permit HBV-infected healthcare workers who have been treated and have posttreatment DNA levels that have fallen to less than 10^4 GE/mL to conduct exposure-prone procedures, so long as the healthcare worker is retested every 3 months to ensure that the viral burden remains below 10^4 GE/mL.[23]

HCV Exposure

Healthcare personnel are at risk for HCV infection as a result of parenteral or mucous membrane exposures to blood from patients infected with HCV. The risk of chronic infection in acutely infected, untreated individuals is 50–80 percent, depending on host and viral factors.[24,25] Individuals who develop chronic HCV infection are at risk for serious sequelae of this infection, namely cirrhosis and hepatocellular carcinoma. Whereas new antiviral treatment for hepatitis C infection may reduce the risk of these long-term sequelae, they can still occur following effective therapy.[26]

Transmission

Occupational risk for HCV transmission is likely linked to the same routes of transmission as those for HBV. Occupational HCV infection has been most frequently associated with parenteral exposures. A few instances of mucous membrane transmission have been reported, and nonapparent parenteral transmission (caused by exposure of nonintact skin to blood of an HCV-infected individual) likely also occurs, albeit at a substantially lower rate than is the case for HBV. The risk for occupational infection associated with a single parenteral exposure has been estimated to be nearly 2 percent.[27,28]

Criteria for Exposure

Occupational medicine staff should consider any healthcare worker who has sustained a percutaneous, mucous membrane, or nonintact skin exposure to blood, or a body fluid potentially containing blood, from an HCV-infected patient as having been exposed. As is the case for HBV infection, in instances in which the source patient for an exposure is unknown, cannot be tested, or is known to have epidemiological risk factors associated with HCV infection, the worker also should be considered exposed.[29]

Postexposure Management

At present, there is no known effective postexposure prophylaxis for hepatitis C. All HCV-exposed individuals should be tested at the time of exposure for antibody to HCV and for HCV RNA (by PCR) and baseline liver enzymes. Personnel should be monitored with serial antibody and viral load testing every 2 months or so. Those who develop reproducibly positive tests should be referred for monitoring and, if spontaneous clearance does not occur,[30] treatment of acute hepatitis C with immunomodulators or antiviral agents.

The healthcare worker also should be encouraged to seek prompt medical attention for any symptoms suggestive of systemic illness or acute hepatitis. Immune serum globulin should not be administered for occupational exposures to HCV, as neutralizing antibody has not shown to be effective against hepatitis C infection, and donors for current immune globulin preparations are screened for hepatitis C antibody (anti-HCV) and eliminated from the donor pool if found to be positive for anti-HCV.

Both "preemptive therapy" and "watchful waiting" strategies have been proposed as reasonable strategies for postexposure management.[27] As yet, data from studies of healthcare workers treated with these approaches are too preliminary to

provide the basis for a formal recommendation of an optimal management strategy. At our own institution, we use the "watchful waiting" strategy.

Control Measures

Avoidance of exposures through the routine use of universal and standard precautions (i.e., primary prevention) is the only effective preventive strategy currently available. Although iatrogenic transmission of HCV from healthcare personnel to patients has been uncommon, particularly in the United States, recent years have seen several clusters of healthcare provider-to-patient HCV transmission. Whereas provider-to-patient transmission clusters occurring in the United Kingdom and Europe have likely been attributable to surgical technique, those documented in the United States have been more related to intravenous drug use and drug diversion by the involved healthcare worker.

Healthcare workers engaging in drug diversion typically inject themselves from a patient supply of narcotics or anesthetic drugs, often repeatedly with the same needle, thereby exposing the patient to their bloodborne pathogens.[19,31,32] The experience in the United Kingdom has been quite distinctive, in that HCV transmission from healthcare workers to patients seems to have occurred primarily (though not exclusively) in the context of exposure-prone procedures, and involve gynecologists, cardiothoracic surgeons, orthopedists, and anesthesiologists.[33–42] Although the magnitude of risk for iatrogenic HCV transmission is likely small, the well-documented transmission events have prompted measures to limit highly viremic HCV-infected providers from the most exposure-prone procedures.

The SHEA guidelines recommend that providers who have HCV viral loads greater than or equal to 10^4 GE/mL use double gloves for all procedures and mucous membrane contact, and avoid performing the most invasive, exposure-prone procedures and be referred to a hepatologist for possible treatment.[19] European consensus guidelines from 2003 recommended only that providers who perform exposure-prone procedures know their HCV status.[23] The increasing availability of effective and curative antiviral therapies for HCV will almost assuredly result in viremic infected providers being cured of their infections and thus able to return to the operating room.

HIV Exposure

The risk of acquiring HIV infection is approximately 0.3 percent per parenteral exposure and approximately 0.09 percent after a mucous membrane exposure.[43,44] Whereas this risk is substantially smaller than that for other bloodborne infections, the consequences of infection are life altering. For a thorough discussion of the issues relating to nosocomial transmission of HIV, see Henderson.[45]

Transmission

HIV is transmitted parenterally, sexually, and vertically between mother and child (i.e., across the placenta, perinatally, or through breastfeeding). Occupational transmission has been reported after percutaneous, mucous membrane, and nonintact skin exposure to HIV-infected blood. HIV is present in much lower amounts in other blood cell–containing body fluids, including inflammatory exudates, amniotic fluid, saliva, and vaginal secretions. The risk of seroconversion following mucous membrane or nonintact skin exposure is too low to be estimated with precision.

Criteria for Exposure

As for HBV and HCV exposures, any healthcare worker who has sustained a percutaneous, mucous membrane, or nonintact skin exposure to the blood or body fluid potentially containing blood from an HIV-infected patient should be considered exposed. The risk for infection associated with any discrete exposure depends on a number of variables, including the route of inoculation, inoculum size, exposure severity, and the stage of the source patient's illness (i.e., circulating viral burden).

Postexposure Management and Postexposure Antiretroviral Prophylaxis

The efficacy of antiretroviral chemoprophylaxis for occupational HIV exposure will likely never be definitively established in a prospective clinical trial. Nonetheless, a variety of types of studies provide indirect evidence of the efficacy of postexposure prophylaxis, including the efficacy of antiretroviral agents in preventing retroviral infection in animal models, the efficacy of antiretrovirals in preventing mother-to-child transmission, the results of the CDC's retrospective case-control study of occupational HIV infection, and our own clinical experience using antiretroviral agents for postexposure prophylaxis at our institution since 1988 (discussed in more detail in Henderson).[45] At approximately 3 to 5 year intervals, the US Public Health Service revises its recommendations for chemoprophylaxis after occupational HIV exposure, taking into account new information about the toxicity of established regimens, the ability of exposed healthcare personnel to adhere to the established regimens, the availability of new antiretroviral agents, and patterns of antiretroviral resistance. The 2013 recommendations regarding postexposure management[46] are summarized in Table 26.2.

A hospital's occupational postexposure prophylaxis program should be up to date and efficient in order to earn the confidence of healthcare personnel. The fact that treatment is immediately accessible should be widely publicized throughout the healthcare institution. All employees should be aware of the postexposure prophylaxis program and how it works. At our institution, we have distributed posters and flyers that emphasize the program, and also include information about the program in mandatory annual education sessions for clinical staff. Occupational medicine staff must be very familiar with what constitutes an exposure and must make certain that they do not overprescribe antiretrovirals. Prescribing physicians should carefully choose a regimen that can be taken by the healthcare worker. More is not necessarily better, especially if all of the drugs are vomited up. Prescribing physicians also need to be cognizant of the source patient's therapy and viral burden (if this information is immediately available) and should use this information in developing an optimal regimen.

Table 26.2 Circumstances in which expert consultation for HIV postexposure prophylaxis (PEP) is recommended[46]

Situation	Action	Caution
Delayed exposure report (i.e., more than 72 hours after time of exposure)	Use of PEP decided on case-by-case basis	Benefits of PEP uncertain after this interval
Exposure from unknown source (e.g., needle in sharps container or laundry)	Use of PEP decided on case-by-case basis, considering severity of exposure and epidemiologic likelihood of HIV exposure	Do not test needles or other sharp instruments for HIV
Exposed person is known or suspected to be pregnant	Choice of PEP regimen decided on case-by-case basis	Provision of PEP should not be delayed while awaiting expert consultation
Exposed person is breastfeeding	Choice of PEP regimen decided on case-by-case basis	Provision of PEP should not be delayed while awaiting expert consultation
Known or suspected antiretroviral drug resistance of source virus	Choice of PEP regimen will include drugs to which the source virus is unlikely to be resistant	Provision of PEP should not be delayed while awaiting resistance testing of source virus
Exposed person experiences toxicity of initial PEP regimen	Symptoms (e.g., vomiting, diarrhea) are often manageable without changing PEP regimen, using antiemetics or antimotility agents	Counseling and support for management of side effects is important to reduce anxiety and bolster ability to cope with side effects
Exposed person has a serious underlying medical illness	Risk of drug-drug interactions or drug toxicity requires careful tailoring of PEP regimen	

To the extent that it is possible, prescribers should become familiar with the antiretroviral agents, their side effects, and the appropriate strategies to manage toxicity. Prescribers should anticipate and prophylactically treat side effects (e.g., providing antiemetics for nausea and antispasmodics for diarrhea). Prescribing staff also should carefully monitor all healthcare personnel who are taking antiretrovirals for the development of signs of toxicity, as well as for adherence to the regimen. Table 26.3 summarizes circumstances in which consultative assistance from HIV specialists is recommended. If no experts are immediately available, expert guidance is available around the clock from PEPline, the National Clinicians' Postexposure Prophylaxis Hotline (sponsored by the CDC and the University of California, San Francisco), either by telephone (at 888–448–4911) or online (http://nccc.ucsf.edu/clinician-consultation/pep-post-exposure-prophylaxis/).

Other Considerations

Several additional issues must be taken into consideration when considering HIV postexposure chemoprophylaxis. Counseling and serologic testing of exposed personnel should be performed as soon as possible after the exposure. These services should be available 24 hours per day. All personnel involved in postexposure evaluation and counseling, including emergency department personnel, must be trained in and familiar with institutional protocols. Follow-up serologic testing should be performed at 6 weeks, 12 weeks, and 6 months after the exposure. Some institutions (including our own) offer additional testing at 1 year after the exposure. Exposed workers should be instructed to return immediately for clinical evaluation if they develop signs or symptoms of either drug toxicity or of acute retroviral syndrome (e.g., fever, rash, and lymphadenopathy). Occupational HIV exposure can cause severe psychological symptoms, including depression, anxiety, anger, fear, sleep disturbances, conversion symptoms, suicidal ideation, and psychosis. Postexposure counselors should be alert to these possibilities and be quick to refer the employee to specialists in crisis intervention and counseling, if necessary.

Healthcare Personnel-to-Patient Transmission

Transmission of HIV from healthcare worker to patient occurs extremely uncommonly. Nonetheless, a few such cases have been described in the literature.[47–57] Current US Public Health Service guidelines recommend that individual states either adopt the 1991 CDC guidelines or construct guidelines that are certified by the states as equivalent to the CDC guidelines.[58] The SHEA infected provider guidelines published in 2010 have become the standard that is followed widely, including by some professional societies representing providers who perform invasive procedures.[59]

The SHEA guidelines recommend that providers who have HIV viral burdens of $5x10^2$ GE/mL or greater use double gloves for all procedures and mucous membrane contact, and avoid performing the most invasive, exposure-prone procedures. The guidelines recommend no restrictions for those who have lower viral burdens, provided they adhere to infection control precautions, comply with twice-yearly viral load monitoring, and heed the advice of the expert review panel.[19] The United Kingdom's National Health Service guidelines updated

Table 26.3 HIV postexposure prophylaxis (PEP) regimens[46]

Preferred regimen	
Raltegravir PLUS Truvada (Tenofovir DF + emtracitabine)	
Alternative regimens	
Regimens combine one drug or drug pair from the left column with one pair of nucleoside/nucleotide reverse-transcriptase inhibitors from the right column.[1,2]	
Raltegravir	
Darunavir + ritonavir	Tenofovir DF + emtracitabine
Etravirine	Tenofovir DF + lamivudine
Rilpivirine	Zidovudine + lamivudine
Atazanavir + ritonavir	Zidovudine + emtracitabine
Lopinavir/ritonavir	

Alternatively, the fixed-dose combination regimen Stribild (elvitegravir, cobicistat, tenofovir DF, emtracitabine)
[1] Prescribers unfamiliar with the agents and their toxicities should consult HIV experts.
[2] Other antiretroviral drug combinations should be assembled only with expert consultation.

in 2014 require providers who perform exposure-prone procedures to undergo testing for HIV, HBV, and HCV. HIV-infected providers who have viral burdens less than 10^2 GE/mL on antiretroviral therapy or are elite controllers may perform exposure-prone procedures with quarterly monitoring.[60] Australian guidelines are more restrictive, proscribing exposure-prone procedures by HIV-infected practitioners, even if their viral loads are undetectable on antiretroviral therapy.[61] The guidelines recommend testing of all healthcare personnel and healthcare students, and prohibit dental students who are infected with HIV or other bloodborne pathogens from continuing dental training.[61]

Individual state guidelines concerning providers infected with bloodborne pathogens vary substantially, so practitioners will need to be cognizant of local and state laws.

Education and Orientation

Employee education is another area in which the biosafety, hospital epidemiology, and occupational medicine programs work together to make their initial contacts with new personnel as effective as possible. New employee orientation should contain basic information about infection control and prevention and should provide a detailed list of resources for additional information. Educational programs for staff should emphasize the basic tenets of infection control, such as use of universal or standard precautions, optimal use of personal protective equipment, hand hygiene, vaccine safety and efficacy, and identification of healthcare personnel injuries (e.g., needlesticks) and communicable illnesses (e.g., conjunctivitis, varicella, skin and soft-tissue infections, influenza-like illness, herpes zoster, other childhood viral illnesses, jaundice, and diarrhea) that require prompt evaluation by occupational medicine staff in order to prevent spread to patients and other staff.

Outbreak Investigation

The occurrence of clusters of infections caused by the same pathogen is another instance in which cooperation and close collaboration among the occupational medicine, hospital epidemiology, and biosafety programs are essential. Depending on the type of outbreak, the hospital epidemiology team will likely conduct the "shoe-leather" investigation, identify healthcare personnel at risk, and refer them to the occupational medicine service. Occupational medicine staff conduct careful interviews, provide postexposure testing and treatment as appropriate, and (in collaboration with hospital epidemiology and biosafety personnel) try to identify factors that are associated with a risk for transmission. During an outbreak, effective communication and daily interaction among these three groups is essential to effective interdiction (see Chapter 11, on outbreak investigations).

Noninfectious Adverse Events Among Hospital Staff

The hospital epidemiology service should also work closely with both the biosafety team and the occupational medicine service to evaluate noninfectious adverse events occurring among hospital staff. Clusters of certain kinds of events (e.g., needlestick injuries associated with similar circumstances of exposure) can become the stimulus for institutional performance improvement activities that can ultimately reduce the risk of these events substantially. Following an occupational HIV infection in a staff member that occurred in 1988, we developed a working group to evaluate the circumstance of every occupational exposure to blood that occurred in our institution, with the expectation that a more complete understanding of the circumstances of these exposures might provide a path to performance improvement through the

continued education and training of our staff about risks and risk reduction, instruction of staff about the appropriate use of infection control precautions, the use of intrinsically safer devices, and the modification of work practices associated with exposures. Thus, as is the case for healthcare-associated infections, noninfectious adverse events in the hospital also have healthcare-associated epidemiology that, when delineated, may provide insight into appropriate interventions and risk-reduction strategies. The hospital epidemiologist is ideally placed in the organization to facilitate the identification of factors contributing risk for such adverse events and for leading the team to design, implement, and evaluate the success of interventions designed to mitigate those risks.

Emerging Infectious Diseases

Many occupational medical services in research-oriented healthcare facilities have extensive experience managing exposures among laboratory researchers who work with communicable pathogens. The Ebola virus outbreak that began in 2014 demonstrated the important role that occupational medical services can play in assuring worker and public safety in the context of potential occupational exposures to emerging pathogens. During the Ebola outbreak that began in 2014, occupational medicine services at US hospitals that cared for Ebola-infected healthcare personnel worked closely with public health officials to monitor healthcare staff for fever and other early symptoms of Ebola infection. At our institution, the occupational medical service managed the employee monitoring program for the staff providing care to the Ebola patients and also conducted pretravel counseling and post-travel symptom monitoring for clinicians who traveled to Ebola-affected countries. Although the monitoring was a public health department responsibility, occupational medicine services in these designated facilities were effectively deputized to conduct the monitoring and followup for personnel at their hospitals.[62]

References

1. Centers for Disease Control. Immunization of health-care personnel: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2011;**60** (RR-7):1–45.
2. Breuer J, Schmid DS, Gershon AA. Use and limitations of varicella-zoster virus-specific serological testing to evaluate breakthrough disease in vaccinees and to screen for susceptibility to varicella. *J Infect Dis.* 2008;**197**(Suppl 2):S147–S151.
3. Jensen PA, Lambert LA, Iademarco MF, Ridzon R. Guidelines for preventing the transmission of Mycobacterium tuberculosis in health-care settings, 2005. *MMWR Recomm Rep*. 2005;**54** (RR-17):1–141.
4. Mazurek GH, Jereb J, Vernon A, LoBue P, Goldberg S, Castro K. Updated guidelines for using Interferon Gamma Release Assays to detect Mycobacterium tuberculosis infection – United States, 2010. *MMWR Recomm Rep*. 2010;**59** (RR-5):1–25.
5. Centers for Disease Control. Updated recommendations for use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine from the Advisory Committee on Immunization Practices, 2010. *MMWR Morb Mortal Wkly Rep*. 2011;**60** (1):13–5.
6. Pearson ML, Bridges CB, Harper SA. Influenza vaccination of health-care personnel: recommendations of the Healthcare Infection Control Practices Advisory Committee (HICPAC) and the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2006;55(RR-2):1–16.
7. Cunney RJ, Bialachowski A, Thornley D, Smaill FM, Pennie RA. An outbreak of influenza A in a neonatal intensive care unit. *Infect Control Hosp Epidemiol.* 2000;**21**(7):449–454.
8. Carman WF, Elder AG, Wallace LA, et al. Effects of influenza vaccination of health-care workers on mortality of elderly people in long-term care: a randomised controlled trial. *Lancet.* 2000;**355**(9198):93–97.
9. Hayward AC, Harling R, Wetten S, et al. Effectiveness of an influenza vaccine programme for care home staff to prevent death, morbidity, and health service use among residents: cluster randomised controlled trial. *BMJ.* 2006;**333**(7581):1241.
10. Potter J, Stott DJ, Roberts MA, et al. Influenza vaccination of health care workers in long-term-care hospitals reduces the mortality of elderly patients. *J Infect Dis.* 1997;**175**(1):1–6.
11. Saito R, Suzuki H, Oshitani H, Sakai T, Seki N, Tanabe N. The effectiveness of influenza vaccine against influenza a (H3N2) virus infections in nursing homes in Niigata, Japan, during the 1998–1999 and 1999–2000 seasons. *Infect Control Hosp Epidemiol.* 2002;**23** (2):82–86.
12. Thomas RE, Jefferson TO, Demicheli V, Rivetti D. Influenza vaccination for health-care workers who work with elderly people in institutions: a systematic review. *Lancet Infect Dis.* 2006;**6**(5):273–279.
13. Infectious Diseases Society of America SfHEoA, Pediatric Infectious Diseases Society, IDSA, SHEA, and PIDS Joint Policy Statement on Mandatory Immunization of Health Care Personnel According to the ACIP-Recommended Vaccine Schedule. 2013.
14. Werner BG, Grady GF. Accidental hepatitis-B-surface-antigen-positive inoculations. *Use of e antigen to estimate infectivity. Ann Intern Med.* 1982;**97**(3):367–369.
15. U.S. Public Health Service. Updated U. S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis. *MMWR Recomm Rep*. 2001;**50**(RR-11):1–52.
16. Schillie S, Murphy TV, Sawyer M, et al. CDC guidance for evaluating health-care personnel for hepatitis B virus protection and for administering postexposure management. *MMWR Recomm Rep*. 2013;**62**(RR-10):1–19.
17. Harpaz R, Von Seidlein L, Averhoff FM, et al. Transmission of hepatitis B virus to multiple patients from a surgeon without evidence of inadequate infection control. *N Engl J Med.* 1996;**334**(9):549–554.
18. Johnston BL, MacDonald S, Lee S, et al. Nosocomial hepatitis B associated with orthopedic surgery–Nova Scotia. *Can Commun Dis Rep.* 1992;**18**(12):89–90.
19. Henderson DK, Dembry L, Fishman NO, et al. SHEA guideline for management of healthcare workers who are infected with hepatitis B virus, hepatitis C virus, and/or human immunodeficiency virus. *Infect Control Hosp Epidemiol.* 2010;**31**(3):203–232.
20. Centers for Disease C, Prevention. Updated CDC recommendations for the management of hepatitis B virus-

infected health-care providers and students. *MMWR Recomm Rep*. 2012;**61**(RR-3):1–12.

21. Recommendations for preventing transmission of human immunodeficiency virus and hepatitis B virus to patients during exposure-prone invasive procedures. *MMWR Recomm Rep*. 1991;**40**(RR-8):1–9.
22. Department of Health (UK). *Hepatitis B Infected Healthcare Workers and Antiviral Therapy.* London; 2007:7235.
23. Gunson RN, Shouval D, Roggendorf M, et al. Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections in health care workers (HCWs): guidelines for prevention of transmission of HBV and HCV from HCW to patients. *J Clin Virol.* 2003;**27**(3):213–230.
24. Grebely J, Page K, Sacks-Davis R, et al. The effects of female sex, viral genotype, and IL28B genotype on spontaneous clearance of acute hepatitis C virus infection. *Hepatology.* 2014;**59**(1):109–210.
25. Farci P, Shimoda A, Coiana A, et al. The outcome of acute hepatitis C predicted by the evolution of the viral quasispecies. *Science.* 2000;**288**(5464):339–344.
26. Aleman S, Rahbin N, Weiland O, et al. A risk for hepatocellular carcinoma persists long-term after sustained virologic response in patients with hepatitis C-associated liver cirrhosis. *Clin Infect Dis.* 2013;**57**(2):230–236.
27. Henderson DK. Managing occupational risks for hepatitis C transmission in the health care setting. *Clin Microbiol Rev.* 2003;**16**(3):546–568.
28. Service USPH. Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis. *MMWR Recomm Rep*. 2001;**50**(RR-11):1–52.
29. Henderson DK. Management of needlestick injuries: a house officer who has a needlestick. *JAMA.* 2012;**307**(1):75–84.
30. Larghi A, Zuin M, Crosignani A, et al. Outcome of an outbreak of acute hepatitis C among healthy volunteers participating in pharmacokinetics studies. *Hepatology*. 2002;**36**(4 Pt 1):993–1000.
31. Hellinger WC, Bacalis LP, Kay RS, et al. Health care–associated hepatitis C virus infections attributed to narcotic diversion. *Ann Intern Med.* 2012;**156**(7):477–482.
32. Warner AE, Schaefer MK, Patel PR, et al. Outbreak of hepatitis C virus infection associated with narcotics diversion by an hepatitis C virus-infected surgical technician. *Am J Infect Control.* 2015;**43**(1):53–58.
33. Duckworth GJ, Heptonstall J, Aitken C. Transmission of hepatitis C virus from a surgeon to a patient. The Incident Control Team. *Commun Dis Public Health*. 1999;**2**(3):188–192.
34. Esteban JI, Gomez J, Martell M, et al. Transmission of hepatitis C virus by a cardiac surgeon. *N Engl J Med.* 1996;**334**(9):555–560.
35. Public Health Laboratory Service. Hepatitis C virus transmission from health care worker to patient. *Commun Dis Rep CDR Wkly*. 1995;**5**(26):121.
36. Public Health Laboratory Service. Transmission of hepatitis C virus from surgeon to patient prompts lookback. *Commun Dis Rep CDR Wkly*. 1999;**9**(44):387.
37. Public Health Laboratory Service. Two hepatitis C lookback exercises – national and in London. *Commun Dis Rep CDR Wkly*. 2000;**10**(14):125–8.
38. Willocks L. Hepatitis C lookback in two healthcare trusts in the south of England. *Euro Surveill.* 2001;**5**(22):1745.
39. Shemer-Avni Y, Cohen M, Keren-Naus A, et al. Iatrogenic transmission of hepatitis C virus (HCV) by an anesthesiologist: comparative molecular analysis of the HCV-E1 and HCV-E2 hypervariable regions. *Clin Infect Dis.* 2007;**45**(4):e32–e38.
40. Ross RS, Viazov S, Thormahlen M, et al. Risk of hepatitis C virus transmission from an infected gynecologist to patients: results of a 7-year retrospective investigation. *Arch Intern Med.* 2002;**162**(7):805–810.
41. Ross RS, Viazov S, Roggendorf M. Phylogenetic analysis indicates transmission of hepatitis C virus from an infected orthopedic surgeon to a patient. *J Med Virol.* 2002;**66**(4):461–467.
42. Ross RS, Viazov S, Gross T, Hofmann F, Seipp HM, Roggendorf M. Transmission of hepatitis C virus from a patient to an anesthesiology assistant to five patients. *N Engl J Med.* 2000;**343**(25):1851–1854.
43. Henderson DK, Fahey BJ, Willy M, et al. Risk for occupational transmission of human immunodeficiency virus type 1 (HIV-1) associated with clinical exposures. a prospective evaluation. *Ann Intern Med.* 1990;**113**(10):740–746.
44. Ippolito G, Puro V, De Carli G. The risk of occupational human immunodeficiency virus infection in health care workers. Italian Multicenter Study. The Italian Study Group on Occupational Risk of HIV infection. *Arch Intern Med.* 1993;**153**(12):1451–1458.
45. Henderson DK. Human Immunodeficiency Virus in Health Care Settings. In: Bennett JE, Dolin, R., Blaser, M.J., eds. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 8th ed. Philadelphia, Pa.: Elseview; 2015:3361–3375.
46. Kuhar DT, Henderson DK, Struble KA, et al. Updated US Public Health Service guidelines for the management of occupational exposures to human immunodeficiency virus and recommendations for postexposure prophylaxis. *Infect Control Hosp Epidemiol.* 2013;**34**(9):875–892.
47. Centers for Disease Control and Prevention. Possible transmission of human immunodeficiency virus to a patient during an invasive dental procedure. *MMWR Morb Mortal Wkly Rep*. 1990;**39**(29):489–493.
48. Centers for Disease Control and Prevention. Update – transmission of HIV infection during an invasive dental procedure – Florida. *MMWR Morb Mortal Wkly Rep*. 1991;**40**(2):21–27, 33.
49. Centers for Disease Control and Prevention. Update: investigations of patients who have been treated by HIV-infected health-care workers. *MMWR Morb Mortal Wkly Rep*. 1992;**41**(19):344–346.
50. Ciesielski C, Marianos D, Ou CY, et al. Transmission of human immunodeficiency virus in a dental practice. *Ann Intern Med.* 1992;**116**(10):798–805.
51. Ciesielski CA, Bell DM, Marianos DW. Transmission of HIV from infected health-care workers to patients. *AIDS.* 1991;**5**(Suppl 2):S93–S97.
52. Ou CY, Ciesielski CA, Myers G, et al. Molecular epidemiology of HIV transmission in a dental practice. *Science.* 1992;**256**(5060):1165–1171.
53. Astagneau P, Lot F, Bouvet E, et al. Lookback investigation of patients potentially exposed to HIV type 1 after a nurse-to-patient transmission. *Am J Infect Control.* 2002;**30**(4):242–245.

54. Blanchard A, Ferris S, Chamaret S, Guetard D, Montagnier L. Molecular evidence for nosocomial transmission of human immunodeficiency virus from a surgeon to one of his patients. *J Virol.* 1998;**72**(5):4537–4540.
55. Bosch X. Second case of doctor-to-patient HIV transmission. *Lancet Infect Dis.* 2003;**3**(5):261.
56. Goujon CP, Schneider VM, Grofti J, et al. Phylogenetic analyses indicate an atypical nurse-to-patient transmission of human immunodeficiency virus type 1. *J Virol.* 2000;**74**(6):2525–2532.
57. Lot F, Seguier JC, Fegueux S, et al. Probable transmission of HIV from an orthopedic surgeon to a patient in France. *Ann Intern Med.* 1999;**130**(1):1–6.
58. Centers for Disease Control and Prevention. Recommendations for preventing transmission of human immunodeficiency virus and hepatitis B virus to patients during exposure-prone invasive procedures. *MMWR Recomm Rep*. 1991;**40**(RR-8):1–9.
59. American College of O, Gynecologists Committee on Gynecologic P. ACOG Committee Opinion No. 489: Hepatitis B, hepatitis C, and human immunodeficiency virus infections in obstetrician-gynecologists. *Obstet Gynecol.* 2011;**117**(5):1242–1246.
60. Public Health England. *The Management of HIV infected Healthcare Workers who perform exposure prone procedures*: updated guidance, January 2014. London; 2014.
61. Communicable Disease Network Australia. Australian National Guidelines for the Management of Health Care Workers known to be Infected with Blood-Borne Viruses. 2012.
62. Palmore TN, Barrett K, Michelin A, et al. Challenges in managing patients who have suspected or confirmed Ebola virus infection at the National Institutes of Health. *Infect Control Hosp Epidemiol.* 2015;**36**(6):623–626.

Chapter

27 Tuberculosis Infection Control in Healthcare Settings

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Introduction and Historical Overview

The World Health Organization (WHO) estimates that there are 9.6 million new tuberculosis (TB) cases and 1.5 million deaths due to TB each year.[1] Tuberculosis is the leading cause of death due to an infectious disease, and the number of TB deaths now exceeds the number of HIV-related deaths each year (1.5 vs. 1.2 million per year). The overwhelming majority of TB cases occur in low- and middle-income countries; <1% of all TB cases occur in the United States.

Tuberculosis is spread person to person by an airborne route. Tuberculosis has been recognized and accepted by the medical community as a potential occupational hazard only for several decades.[2] The risk of transmission of *Mycobacterium tuberculosis* from patients with tuberculosis disease to other hospitalized patients and healthcare workers (HCWs) was established by the 1950s when, as noted by Myers et al., "a rapid decline of tuberculosis in the general population made the disease among physicians more conspicuous."[2,3] With the introduction of effective chemotherapy in the 1950s and a progressive decline in the incidence of tuberculosis in the US until the mid-1980s, the risk of occupational infection and clinical tuberculosis declined among US HCWs. With this decline, less attention was paid toward TB infection control measures in hospitals. Thus few healthcare facilities in the US were prepared for the changing epidemiology of TB since the mid-1980s.

Between 1985 and 1992, there was a resurgence of TB in the US with a 20 percent increase in the number of reported cases. This resurgence was fueled by the decay of the public health infrastructure (due to underfunding) and the HIV epidemic.[4–6] The surge of cases combined with neglect toward TB infection control activities and ineffective control measures led to a number of reports of nosocomial transmission of TB in the late 1980s and early 1990s.[7–20] A number of these explosive and unfortunate outbreaks involved transmission of multidrug-resistant (MDR) resistant strains of *M. tuberculosis* (resistance to at least both isoniazid and rifampin) to patients and HCWs that was associated with significant morbidity and mortality, especially among HIV-infected and other immunocompromised persons.[7] Outbreaks of MDR-TB and extensively drug-resistant (XDR)-TB have also been reported from lower and middle income countries (LMIC).[21–27] XDR-TB is defined as resistance to isoniazid and rifampin (MDR-TB) plus a fluoroquinolone and at least one second line injectable agent (such as amikacin, capreomycin, or kanamycin). Transmission of TB is ongoing in many locations in high-burden, low- and middle-income countries and may not be fully recognized because of lack of adequate laboratory infrastructure and surveillance of HCWs for TB. This is reflected by much higher rates of TB and latent TB infection among HCWs in resource-limited settings.[28,29]

Nosocomial transmission of XDR-TB at a small rural hospital in Kwazulu-Natal province in South Africa in 2005 and 2006 highlights the devastating nature of outbreaks of highly drug-resistant TB and brought attention of the impact of healthcare-associated TB transmission to the global community.[21,22] In the initial report, 52 of 53 persons (patients and healthcare workers at the hospital) who acquired XDR-TB died, and all those tested were HIV co-infected[21]. A follow-up report on this outbreak noted that among 148 patients with XDR-TB, 98 percent were HIV-infected, and genotyping identified a predominant cluster comprising 96 percent of *M. tuberculosis* isolates.[22] Network analysis demonstrated a high degree of interconnectedness that resulted in multiple generations of nosocomial transmission. Similarities were seen between this XDR-TB outbreak in South Africa and outbreaks of MDR-TB reported from the US in the late 1980s and early 1990s.[7,8]

Several factors have contributed to outbreaks of TB, including MDR- and XDR-TB in hospitals and other institutional settings (Tables 27.1 and 27.2).[7,22,30–35] Failure to implement effective TB infection control strategies has resulted in delays in the suspicion and diagnosis of TB, identification of drug resistance, and in initiation of appropriate therapy; this has resulted in lack of separation or delayed separation of infectious patients from others. In addition, inadvertent clustering of patients with infectious TB (often unrecognized and not diagnosed) with susceptible immunocompromised patients (most often HIV-infected persons) has facilitated and amplified nosocomial transmission of TB, including highly drug-resistant TB. Second, environmental controls were often nonexistent (e.g., in low and middle-income country settings) or inadequate. For example, airborne infection isolation rooms did not exist or when present, had positive rather than negative pressure, air recirculated from isolation rooms to other areas, doors to isolation rooms were left open, isolation precautions were discontinued too soon, and HCWs did not wear adequate respiratory protection.[34] A lack of adequate laboratory infrastructure has also contributed to healthcare-associated TB transmission. In many settings, especially in resource-limited areas, there is lack of resources for the rapid diagnosis of TB and rapid diagnosis of MDR-TB through the use of nucleic acid amplification tests.

Implementation of effective TB infection control measures[36,37] based on a hierarchy of control measures (administrative controls, environmental controls, and personal respiratory protection), which are now recommended by the Centers for Disease Control and Prevention (CDC), WHO, and others[30–32] and the decreasing incidence of TB in the community since 1992 have led to a dramatic decrease in the risk of transmission of TB in healthcare settings in the US.[38–41] The control of TB in healthcare settings in the US contributed to enhanced control in the community, which was also facilitated by rebuilding of the public health infrastructure and expanded use of directly observed therapy (DOT) beginning in the 1990s.[42] CDC last updated TB infection control guidelines for the US in 2005 ("Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Healthcare Settings").[31] The 2005 guidelines do not fully address the changing epidemiology of TB in the US and the current low risk of most US HCWs and may result in over-testing of low-risk healthcare workers for latent TB infection, which can lead to false positive results, especially when the pretest probability of infection is quite low.[43] This is a particular issue when interferon-gamma release assays are used for serial testing of low-risk HCWs.[44] Despite the decreasing incidence of TB in the US since 1992[45] and lower risk of transmission in US healthcare facilities, TB infection control remains an important responsibility of healthcare personnel. Reports have highlighted delays in the diagnosis of patients with TB

Table 27.1 Factors facilitating nosocomial transmission of tuberculosis (TB)

1. *Inefficient infection-control procedures*
   A. Delayed suspicion and diagnosis
      - Clustering of patients with unsuspected TB with susceptible immunocompromised patients including persons living with HIV
      - Delayed recognition of TB in HIV-infected patients because of "atypical" presentation or low clinical suspicion leading to misdiagnosis (HIV+ or HIV-)
      - Failure to recognize and isolate patients with active pulmonary disease
   B. Failure to recognize ongoing infectiousness of patients
2. *Laboratory delays in identification and susceptibility testing of M. tuberculosis isolates*
3. *Inadequate airborne infection (respiratory) isolation facilities and engineering controls*
   Lack of airborne infection (respiratory) isolation rooms
   Recirculation of air from airborne infection isolation rooms to other parts of the hospital
4. *Delayed initiation of effective antituberculosis therapy*

[Adapted from references[7,30–32]]

Table 27.2 Factors that may facilitate nosocomial transmission of tuberculosis (TB) in low- and middle-income countries

Area	Factor
Factors that increase risk for nosocomial exposure	• Delayed diagnosis of patients with infectious TB and lack of laboratory infrastructure to provide a rapid diagnosis
	• Overwhelming numbers of TB patients and repeated exposure to patients with smear-positive TB
	• Unnecessary or prolonged hospitalization of patients with smear-positive pulmonary TB
	• Delays in initiating anti-TB treatment for those with active TB disease
	• Poor adherence to treatment, use of suboptimal treatment regimens, and lack of adequate patient support to improve adherence
	• Interruptions in supply of TB medications in healthcare facilities
Lack of effective infection-control procedures	• Failure to recognize and isolate or separate patients with active pulmonary TB
	• Laboratory delays in identification of TB, and poor use of tests such as sputum microscopy to identify infectious TB cases
	• Clustering patients with TB with susceptible and vulnerable patients (e.g., HIV-infected patients)
	• Lack of HIV testing services and delayed recognition of TB in HIV-infected patients because of atypical presentation and low level of clinical suspicion
	• Inadequate airborne infection (respiratory) isolation facilities and environmental controls
	• Overcrowded hospital wards and outpatient departments
	• Poorly ventilated wards and rooms
	• Lack of airborne infection isolation rooms

Table 27.2 (cont.)

Area	Factor
	• Lack of personal protection equipment (e.g., respirators)
	• Lack of screening programs to detect and treat latent TB infection and active TB among healthcare workers
	• Lack of commitment on the part of hospitals to invest in infection control programs
	• Lack of national guidelines on nosocomial TB tailored to the local country's healthcare environment
Gaps in knowledge and awareness	• Lack of awareness about nosocomial TB transmission in healthcare settings
	• Lack of political will to provide adequate resources to implement effective TB infection control measures
	• Belief by some hospital administrators and healthcare workers that nosocomial infection is an occupational hazard that cannot be avoided
	• Lack of educational programs on occupational safety and hygiene
	• Poor patient education regarding cough etiquette and sputum disposal

Adapted from reference (53).

that have contributed to prolonged infectiousness of index cases and TB outbreaks in the US.[46,47] Failure to be vigilant and recognize undiagnosed patients with TB has resulted in nosocomial transmission in the US in the twenty-first century, even in an era of improved TB control as noted in reports from CDC and others.[1,48]

Unlike the United States, Canada and other high-income, low-incidence countries, exposure to and acquisition of tuberculosis remains a major occupational hazard in high TB burden, resource-limited areas.[28,29,49–52] Unfortunately, despite guidelines by WHO about prevention of healthcare-associated transmission of TB in resource-limited areas, in the past little attention has been given to TB infection control measures in most low- and middle-income countries.[30,33] Acquisition of TB by HCWs in low- and middle-income countries has too often been accepted as an occupational hazard in resource-limited countries.[53] However, given the emergence and spread of MDR- and XDR strains of TB, including outbreaks of XDR-TB in South Africa affecting both patients and HCWs and associated with high morbidity and mortality, TB infection control measures can no longer be ignored.[21,22,50] Political commitment for support of TB infection control has not generally been a priority for the international community or funders. Advocacy by HCWs and others[33] is essential in efforts to enhance TB infection control, especially in high-burden, low-resource areas where HIV/TB co-infection is prevalent. Furthermore, effective global control of MDR- and XDR-TB will also require implementation of measures to prevent institutional spread of drug-resistant TB.

This chapter is not intended to provide an exhaustive summary of TB infection control measures; the 2005 CDC guidelines outline recommendations for US healthcare facilities, while more recent 2014 Canadian guidelines provide updated recommendations that may better reflect the current epidemiology of TB in North America, especially the negative consequences of over-testing of low-risk healthcare workers.[31,32] The WHO TB infection control recommendations focused on resource-limited countries.[30] Guidelines and suggestions on how to implement TB infection control measures in resource-limited settings have been published and need greater attention by the international community.[54,55]

This chapter outlines the basic framework for developing a TB control program including how to assess the risk of TB transmission in a healthcare setting, how to prioritize control measures based on effectiveness, and how to meet current US regulatory requirements. Also highlighted are some of the challenges for TB infection control in high-incidence, resource-limited areas.

Institutional Controls for the Prevention of Nosocomial Tuberculosis

Nosocomial TB is driven by the prevalence of disease in the community served by the hospital or healthcare system[56] and the efficacy of TB infection control measures instituted. Rates of TB in the US have decreased significantly since 199245 but still vary widely by geographic area. Frequently, urban areas[57] and areas with large numbers of foreign-born persons from TB endemic areas have the highest rates of TB disease. The global epidemic of TB has had a significant impact upon the US; 66 percent of US TB cases occurred among foreign-born persons in 2015[58]; foreign-born persons account for 85 percent of MDR TB cases reported in the US.[45]

An effective TB infection control program requires early identification, separation of potentially infectious persons by

Table 27.3 Major goals in the control and prevention of nosocomial tuberculosis

1. Implementation of a hierarchy of tuberculosis infection control measures (see Table 27.3).
2. Airborne infection isolation (AII) of patients as soon as tuberculosis is suspected, whether during emergency care or on admission to the institution.
3. Start empirical antituberculosis therapy as soon as tuberculosis is suspected with an appropriate regimen (generally, a four-drug regimen of rifampin, isoniazid, pyrazinamide, and ethambutol will be employed unless there is high suspicion for multidrug-resistant [MDR]-TB.)
4. Comply with airborne infection isolation procedures during the patient's hospitalization until laboratory and clinical evidence excludes the possibility of tuberculosis or the risk of transmission.
5. Conduct laboratory studies as soon as possible to confirm or exclude the presence of tuberculosis and to identify multidrug-resistant strains of *M. tuberculosis*; molecular diagnostic tests can help provide rapid assessment of whether a patient has tuberculosis.
6. Enhance occupational health services to monitor for tuberculosis infection and disease in healthcare workers.
7. Discharge patients with tuberculosis from acute care only when arrangements have been made for appropriate isolation from contact with susceptible individuals (e.g., in a stable home or another stable location with no new persons exposed).
8. Cooperate closely with public health and other community agencies to provide resources that ensure the completion of therapy (e.g., directly observed therapy).
9. Tuberculosis-related healthcare worker education to support the above goals.

Adapted from reference (31).

airborne infection isolation, rapid diagnosis, and early initiation of effective treatment of active TB disease.[30–32,54] The termination of outbreaks in the US and prevention of nosocomial transmission of TB followed implementation of effective infection control programs.[31,36,37,59] Policies and procedures regarding TB infection control should be developed by all healthcare facilities that reflect their risk and patient population served. All healthcare settings should implement an effective TB infection-control program designed to detect disease early and to isolate or geographically separate patients with known or suspected TB and promptly refer or treat those who have TB disease. The major goals of a TB infection control program are outlined in Table 27.3.

A Assignment of Responsibility

The first step in establishing an effective TB infection control program is for an institution to assign responsibility to a specific person or persons and ensure they have the authority and support to implement such a program. The person or persons should have expertise or access to expertise in the areas of infection control and healthcare epidemiology, public health, occupational health, engineering, and clinical microbiology. Frequently this responsibility is given to institution's Infection Control Committee. The group should develop written tuberculosis infection control policies based on the institution's risk assessment. Policies and procedures should be reviewed on at least an annual basis and updated as indicated. At large institutions located in urban areas that care for sizable numbers of patients with active TB, it has been helpful to designate an individual (e.g., one of the Infection Control Practitioners) to serve as the coordinator of TB infection control activities.

B Risk Assessment

All healthcare settings should conduct regular, periodic (at least annual) TB risk assessments regardless of whether or not patients with suspected or confirmed TB disease will receive care at their institution. The TB risk assessment determines the risk of nosocomial transmission of *M. tuberculosis* in the healthcare setting by examining a numbers of factors, including 1) community incidence of TB disease; 2) number of patients with TB presenting for care at the healthcare facility, regardless of whether they receive care in the setting or are transferred to another healthcare setting; 3) timeliness of the recognition, isolation, and evaluation of patients with suspected or confirmed TB; and 4) evidence for transmission of *M. tuberculosis* in the setting. Local and state public health departments can help infection control personnel obtain information about their community's TB profile. Other sources of information on TB cases include extended-care facilities, schools, homeless shelters, and prisons. Even if there are no reported cases of TB in a community, infection control staff still should determine if patients with TB may have been admitted or treated in the facility. Good sources for this information are the microbiology laboratory's database, infection control records, and medical records databases containing discharge diagnoses, autopsy, and surgical pathology reports.

CDC has recommended using a risk classification system for US healthcare settings based on the size of the institution and the number of persons with active TB disease seen at the institution; this CDC-recommended system includes low-risk, medium risk, or ongoing transmission categories.[31] While risk assessment is important, the parameters used to determine the degree of risk in these CDC guidelines are somewhat arbitrary and not evidence based, as discussed below. In general, a risk classification is determined for the entire setting although in certain circumstances such as a large healthcare organization that encompasses several sites, specific areas can be defined by geography, functional units, or location.

CDC guidelines[31] recommend that hospitals with >200 beds that provide care for <6 patients with TB per year are categorized as *low-risk* while those that care for >6 patients with TB per year are considered *medium risk* (regardless of occupational risk to HCWs based on results of tuberculin skin testing). For inpatient settings with <200 beds, those that

provide care to <3 patients with TB in the past year are considered *low-risk*, and those with >3 TB cases in the past year are considered *medium risk*. Outpatient clinics, outreach or home health settings that provide care to <3 patients with TB per year are considered *low risk*, and those that provide care for >3 patients are considered *medium risk*. Tuberculosis clinics and outreach programs as well as other outpatient settings where care of persons with TB is provided should be classified as *medium risk*. Any institution, clinic, or setting with evidence of patient-to-patient or patient-to-healthcare worker transmission of *M. tuberculosis* or evidence of ongoing nosocomial transmission of TB should be classified as *potential ongoing transmission* until appropriate infection control measures have been implemented and transmission has been demonstrated to have been stopped. *Potential ongoing transmission* should be a temporary classification only. When nosocomial transmission of TB is suspected, an immediate investigation, active and corrective steps should be implemented. This may include consultation with public health officials or other experts in healthcare epidemiology and infection control. Evidence of potential nosocomial transmission of TB includes clusters of new positive tests for latent TB infection (tuberculin skin test [TST] or interferon-γ release assays [IGRA] including the QuantiFERON-TB Gold in Tube or TSPOT.TB tests) among healthcare workers, increased rates of healthcare worker TST or IGRA conversions, a HCW with potentially infectious TB, unrecognized disease in patients or HCWs, or recognition of an identical strain of *M. tuberculosis* in patient or HCW with TB disease.

Based on the finding of the risk assessment, the appropriate level of administrative, environmental, and respiratory protection policies to prevent occupational exposure to and nosocomial transmission of TB can be determined. CDC recommends that the frequency of diagnostic testing for latent TB infection (with either the TST or IGRA) of HCWs be based on the finding of the risk assessment and is discussed in additional detail below. Unfortunately, current CDC TB infection control guidelines published in 2005[31] likely misclassify many institutions into the "medium" risk category that will lead to overtesting of low-risk HCWs for latent TB infection in serial (annual) testing programs. This can lead to the majority of positive tests (TST or IGRA) being false positive results due to testing of very low-risk HCWs, even when using a highly sensitive and specific diagnostic test.[43,60]

Hierarchy of Tuberculosis Infection Control Measures

A "hierarchy of controls" that include administrative controls, engineering controls, and respiratory protection (Table 27.4) are recommended by CDC, the Public Health Agency of Canada, and WHO to prevent nosocomial transmission of tuberculosis.[30–32] Implementation of this hierarchy has been noted to be effective in terminating outbreaks and preventing nosocomial transmission of TB.[30,31,36,38] An infection control program should achieve the following goals: early identification of patients with TB disease, prompt airborne infection isolation that ensures patients who may have infectious TB are separated from other patients, and prompt diagnosis and effective treatment of persons with active disease (or rapid transfer of the patient to another facility that treats patients with TB if the admitting facility does not). The specific control measures can be prioritized based on their relative effectiveness in reducing risk of transmission and are discussed below.

Table 27.4 Hierarchy of tuberculosis infection control measures

1. Administrative controls (most essential component)
   - Careful screening of patients, isolation, early diagnosis, and treatment
   - Healthcare worker–directed measures
   - Comprehensive tuberculin skin testing program for healthcare workers
   - Healthcare worker education
2. Environmental controls
   - Airborne Infection Isolation (i.e., negative pressure) rooms; a single pass ventilation system is preferred; use HEPA filtration If recirculation of air is necessary
   - Ultraviolet germicidal irradiation (UVGI) can be used as a supplement or adjunct to other environmental controls (e.g., ventilation) in settings where persons with undiagnosed and infectious TB could potentially contaminate the air (e.g., waiting rooms, emergency rooms, corridors, central areas) or as an adjunct to negative pressure ventilation in rooms or areas where suspected or confirmed infectious TB patients are isolated or high-risk procedures are performed (e.g., bronchoscopy, sputum induction)
3. Personal respiratory protection equipment (including use of N-95 respirators)

Adapted from references (30–32).

A Administrative Controls

Administrative controls are the most important TB infection control measures[36] and consist of measures to reduce the risk of exposure to persons with infectious TB (Table 27.4). A healthcare facility should implement administrative controls first, because these controls most effectively reduce the risk of nosocomial transmission.[36,38,41,61] Administrative controls include developing and implementing effective policies and protocols to assure that persons likely to have TB disease are identified rapidly, isolated properly, evaluated clinically, and treated appropriately. This requires that HCWs carefully evaluate patients upon their initial encounter and promptly isolate any patient who they suspect may have TB until laboratory and clinical evidence eliminates this diagnosis. Hospitals can implement an early identification and isolation protocol more efficiently by authorizing both nurses and physicians to isolate patients with suspected TB and by developing policies that allow staff to automatically isolate certain patients (e.g.,

patients for whom TB is in the differential diagnosis or from whom specimens are ordered for acid-fast bacilli (AFB) smear, culture, and/or for nucleic acid amplification tests).[36,62] Many institutions have implemented policies that include mandatory airborne infection isolation (AII) for certain patients in order to facilitate the success of administrative controls.[2,36,63] Moreover, because patients with HIV infection may present with atypical signs and symptoms, some facilities isolate all patients with HIV infection who have clinical symptoms suggestive of TB (e.g., fever, cough, and/or an abnormal chest radiograph) until appropriate diagnostic tests are negative for TB. For example, at Grady Memorial Hospital in Atlanta, which cares for relatively large numbers of patients with TB, including those who are HIV co-infected, the airborne infection isolation policy requires that all patients admitted to the hospital with known TB, those with TB in the differential diagnosis or who have sputum or respiratory specimens for AFB ordered; and those who are HIV infected and have an abnormal chest radiograph (CXR), be placed in airborne infection isolation until TB is ruled out. Generally, the diagnosis is excluded by obtaining two or three negative AFB smears of sputum or other respiratory specimens and/or negative nucleic acid amplification test results (e.g., Xpert MTB/RIF).[64–66] Airborne infection isolation precautions policies and procedures should be developed based on the local epidemiology of the disease in the community served by a particular facility.

The protocol for early identification of patients with TB and patient population served by a healthcare facility will determine the number of negative-pressure airborne infection isolation rooms required. It should be anticipated that some patients who do not have TB disease will be isolated to prevent nosocomial transmission of *M. tuberculosis*. At Grady Memorial Hospital in Atlanta, which provides care to more patients with TB than any other hospital in the Southeast, the "rule out" ratio of patients isolated to patients found to have TB disease was reported to be 10:1 although this ratio may increase if TB case rates continue to fall.[63] Reports from other US institutions suggested a range of 8:1 to 14:1 in the 1990s.[67] In a low prevalence Midwestern state (Iowa), a group of investigators predicted that as many as 93 patients without TB would be isolated for every case diagnosed.[68] The expected "rule out" ratio is not well defined, especially in recent years, and likely varies by geographic area based on the prevalence of tuberculosis in the community and at the facility served. However, because there is little or no margin of error when detecting persons with TB in that a single person with undiagnosed disease can lead to an outbreak,[31,69] a high sensitivity is required and therefore some degree of "overisolation" is to be expected. At large institutions, increased efficiency in the evaluation of patients who subsequently "rule out" for TB has been demonstrated by clustering AII rooms on a respiratory isolation ward.[63] While CDC TB infection control guidelines recommend obtaining three sputum samples for AFB smear and culture when evaluating patients for pulmonary tuberculosis, some institutions in the US and elsewhere have switched to obtaining two samples in an effort to enhance efficiency given that the addition of a third specimen adds little to the sensitivity of a TB diagnosis.[31,70–72] In addition, the Food and Drug Administration (FDA) has approved use of the Xpert MTB/RIF assay (a nucleic acid amplification test that employs real-time PCR technology)[73] to include testing of either one or two sputum specimens as an alternative to examination of serial acid-fast stained sputum smears to aid in the decision of whether continued airborne infection isolation is warranted.[65] This change reflects the outcome of a recent multicenter international study demonstrating that negative Xpert MTB/ RIF assay results from either one or two sputum specimens are highly predictive of the results of two or three negative acid-fast sputum smears.[74] A single Xpert MTB/RIF assay result detected approximately 97 percent of patients who were AFB smear–positive and culture-confirmed as infected with *M. tuberculosis*, and a single negative Xpert MTB/RIF assay result predicted the absence of AFB smear–positive pulmonary TB with a negative predictive value of 99.7 percent.

Several of the measures mentioned above can enhance efficiency and provide significant cost savings to the institution and better use of AII rooms, which are often in limited supply.

In addition, it should be noted that individuals with suspected or known infectious TB should wear a surgical mask when not in an airborne infection isolation (negative pressure) room or a local exhaust ventilation enclosure (for example, when transported to have a procedure or diagnostic test).[31] The purpose of the surgical mask is to block aerosols produced by coughing, talking, and breathing. In general, the time outside of an airborne infection isolation room should be minimized and compliance with wearing a mask should be monitored.

Administrative Controls in Resource-Limited Areas: Unfortunately, adequate TB infection control measures have generally not been implemented at healthcare facilities in many resource-limited settings. Health system factors including lack of staff, lack of space to separate infectious patients from those without TB (e.g., absence of airborne infection isolation rooms), and lack of adequate resources and infrastructure (including laboratory infrastructure) are among the barriers.[75] Healthcare workers in resource-limited countries are often very knowledgeable and familiar with the risk of occupational exposure to tuberculosis and have concerns about their risk of contracting tuberculosis.[33,76–79] Strengthening health systems and the political will is an essential component in improving patient and healthcare worker safety at healthcare facilities in resource-limited areas. Demonstration projects on how best to implement effective TB infection control measures in resource-limited areas are urgently needed. One proposed approach that provides a framework for the implementation of administrative controls in resource-limited areas is called F-A-S-T (Table 27.5).[54] The availability of rapid molecular diagnostic tests such as the Xpert MTB/RIF[73] provides the laboratory infrastructure that can support rapid diagnosis of pulmonary TB among patients at the time of admission to healthcare facilities. This will allow for cohorting of patients at resource-limited facilities by the presence of drug susceptible TB versus MDR-TB. A few demonstration projects are currently in progress in high-

Table 27.5 **F-A-S-T**: a refocused, intensified, administrative tuberculosis transmission control strategy for resource-limited areas

*F*ind TB cases – rapid diagnosis of TB cases on admission
• Focus on *rapid molecular diagnosis* using rapid molecular diagnostic tests such as the Gene Xpert MTB/RIF
• Sputum smear – can be rapid, but limited diagnostic capacity
*A*ctive TB case finding
• Focus on cough surveillance at all entrance points to a healthcare facility
*S*eparate patients with active TB from others *to reduce exposure*
• Building design and engineering
• Cough hygiene and triage
*T*reat *effectively, based on rapid Drug Susceptibility Testing (DST)*
• Focus on rapid molecular DST – such as the Xpert MTB/RIF, which can provide rapid TB diagnosis and rifampin resistance (which is generally a marker for MDR-TB)

Adapted from reference (54).

burden, low- and middle-income countries,[54] but data are urgently needed on the effectiveness of this approach. If this approach is shown to be an effective method of implementing administrative controls, resources need to be made available to scale up this intervention in resource-limited areas.

Surveillance for Latent Tuberculosis Infection

Surveillance for latent TB infection (LTBI) in HCWs is a component of the administrative controls. The appropriate frequency of performing diagnostic tests (either tuberculin skin testing or commercially available and FDA-approved interferon-gamma release assays [IGRAs] including QuantiFERON-TB Gold in Tube or TSPOT.TB) of HCWs should be determined by a risk assessment that reflects the occupational risk of acquisition of *M. tuberculosis* among HCWs. Given the low positive predictive value of diagnostic tests when testing low-risk and low-prevalence populations for LTBI, frequent (serial) testing of HCWs in low-risk settings in North America is not recommended because it will lead to false positive results.[43,44,60] However, because current CDC guidelines define "medium" risk to be present in all healthcare facilities that have >200 beds and see 6 or more patients with TB, the CDC recommendation[31] of annual testing of US HCWs working at "medium" risk facilities results in over-testing of many low-risk HCWs in the US.[60,80]

All HCWs should undergo baseline testing with a diagnostic test for LTBI (TST or IGRA). For those who have a TST performed, two-step testing is recommended at the time of employment if the HCW has not been previously tested in the preceding year. Two-step baseline tuberculin skin testing can help infection control staff identify LTBI in new personnel who otherwise would be classified as recent conversions. Two-step testing is not required if an IGRA is used. Current guidelines from CDC on the use of IGRAs recommend that either a TST or IGRA can be used for serial testing of HCWs.[81] However, recent reports have demonstrated that serial testing of low-risk HCWs with IGRAs results in high rates of false positive tests rather than a true conversion and recent infection and frequent reversion of these tests.[44] Because of multiple reports suggesting false positive conversions among healthcare workers when using IGRAs for serial testing among low-risk US and Canadian healthcare workers, the Public Health Agency and Canadian Thoracic Society have recommended that IGRAs not be used for serial testing of healthcare workers (i.e., in North America).[32,44,82–85] CDC 2005 guidelines[31] would benefit from revisions that incorporate data from these studies. Interestingly, when carrying out serial testing of low-risk US healthcare workers, the TST performed significantly better than IGRAs in a head-to-head comparison, but reversions of TST conversions were also seen.[44] These results emphasize the needs to refine current CDC guidelines on frequency of testing and the need for serial testing of low-risk US healthcare workers. Canadian TB infection control guidelines do in fact recommend that the frequency of testing of healthcare workers be switched if the risk is low; in particular they recommend that if the annual risk of HCW infection is <0.5% that consideration should be given to decreasing frequency of testing to every other year or establish criteria for only annual testing of selected "high-risk" HCWs at an institution that overall is low risk.[32]

It is not recommended that HCWs in "low-risk" settings undergo routine periodic follow up testing because as noted above, serial testing of low-risk healthcare workers will result in primarily false positive results (with any type of diagnostic test for LTBI). For low-risk healthcare workers as defined by CDC based on their recommended risk assessment, CDC recommends follow-up testing is recommended only if there is an exposure to a patient with active TB (i.e., patient not initially isolated but later found to have laryngeal or pulmonary tuberculosis).[31] CDC recommends that HCWs working at "medium risk" settings should undergo baseline and annual testing as well as testing after a tuberculosis exposure episode. Institutions with ongoing nosocomial transmission should carry out diagnostic testing for LTBI of at-risk HCWs every three months until it is documented that the transmission has been terminated.[31] For institutions with high risk for ongoing transmission, intensive surveillance for healthcare work infection by testing for LTBI conversions is one way to assess the efficacy of an infection control program and demonstrate termination of transmission in situations where there has been ongoing nosocomial transmission.

When performing TST of HCWs, the Mantoux method should be used. PPD is injected intradermally (0.1 mL of 5 tuberculin units), and the degree of induration is recorded in mm at 48 to 72 hours after placement.[86] HCWs with a positive TST or IGRA (either at baseline or during follow-up testing) should have a chest radiograph performed to exclude active disease. If an abnormal CXR is found, the HCW should be removed from the work setting until active

TB disease is excluded. Those with a negative chest radiograph found to have LTBI who are at increased risk for progression to active disease (e.g., true recent conversion, HIV co-infection or other underlying medical conditions, etc.),[86,87] should be strongly encouraged to take and complete therapy for LTBI (see Treatment below). Infection control staff working closely with employee health staff should consider several issues when developing a program for diagnostic testing for LTBI among HCWs. Institutions should assume responsibility for surveillance and mandate testing of all HCWs working at a particular institution (including unpaid staff, students, and volunteers) and not just employees. This is particularly important in an era of outsourcing when many HCWs may not be employees of the institution that they are working at. For institutions where routine follow-up testing is warranted based on risk, diagnostic test results should be recorded in the individual employee's health record and in an aggregate database of all results. TST (or IGRA) conversion rates should be calculated for the facility as a whole and, if appropriate, for specific areas of the facility and for occupational groups. Conversion rates should be calculated by dividing the number of TST (or IGRA)-test conversions among healthcare workers in each area or group (i.e., the numerator) by the total number of previously TST (or IGRA)-negative healthcare workers tested in each area or group (i.e., the denominator). In collaboration with occupational health staff, infection control and prevention personnel should interpret TST (or IGRA) conversion rates. Because of the substantial risk of false positive tests when the IGRA is used for serial testing of low-risk HCWs,[44] it is important for programs to determine if the IGRA should even be used for serial testing and whether an increase in the number of "conversions" are real or related to the use of serial IGRA. False positive conversions have also been reported when healthcare facilities switched brands of tuberculin they used for serial testing of HCWs (from Tubersol to Aplisol).[88,89] This is likely due to the difference in specificity between the two brands of tuberculin.[90]

If healthcare workers have a conversion (positive test following a previous negative test) when testing for LTBI (TST or IGRA), infection control and prevention staff should investigate to determine whether the likely source is in the facility or in the community. Of note, in areas that have low rates of TB in the community and/or have implemented effective TB infection control measures, HCWs in some facilities are more likely to be exposed to TB in the community than in the hospital.[39,91,92] One challenge of TB screening programs for HCWs is to ensure that staff report to employee health for LTBI diagnostic testing and for follow-up assessment. Some facilities have improved compliance by offering testing at the work site. Others have tied testing to issuance of employee identification badges that are required to work at the facility and to the physician-credentialing process.

Education

HCW education is an important component of an effective TB infection control program.[31] HCWs should receive training and education on the variety of components of an effective TB infection control program and their responsibilities in implementing and carrying out the institution's infection control plan. HCWs need to appreciate the risk of occupational exposure to patients with TB as well as the measures (e.g., hierarchy of controls) and policies adopted by the healthcare facilities to prevent nosocomial transmission. TB education should be provided upon employment and then each subsequent year. Basic information should be provided to all HCWs, and more in-depth education and training can be provided on a targeted basis to HCWs working in areas or settings where patients at risk or with TB may receive care. OSHA requires that US healthcare facilities provide annual training, and one way a number of institutions have incorporated this is into OSHA-mandated bloodborne pathogen training.

Extended Care Facilities

Many of the considerations for control of TB in hospitals apply to extended care facilities (ECFs) including the risk assessment recommendations. Elderly persons residing in a nursing home are at a higher risk of developing active TB than those living at home in the community.[93,94] Older adults residing in ECFs are more likely to have comorbidities associated with the risk of reactivation, and residence in congregate settings can promote transmission.[95] As in the hospital setting, effective TB control measures for ECFs include a high index of suspicion, prompt detection of active TB cases, isolating infectious cases, initiating appropriate therapy, identifying and evaluating contacts, and, when appropriate, conducting targeted testing and treatment of LTBI. Generally, ECFs do not have airborne infection isolation rooms, and therefore patients with suspected TB should be referred to an acute care hospital and not cared for at an ECF while they are infectious. Public health guidelines include recommendations for all residents (and HCWs) entering long-term care facilities to have a baseline diagnostic test for LTBI performed (either a TST or IGRA) unless documented to be previously positive.[31,93] The risk will vary based on the location and setting of the LTCF and the community it services. A cost-effectiveness analysis performed in a low-risk setting in Canada questioned the cost effectiveness of screening programs in LTCFs in low TB incidence and low-risk areas.[95] If a TST is used as the diagnostic test for TB screening at the time of resident entry into an ECF, two-step testing should be performed unless the newly admitted patient had previously received a TST during the prior 12 months. Persons found to have a positive TST or IGRA should have a chest radiograph performed and if negative, be evaluated for treatment of LTBI.[86]

B Environmental Controls

The second level of controls are *environmental controls* that reduce or eliminate *M. tuberculosis*–laden droplet nuclei in the air. These controls include local exhaust ventilation, general or central ventilation, air filtration with high-efficiency particulate air (HEPA) filters, and air disinfection with ultraviolet germicidal irradiation (UVGI).

Local Exhaust Ventilation

Local exhaust ventilation is a source control method used for capturing airborne contaminants including infectious droplet nuclei or other infectious particles before they are dispersed into the general environment. Local exhaust ventilation using a booth, hood, or tent can be an efficient engineering control technique, because it captures a contaminant at its source. Local exhaust ventilation should be used for cough-inducing (e.g., sputum induction booth) and aerosol-generating procedures (e.g., bronchoscopy). If local exhaust ventilation is not feasible, cough-inducing and aerosol-generating procedures should be performed in a room that meets the requirements of an airborne infection isolation room.

General Ventilation

General ventilation includes mechanisms that dilute and remove contaminated air and control the direction of airflow to prevent an infectious source from contaminating the air in nearby areas. These mechanisms include maintaining negative pressure and circulating air to dilute and remove infectious droplet nuclei (e.g., room air exchanges). Airflow should be from cleaner areas to more contaminated areas;[31,96] thus air should flow from corridors into AII rooms to prevent the spread of tuberculosis. AII rooms are used to house patients with suspected or confirmed TB being cared for at a healthcare facility. Airborne infection isolation rooms should have negative pressure to prevent the escape of droplet nuclei, and CDC recommends a minimum of 6 air exchanges per hour (and 12 air changes per hour if feasible), to decrease the concentration of infectious particles. For newly constructed or renovated facilities, a minimum of 12 air exchanges per hour for AII rooms is recommended by CDC.[31] A single-pass ventilation system is preferred; in such cases after air passes through the room or area, 100 percent of that air is exhausted to the outside. If this is not possible, HEPA filtration must be employed to filter air from an AII room that is recirculated into the general ventilation system. HEPA filtration must also be used when discharging air from local exhaust ventilation booths or enclosures (e.g., sputum induction booths).

The number of airborne infection isolation rooms and the location of these rooms (e.g., inpatient wards, emergency department, intensive care unit, etc.) should be determined based on results of the risk assessment. Grouping of airborne infection isolation rooms in one area (e.g., respiratory isolation ward) may facilitate the care of patients with suspected or proven TB[63] and the installation and maintenance of optimal environmental controls. Airborne infection isolation rooms should be checked regularly to ensure they are under negative pressure using smoke tubes or other devices. CDC recommends that these rooms be checked before occupancy and then daily while occupied by a patient with suspected or confirmed TB. When negative pressure is required, CDC recommends the pressure differential should be >0.01 inch of water gauge compared with adjacent areas. Detailed recommendations for designing and operating ventilation systems have been published.[31,96–98] A maintenance plan that outlines the responsibility and authority for maintenance of the environmental controls and addresses staff training needs should be part of the written tuberculosis control plan. Standard operating procedures should include the notification of infection control personnel before performing maintenance on ventilation systems serving TB patient care areas.

Portable Air Filtration Units

Portable room-air recirculation units (which are often referred to as portable air filtration units or portable high-efficiency particulate air [HEPA] filters) appear to be effective in removing bioaerosols and aerosolized particles from room air,[99,100] and therefore may be helpful in reducing airborne disease transmission. If portable devices are used, units with relatively high volumetric airflow rates that provide maximum flow through the HEPA filter are preferred. Portable HEPA units should be designed to achieve >12 equivalent air exchanges per hour, ensure adequate air mixing in all areas of the rooms, and be compatible with the ventilation system.[31] Placement of the units is important and should be selected to optimize the recirculation of AII room air through the HEPA filter. These portable units are not a permanent solution but may be useful as an interim measure and enable hospitals to establish TB isolation rooms in outpatient departments and areas when other TB isolation rooms are in use. In addition, facilities that do not have isolation rooms can use these units to convert general patient rooms to TB isolation rooms. Effectiveness of these portable units is affected by the room's configuration, the furniture and persons in the room, and the placement of the HEPA filtration unit relative to the supply air vent and exhaust grilles. Portable air filtration units may also include ultraviolet germicidal irradiation as discussed below.

Ultraviolet Germicidal Irradiation

Ultraviolet germicidal irradiation (UVGI) is an air-cleaning technology that can be used in a room or corridor to irradiate the air in the upper portion of the room (upper air irradiation), installed in a duct to irradiate air passing through the duct (duct irradiation), or incorporated into room air-recirculation units. The effective use of UVGI is associated with exposure of *M. tuberculosis*, as contained in an infectious droplet, to a sufficient dose of UV-C at 253.7 nm to ensure inactivation.[31] Germicidal lamps used in upper-room UVGI systems consist of low-pressure mercury vapor enclosed in special UV-transmitting glass tubes. Approximately 95 percent of the energy from these lamps is radiated at 253.7 nm in the UV-C range.[101] The CDC considers UVGI to be a supplementary measure for TB control and recommends against UVGI being used as a substitute for negative pressure or HEPA filtration.[31,101] Others have advocated more vigorously for an expanded role of UVGI for TB infection control and have suggested that it is the most cost-effective way to achieve high levels of air disinfection.[102–104] Reports from investigations carried out in Peru and South Africa indicate that that upper room UV lights, combined with adequate air mixing prevented most airborne TB transmission to guinea

pigs exposed to hospital room air (from rooms with patients with active TB disease).[104,105] This approach has been proposed as a relatively low-cost intervention for use in low- and middle-income countries as well as areas where other types of environmental controls are hard to implement such as waiting rooms and other overcrowded settings in healthcare facilities.[102,104] Concerns exist about proper maintenance of UVGI in low- and middle-income countries as well as the impact of high humidity on the efficacy of UVGI.

Air-cleaning technologies, such as UVGI and HEPA filtration, can be used to increase equivalent air changes per hour (ACH) in waiting areas and AII rooms. Air mixing, air velocity, relative humidity, UVGI intensity, and lamp configuration affect the efficacy of UVGI systems. In practical terms, it can be difficult to achieve the desired effects unless the system is properly designed. It is strongly recommended that healthcare facility managers consult a UVGI system designer to address safety and efficacy considerations before such a system is procured and installed.[31,101] Experts who can be consulted include industrial hygienists, engineers, and health physicists.

In upper-room air irradiation, UVGI lamps are suspended from the ceiling or mounted on the wall with a shield at the bottom of the lamp to direct the rays upward. As the air circulates, nonirradiated air moves from the lower to the upper part of the room, and irradiated air moves from the upper to the lower part of the room. For upper-room air systems, airborne microorganisms in the lower, occupied areas of the room must move to the upper part of the room to be killed or inactivated by upper-air UVGI. For optimal efficacy of upper-air UVGI, relative humidity should be maintained at <60 percent, a level that is consistent with current recommendations for providing acceptable indoor air quality and minimizing environmental microbial contamination in indoor environments.[106] The most useful places to consider using UVGI include locations in high TB prevalence areas that are difficult to control through ventilation measures alone such as waiting rooms, emergency rooms, corridors, and other central areas of a facility where patients with undiagnosed TB could contaminate the air, including operating rooms and adjacent corridors where procedures are performed on patients with TB disease. Details about the types of UVGI, their applications, and limitations can be found in CDC and NIOSH guidelines, and in other resources.[31,101–103,107] Suggestions on the use of UVGI in high TB incidence, resource-limited areas have been published.[102]

There are a number of health and safety issues related to the use of upper room UVGI lamps. For example, short-term overexposure to UV radiation can cause erythema, photokeratitis, and conjunctivitis. If UVGI is used (e.g., in upper air UVGI systems), it is important that the UVGI fixtures be designed and installed to ensure that UVGI exposures to occupants are below current safe exposure levels. Health-hazard evaluations by CDC/NIOSH have identified potential problems at some facilities using UVGI systems.[31,101] These include overexposure of HCWs to UVGI and inadequate maintenance, training, labeling, and use of personal protective equipment (PPE). It is believed that in most instances, properly designed, installed, and maintained UVGI fixtures provide protection from most, if not all, of the direct UVGI in the lower room.[103] When UVGI is used, it is important that these systems be monitored and maintained appropriately and that HCWs receive appropriate education about UVGI safety.

C Personal Respiratory Protection

Personal respiratory protection is the last step in the hierarchy of TB infection control measures. It is recommended that personal respiratory equipment (e.g., N-95 respirators) be used by HCWs when entering high-risk areas where exposure to airborne *M. tuberculosis* may occur (e.g., AII rooms, rooms where cough-producing or aerosol-producing procedures are performed, including the bronchoscopy suite where procedures are performed on patients with suspected or proven tuberculosis).[30,31] Although recommended as part of a combination of TB infection control measures, the efficacy of masks or respirators in preventing tuberculosis infection or disease in healthcare workers has not been demonstrated; in efforts to terminate outbreaks, multiple interventions were implemented simultaneously.[108]

The most controversial area of TB infection control has involved personal respiratory protection because of federal mandates from the OSHA regarding fit-testing, and due to lack of data on the precise level of effectiveness of respiratory protection in protecting HCWs from *M. tuberculosis* transmission in healthcare settings has not been determined. Prior to 1996, OSHA had mandated the use of HEPA respirators in healthcare facilities. Two cost-effectiveness analyses performed at the University of Virginia suggested that HEPA respirators would offer negligible additional efficacy at a great cost (e.g., $7 million per case of tuberculosis prevented).[109,110] Current recommendations from US federal agencies involved in this issue (National Institute for Occupational Safety and Health [NIOSH], OSHA, and the CDC) are in agreement that the minimal acceptable respiratory protection is a NIOSH-certified N-95 respirator.[31]

In 1997, OSHA published a proposed standard for occupational exposure to TB.[111] The Institute of Medicine (IOM) was subsequently asked by the US Congress to evaluate the risk of TB among HCWs and the impact of the proposed OSHA TB standard. The IOM published a report in 2001 entitled, "Tuberculosis in the Workplace."[38] The IOM report questioned the validity of the OSHA risk assessment that the standard was based on and noted that the risk of occupational exposure to TB and HCW risk of occupationally acquired infection had decreased significantly following implementation of CDC-recommended TB infection control guidelines and given the decreasing incidence of TB in the community. The IOM report also concluded that the CDC 1994 TB infection control guidelines[112] were effective in terminating outbreaks and preventing nosocomial infection of TB. Occupational risk to healthcare workers in most US healthcare facilities has continued to decrease over the past two decades, given a combination of reduced incidence of TB in the community and implementation of effective TB infection control measures. In 2003, OSHA announced that it

has decided to withdraw this proposal,[113] because "it does not believe a standard would substantially reduce the occupational risk of TB infection." Despite not issuing a separate TB standard, OSHA maintains regulatory control over TB in healthcare settings under the Code of Federal Regulations (CFR) Title 29, Part 1910.134 and Section 5(a)(1) of the OSH Act, often referred to as the General Duty clause.[114] The impact of this decision is that healthcare facilities are now required by OSHA to perform annual fit-testing of all healthcare workers who use N-95 respirators rather than just at the time of employment as had been the case previously.[115]

Fit-testing of N-95 respirators has been a contentious issue. Observational studies have demonstrated that TB outbreaks in the US were terminated prior to the availability or use of N-95 or HEPA respirators or use of fit-testing.[56] Fit-testing is time consuming, logistically difficult, and can be expensive at large institutions that may have thousands of HCWs. There are no definitive data of the benefit of fit-testing, and recent publications by NIOSH have demonstrated a variety of problems with fit-testing. Coffey et al. reported that when the most rigorous criterion of fit-testing was used (the 1 percent pass/fail criterion recommended by the American National Standards Institute and required by OSHA), a substantial majority of tested individuals failed the fit-test for 17 of 21 brands of N-95 respirators tested; thus most individuals could not be "successfully" fitted.[38,116] There are a number of different methodologies available for fit-testing although in healthcare facilities, the qualitative fit method is most commonly used. In an additional investigation, Coffey et al. compared five methods for fit testing N-95 respirators, using both qualitative and quantitative methods.[117] The authors found wide variation in results between these fit-testing methods and that none of the five methods met criteria for determining whether a fit-test adequately screened out poorly fitting respirators. They concluded that the accuracy of fit-testing methods and the fitting characteristics of N-95 respirators need to be improved.

Coffey and colleagues at NIOSH also have reported on the fitting characteristics of 18 different models of N-95 respirators using 4 different analytical methods used to measure the performance of N95-respirators.[118] Only 3 of the 18 N-95 respirators had good-fitting characteristics and met the expected level of protection without fit-testing. Passing a fit-test however did not guarantee the wearer an adequately fitting respirator. There was no significant additional benefit of fit-testing for those models of respirators with good-fitting characteristics. Poor-fitting respirators with fit-testing continued to be inferior to good-fitting respirators without fit-testing. Thus, those respirators with good-fitting characteristics provided better protection out of the box without fit-testing than did respirators with poor-fitting respirators after fit-testing. These findings led the authors from NIOSH to conclude that given the "current state of fit-testing, it may be of more benefit to the user to wear a respirator model with good-fitting characteristics without fit-testing than to wear a respirator model with poor-fitting characteristics after passing a fit-test."[118] In 1995, NIOSH published new certification regulations for particulate respirators; a list of NIOSH-approved N-95 respirators is available on the CDC website.[119] Unfortunately, there is no provision requiring good fit characteristics as part of the NIOSH certification process.

OSHA requires healthcare facilities in which HCWs use respiratory protection to develop, implement, and maintain a respiratory-protection program.[31] OSHA permits a HCW to reuse a respirator as long as it maintains its structural and functional integrity and the filter material is not damaged or soiled. Each facility should include in its TB control program policy a protocol that defines when a disposable respirator must be discarded (e.g., if it becomes contaminated with blood or other body fluids). Healthcare facilities should strongly consider selecting a brand of N-95 respirator based on its fitting characteristics as outlined by Coffey et al.[118] In addition to selecting N-95 respirators, each healthcare facility needs a complete respiratory protection program. Components of the OSHA respiratory protection standard require that an institution:

- Assign responsibility for the program to a specific person or group.
- Write procedures for all aspects of the program.
- Screen all employees for medical conditions that prevent them from wearing respirators.
- Train and educate employees about respiratory protocols (and TB infection control measures).
- Fit-test the respirators on each employee (on an annual basis) and have employees check the fit each time they use a respirator.
- Develop policies and procedures that describe how to inspect, maintain, and reuse respirators, and define when respirators are contaminated and must be discarded.
- Evaluate the program periodically.

Despite the limitations of fit-testing,[38,116–118,120–122] OSHA regulations require fit-testing of healthcare workers be performed on an annual basis. Several different fit-testing methods are available[117,121] although a qualitative fit-testing method is generally used for fit-testing disposable N-95 respirators at most US healthcare facilities. This method involves exposing the employee to saccharin. It is been recommended that healthcare facilities should follow the manufacturer's instructions and recommendations for fit-testing[31]. OSHA requires that healthcare facilities screen employees to determine whether they can wear respirators. Other than severe cardiac or pulmonary disease, few medical conditions should preclude the use of disposable respirators. Many facilities use a general questionnaire to screen employees for medical conditions and to determine whether an employee should be evaluated further. Personal respiratory protection (e.g., N-95 respirators) should be used by persons entering rooms in which patients with suspected or confirmed infectious TB are being isolated (e.g., airborne infection isolation rooms), persons present during cough-inducing or aerosol-generating procedures performed on patients with suspected or confirmed infectious TB, and persons in other settings where

administrative and environmental controls are not likely to protect them from inhaling infectious airborne droplet nuclei. This includes emergency medical technicians and other persons who transport patients who might have infectious TB in ambulances or other vehicles and persons who provide urgent surgical or dental care to patients who might have infectious TB. In addition, laboratory workers conducting aerosol-producing procedures involving specimens that might contain *M. tuberculosis* should also use respiratory protection. Detailed recommendations about the environment (including use of a biosafety cabinet and other biosafety procedures) used for carrying out such procedures have been published by CDC and the National Institutes of Health.[123] It is recommended that visitors to isolation rooms or other areas where patients with suspected or confirmed infectious tuberculosis are present should wear a N-95 respirator. Visitors can be given N-95 respirators and instructed in their use, but do not need to be fit-tested.

As discussed above, OSHA's minimum requirement for respiratory protection is the N95 respirator. However, particular situations may warrant more-protective respirators. Modeling studies have suggested that the benefits of respiratory protection are directly proportional to the presence of the risk.[124] For example, personnel who perform extremely high-risk procedures, such as bronchoscopy on patients with known or suspected MDR-TB may need additional respiratory protection. One example of a more-protective respirator is a powered air-purifying respirator (PAPR). NIOSH has published a guide on respirators for TB that describes the type of respirators that are available.[125]

Laboratory Diagnosis

Laboratory tests (e.g., AFB smear and culture and/or molecular diagnostic tests) are necessary to confirm or exclude the diagnosis of tuberculosis and to identify drug-resistant isolates of *M. tuberculosis*.[126–128] If a clinical laboratory cannot perform the most rapid tests, the hospital may need to send specimens to a referral laboratory. The healthcare facility must ensure that arrangements comply with the CDC's guidelines for transporting specimens and reporting results (e.g., AFB smear results should be reported within 24 hours of specimen collection).[129] The use of nucleic acid amplification tests (NAATs) provide rapid diagnosis of TB and can indicate the presence of drug-resistant disease (e.g., rifampin resistance, generally a marker for MDR-TB, can be identified through use of the FDA-approved Xpert MTB/RIF test).[73,130,131] This can facilitate initiation of more appropriate therapy, better patient outcomes, and enhance infection control efforts, especially in low- and middle-income countries or other areas where rates of MDR-TB are high.[132,133] In the US, NAATs have proven useful and cost-effective in certain circumstances such as those encountered at Grady Memorial Hospital in Atlanta, which is located in a relatively high HIV/TB prevalence area and where recovery of nontuberculous mycobacteria is common among HIV-infected patients.[62] Given the relatively low positive predictive value of a positive AFB smear of sputum for TB from an HIV-infected person in this setting, the NAAT is useful in identifying whether *M. tuberculosis* is present and can help facilitate more appropriate and efficient care of patients.[62] CDC and WHO have published updated guidelines on the use of nucleic acid amplification tests.[66,134] These tests have a high sensitivity and specificity when performed on AFB smear positive specimens and a somewhat lower sensitivity when performed on smear-negative, culture-positive respiratory specimens.[62,73,130,131] Those patients who are AFB respiratory smear-positive but found to not have TB based on nucleic acid amplification test results (and clinically not thought to have TB) could have isolation and therapy discontinued in an expeditious fashion.[62,135]

Current CDC guidelines recommend obtaining three respiratory specimens (e.g., sputum) 8 to 24 hours apart when evaluating a patient with suspected pulmonary tuberculosis.[31,136] However, the utility of the third specimen in diagnosing pulmonary tuberculosis is minimal.[70,71] This has led some healthcare facilities in the US to switch to obtaining two respiratory specimens when "ruling out" patients for tuberculosis in an effort to further enhance efficiency and use of AII rooms and reduce costs. In addition, in 2015 the US Food and Drug Administration (FDA) approved an expanded use of the Xpert MTB/RIF nucleic amplification assay that includes testing of either one or two sputum specimens as an alternative to examination of serial acid-fast stained sputum smears to aid in the decision of whether continued airborne infection isolation is warranted for patients with suspected pulmonary tuberculosis.[65] This decision was based on the availability of further data that showed that a negative Xpert MTB/RIF test (1 or 2 tests) was highly predictive of the results of 2 or 3 negative AFB smears of sputum. A single negative Xpert test predicted the *absence* of AFB smear positive pulmonary TB with a negative predictive value of 99.7 percent. A single Xpert MTB/RIF detected 97 percent of patients who were AFB smear-positive and culture-positive for *M. tuberculosis*; two serial Xpert tests detected 100 percent.[65] Further data regarding the impact of Xpert on AII room utilization in the US and other high-income countries is needed. The availability of a rapid diagnostic test in settings where TB diagnostics have been limited (often limited to only smear microscopy), provides a mechanism to enhance TB infection control and implement rapid screening and cohorting and separation of patients with drug-susceptible TB and MDR-TB from those without TB.[54]

Treatment of Tuberculosis Disease and Latent Tuberculosis Infection

Clinicians should start empirical therapy as soon as they suspect that the patient has TB disease. The current recommendation is to begin therapy with a four-drug regimen (isoniazid, rifampin, pyrazinamide, and ethambutol)[54,126] unless there is high suspicion for or a rapid molecular diagnostic test suggests MDR-TB. Definitive therapy depends on results of drug susceptibility testing results. The American Thoracic Society, the Infectious Diseases Society of America (IDSA), and CDC have published guidelines on the treatment of tuberculosis disease

Table 27.6 Abbreviated guidelines for the treatment of latent tuberculosis infection

Drug	Interval and duration	Comments*
Isoniazid	Daily for 9 months**+	In HIV-infected persons, isoniazid may be administered concurrently with nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), integrase inhibitors, and protease inhibitors.
	Twice weekly for 9 months**+	Directly observed therapy (DOT must be used with twice-weekly dosing.
Isoniazid	Daily for 6 months**	6 mo regimen not recommended by CDC for HIV-infected persons in the US, those with fibrotic lesions on chest radiographs, or children.
	Twice weekly for 6 months**	DOT must be used with twice-weekly dosing.
Rifampin	Daily for 4 months	Used for persons who are contacts of patients with isoniazid-resistant, rifampin-susceptible TB; can also be used for the treatment of LTBI due to presumed drug-susceptible strains of *M. tuberculosis*. In HIV-infected persons, most protease inhibitors or delavirdine should not be administered concurrently with rifampin. Rifabutin with appropriate dose adjustments can be used with some protease inhibitors and NNRTIs (except delavirdine). Clinicians should consult web-based updates for the latest specific recommendations.*
Isoniazid (INH) plus rifapentine*	Weekly for 12 weeks	DOT should be used for this weekly regimen. This regimen is not recommended for the following patients: children aged <2 years, because the safety and pharmacokinetics of rifapentine have not been established for them; HIV-infected patients receiving antiretroviral treatment, because the drug interactions have not been studied; pregnant women or women expecting to become pregnant during treatment, because safety in pregnancy is unknown; and patients who have LTBI with presumed isoniazid or rifampin resistance.

*. Interactions with human immunodeficiency virus (HIV)-related drugs are updated frequently and are available at www.aidsinfo.nih.gov/guidelines.
+. Recommended regimen for persons aged <18 years.
**. Recommended regimen for pregnant women.Adapted from references (87,144,146).

that provide detailed guidance for the treatment of TB in North America.[126] A recent review provides an updated perspective.[137] Directly observed therapy is an important component of therapy and has been reported to improve completion rates and outcome.[138,139]

Treatment of LTBI has been demonstrated to be effective in reducing the risk of progression to active disease and is recommended for those individuals at increased risk of progression, including HCWs.[87,140,141] Recommendations for the treatment of LTBI have been published and updated (Table 27.6);[87,142–144] CDC recommended regimens for the treatment of LTBI include isoniazid for nine months, rifampin for four months, or 12 weeks of weekly isoniazid plus rifapentine (given by directly observed therapy).[145,146]

Despite the benefits of therapy for the treatment of LTBI, HCWs have historically had poor rates of initiation and completion of LTBI therapy with the majority of HCWs not initiating or completing therapy.[147–149] However, in the context of a comprehensive TB infection control program[150] and programs that have focused efforts on delivering LTBI therapy to HCWs,[151] much higher rates of initiation and completion have been reported. For example, 98 percent of healthcare workers with LTBI initiated isoniazid therapy and 82 percent completed therapy at Barnes-Jewish Hospital in St. Louis. The authors of this study attributed their high initiation and completion rates to active follow up, consisting of physician counseling and monthly phone consultations by nurses at the institution's occupational health department along with free services and medication. Foreign-born HCWs who had received bacille Calmette-Guerin (BCG) were less likely to complete LTBI therapy in the St. Louis study, and the authors recommend addressing cultural barriers that may lead to refusal and/or nonadherence with therapy. Some have suggested that use of an IGRA test[152] (e.g., at baseline testing) may enhance acceptance of LTBI therapy among foreign-born BCG-vaccinated HCWs.[153]

Improved infection control measures and decreasing incidence of TB since 1992 in the US have led to a significant reduction in HCW risk.[38,60] Following the establishment of effective TB control measures in hospitals, for many HCWs community factors pose a greater risk for infection than occupational exposure.[39,92] At many institutions, a large proportion of HCWs are foreign-born and may be found to have LTBI at the time of employment, presumably due to in large part to infection acquired in their higher-incidence home country. Thus in part, surveillance for LTBI among HCWs at the time of employment is part of a public health strategy for treating those with LTBI who may be at increased risk for progression (e.g., immigrants to the US within the past five years).

Discharge Planning and Collaboration with Public Health

Healthcare facilities and local and state public health officials have responsibilities to work closely with each other to further TB control in the community and state. Public health officials can provide important data to healthcare facilities regarding incidence of TB in the community that is needed for the institution's risk assessment. All US states require that TB cases be reported; often the physician caring for the patient is responsible for this. Frequently infection control departments have assumed this responsibility for their facility to ensure that reporting occurs in a timely fashion. Healthcare facilities and public health officials also need to work closely with regards to discharge planning in order to ensure a seamless transition of care from an inpatient setting to an outpatient clinic (e.g., TB Clinic at the patient's local health department) and to help ensure that patients are not lost to follow-up after discharge. A written policy or critical pathway management of TB patient discharges that provides guidance as to what constitutes an appropriate transfer (for programs that do not provide care to patients with proven or suspected TB but refer to other sites) or discharge (for sites that do provide care) should be established and included as part of a TB infection control program.[56] For example these measures may include ensuring that 1) patients are discharged on an appropriate antituberculosis regimen; 2) have arrangements to ensure close follow-up after discharge (e.g., patient is contacted in the hospital by the public health outreach worker who will provide directly observed therapy following hospital discharge; 3) meet appropriate criteria for discharge (e.g., be medically ready for discharge and have a stable home or other stable location if potentially infectious). Public health officials are responsible for carrying out contact investigations among close contacts of active TB cases (including both family and nonfamily close contacts) where the index or source case is infectious.[154] Healthcare facilities are responsible for carrying out contact investigation among exposed HCWs when an infectious TB case was not appropriately placed in airborne infection isolation on admission to the hospital.

Summary

Much progress has been made over the past two decades in greatly reducing the risk of occupational exposure to TB and occupationally acquired infection due to *M. tuberculosis* in the US and Canada. CDC-recommended guidelines (i.e., a three-level hierarchy of controls that include administrative controls, environmental controls, and use of respiratory protective equipment) have been shown to be effective in terminating outbreaks and in preventing nosocomial transmission of TB.[31,32,36] The improved safety for HCWs (and patients) has been due to a combination of improved infection control measures implemented in US and Canadian hospitals and a decrease in the incidence of TB in the community. The annual risk of TST conversion among HCWs has been reported to be <4 per 1000 person years worked, even in higher–TB prevalence areas in the US.[39] More recent data suggest that the risk in the US can be as low as 1 per 1000 person years worked.[80] Recommendations made in this chapter focus on TB infection control for the United States (and would be applicable to other high-income and low TB incidence countries including Canada). CDC last published detailed TB infection control guidelines in 200531 and revisions are needed with regards of when serial testing of US healthcare workers should be performed, given the low incidence of TB infection and the low positive predictive value of diagnostic tests when testing low-risk populations. Updated Canadian guidelines help address this issue.[32] Despite substantial progress made in the US over the past two decades, a number of controversial areas remain, especially regarding respiratory protection and fit-testing. It is important that guidelines and regulatory requirements be evidenced based and that research continue into unresolved scientific issues. Finally, HCWs must remain vigilant. Even in an era of decreasing TB in the US and Canada, failure to consider the diagnosis and take appropriate infection control measures can lead to nosocomial transmission.

While the risk of occupational acquisition of *M. tuberculosis* is very low for the vast majority of US HCWs, nosocomial transmission of tuberculosis remains a serious public health problem in high TB incidence areas in low- and middle-income countries where the vast majority of TB cases occur. There remains a substantial risk of occupational acquisition of TB among HCWs in low- and middle-income countries.[28,29,33,51,52] The emergence of MDR- and XDR-TB and devastating outbreaks among HIV-infected persons has raised awareness about the importance of infection control measures throughout the world. However, fundamental changes in how patients are cared for are needed in LMIC in order to adequately address TB infection control. Urgent attention, including adequate resources, is needed to implement effective TB infection control measures in high-burden, resource-limited areas. This includes an urgent need for demonstration projects on how best to implement TB infection control measures (especially administrative controls) in high-burden resource-limited countries[54] and the need to scale up implementation of effective TB infection control measures.

References

1. Organization WH. *Global Tuberculosis Report 2015*. Geneva, Switzerland: World Health Organization; 2015.
2. Sepkowitz KA. Tuberculosis and the health care worker: a historical perspective. *Ann Intern Med.* 1994;**120**:71–79.
3. Myers JA, Diehl HS, Boynton RE, Horns HL. Tuberculosis in physicians. *JAMA.* 1955;**158**:1–8.
4. Iademarco MF, Castro KG. Epidemiology of tuberculosis. *Semin Respir Infect.* 2003;**18**: 225–240.
5. Menzies D, Fanning A, Yuan L, Fitzgerald M. Tuberculosis among health care workers. *N Engl J Med.* 1995;**332**:92–98.
6. Snider DE, Jr., Roper WL. The new tuberculosis. *N Engl J Med.* 1992;**326**:703–705.

7. Jarvis WR. Nosocomial transmission of multidrug-resistant Mycobacterium tuberculosis. *Res Microbiol.* 1993;**144**:117–122.
8. Daley CL, Small PM, Schecter GF, et al. An outbreak of tuberculosis with accelerated progression among persons infected with the human immunodeficiency virus: an analysis using restriction-fragment-length polymorphisms. *N Engl J Med.* 1992;**326**:231–235.
9. Castro KG, Dooley SW, Curran JW. Transmission of HIV-associated tuberculosis to healthcare workers. *Lancet.* 1992;**340**:1043–1044.
10. Fischl MA, Uttamchandani RB, Daikos GL, et al. An outbreak of tuberculosis caused by multiple-drug-resistant tubercle bacilli among patients with HIV infection. *Ann Intern Med.* 1992;**117**:177–183.
11. Beck-Sague C, Dooley SW, Hutton MD, et al. Hospital outbreak of multidrug-resistant Mycobacterium tuberculosis infections: factors in transmission to staff and HIV-infected patients. *JAMA.* 1992;**268**:1280–1286.
12. Coronado VG, Beck-Sague CM, Hutton MD, et al. Transmission of multidrug-resistant Mycobacterium tuberculosis among persons with human immunodeficiency virus infection in an urban hospital: epidemiologic and restriction fragment length polymorphism analysis. *J Infect Dis.*1993;**168**:1052–1055.
13. Zaza S, Blumberg HM, Beck-Sague C, et al. Nosocomial transmission of Mycobacterium tuberculosis: role of health care workers in outbreak propagation. *J Infect Dis.*1995;**172**:1542–1549.
14. Pearson ML, Jereb JA, Frieden TR, et al. Nosocomial transmission of multidrug-resistant Mycobacterium tuberculosis: a risk to patients and health care workers. *Ann Intern Med.* 1992;**117**:191–196.
15. Jereb JA, Klevens RM, Privett TD, et al. Tuberculosis in health care workers at a hospital with an outbreak of multidrug-resistant Mycobacterium tuberculosis. *Arch Intern Med.* 1995;**155**:854–859.
16. Ikeda RM, Birkhead GS, DiFerdinando GT, Jr., et al. Nosocomial tuberculosis: an outbreak of a strain resistant to seven drugs. *J Infect Control Hosp Epidemiol.* 1995;**16**:152–159.
17. Edlin BR, Tokars JI, Grieco MH, et al. An outbreak of multidrug-resistant tuberculosis among hospitalized patients with the acquired immunodeficiency syndrome. *N Engl J Med.* 1992;**326**:1514–1521.
18. Dooley SW, Jarvis WR, Martone WJ, Snider DE, Jr. Multidrug-resistant tuberculosis. *Ann Intern Med.* 1992;**117**:257–259.
19. Dooley SW, Villarino ME, Lawrence M, et al. Nosocomial transmission of tuberculosis in a hospital unit for HIV-infected patients. *JAMA.* 1992;**267**:2632–2634.
20. Wells DA, Ross JS, Detsky AS. What is different about the market for health care? *JAMA.* 2007;**298**:2785–2787.
21. Gandhi NR, Moll A, Sturm AW, et al. Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural area of South Africa. *Lancet.* 2006;**368**:1575–1580.
22. Gandhi NR, Weissman D, Moodley P, et al. Nosocomial transmission of extensively drug-resistant tuberculosis in a rural hospital in South Africa. *J Infect Dis.* 2013;**207**:9–17.
23. Aita J, Barrera L, Reniero A, et al. Hospital transmission of multidrug-resistant Mycobacterium tuberculosis in Rosario, Argentina. *Medicina (B Aires).* 1996;**56**:48–50.
24. Bock NN, Jensen PA, Miller B, Nardell E. Tuberculosis infection control in resource-limited settings in the era of expanding HIV care and treatment. *J Infect Dis.* 2007;**196** Suppl 1:S108–S113.
25. Ritacco V, Di Lonardo M, Reniero A, et al. Nosocomial spread of human immunodeficiency virus–related multidrug-resistant tuberculosis in Buenos Aires. *J Infect Dis.* 1997;**176**:637–642.
26. Sacks LV, Pendle S, Orlovic D, Blumberg L, Constantinou C. A comparison of outbreak- and nonoutbreak-related multidrug-resistant tuberculosis among human immunodeficiency virus–infected patients in a South African hospital. *Clin Infect Dis.* 1999;**29**:96–101.
27. Campos PE, Suarez PG, Sanchez J, et al. Multidrug-resistant Mycobacterium tuberculosis in HIV-infected persons, Peru. *Emerg Infect Dis.* 2003;**9**:1571–1578.
28. Menzies D, Joshi R, Pai M. Risk of tuberculosis infection and disease associated with work in health care settings. *Int J Tuberc Lung Dis.* 2007;**11**:593–605.
29. Joshi R, Reingold AL, Menzies D, Pai M. Tuberculosis among health-care workers in low- and middle-income countries: a systematic review. *PLoS Med.* 2006;**3**:e494.
30. World Health Organization. WHO policy on TB infection control in health-care facilities, congregate settings and households: World Health Organization; 2009.
31. Jensen PA, Lambert LA, Iademarco MF, Ridzon R, CDC. Guidelines for preventing the transmission of Mycobacterium tuberculosis in healthcare settings, 2005. *MMWR Recomm Rep.* 2005;**54:** 1–141.
32. (PHAC). CTSCotCLACatPHAoC. Canadian Tuberculosis Standards, 7th ed. Public Health Agency of Canada; 2014.
33. von Delft A, Dramowski A, Khosa C, et al. Why healthcare workers are sick of TB. *Int J Infect Dis.* 2015;**32**:147–151.
34. Jarvis WR. Nosocomial transmission of multidrug-resistant Mycobacterium tuberculosis. *Am J Infect Control.* 1995;**23**:146–151.
35. Wells CD, Cegielski JP, Nelson LJ, et al. HIV infection and multidrug-resistant tuberculosis: the perfect storm. *J Infect Dis.* 2007;**196**(Suppl 1):S86–S107.
36. Blumberg HM, Watkins DL, Berschling JD, et al. Preventing the nosocomial transmission of tuberculosis. *Ann Intern Med.* 1995;**122**:658–663.
37. Wenger PN, Otten J, Breeden A, Orfas D, Beck-Sague CM, Jarvis WR. Control of nosocomial transmission of multidrug-resistant Mycobacterium tuberculosis among healthcare workers and HIV-infected patients. *Lancet.* 1995;**345**:235–240.
38. Institute of Medicine (IOM). Committee on Regulating Occupational Exposure to Tuberculosis MJF, ed. *Tuberculosis in the Workplace*. Washington, D.C.: National Academy Press; 2001.
39. Larsen NM, Biddle CL, Sotir MJ, White N, Parrott P, Blumberg HM. Risk of tuberculin skin test conversion among health care workers: occupational versus community exposure and infection. *Clin Infect Dis.* 2002;**35**:796–801.
40. Choudhary M, Ramirez L, Long R, et al. A university hospital's 10-year experience with tuberculin testing: value of the 2-step tuberculin skin test. *Am J Infect Control.* 2006;**34**:358–361.

41. Welbel SF, French AL, Bush P, DeGuzman D, Weinstein RA. Protecting health care workers from tuberculosis: a 10-year experience. *Am J Infect Control.* 2009;**37**:668–673.
42. Frieden TR, Fujiwara PI, Washko RM, Hamburg MA. Tuberculosis in New York City–turning the tide. *N Engl J Med.* 1995;**333**:229–233.
43. Agoritsas T, Courvoisier DS, Combescure C, Deom M, Perneger TV. Does prevalence matter to physicians in estimating post-test probability of disease? A randomized trial. *J Gen Intern Med.* 2011;**26**:373–378.
44. Dorman SE, Belknap R, Graviss EA, et al. Interferon-gamma release assays and tuberculin skin testing for diagnosis of latent tuberculosis infection in healthcare workers in the United States. *Am J Respir Crit Care Med.* 2014;**189**:77–87.
45. CDC. *Reported Tuberculosis in the United States, 2014*. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2015.
46. Haddad MB, Mitruka K, Oeltmann JE, Johns EB, Navin TR. Characteristics of tuberculosis cases that started outbreaks in the United States, 2002–2011. *Emerg Infect Dis.* 2015;**21**:508–510.
47. Sreeramareddy CT, Panduru KV, Menten J, Van den Ende J. Time delays in diagnosis of pulmonary tuberculosis: a systematic review of literature. *BMC Infect Dis.* 2009;**9**:91.
48. Lee EH, Graham PL, 3rd, O'Keefe M, Fuentes L, Saiman L. Nosocomial transmission of Mycobacterium tuberculosis in a children's hospital. *Int J Tuberc Lung Dis.* 2005;**9**:689–692.
49. Baussano I, Nunn P, Williams B, Pivetta E, Bugiani M, Scano F. Tuberculosis among health care workers. *Emerg Infect Dis.* 2011;**17**:488–494.
50. O'Donnell MR, Jarand J, Loveday M, et al. High incidence of hospital admissions with multidrug-resistant and extensively drug-resistant tuberculosis among South African health care workers. *Ann Intern Med.* 2010;**153**:516–522.
51. Whitaker JA, Mirtskhulava V, Kipiani M, et al. Prevalence and incidence of latent tuberculosis infection in Georgian healthcare workers. *PloS One* 2013;**8**:e58202.
52. Adams S, Ehrlich R, Baatjies R, et al. Incidence of occupational latent tuberculosis infection in South African healthcare workers. *Eur Respir J.* 2015;**45**:1364–1373.
53. Pai M, Kalantri S, Aggarwal AN, Menzies D, Blumberg HM. Nosocomial tuberculosis in India. *Emerg Infect Dis.* 2006;**12**:1311–1318.
54. Barrera E, Livchits V, Nardell E. F-A-S-T: a refocused, intensified, administrative tuberculosis transmission control strategy. *Int J Tuberc Lung Dis.* 2015;**19**:381–384.
55. IMPLEMENTING the WHO Policy on TB Infection Control in Healthcare Facilities, Congregate Settings and Households. Available at: www.stoptb.org/wg/tb_hiv/assets/documents/tbicimplementationframework1288971813.pdf.
56. McGowan JE, Jr. Nosocomial tuberculosis: new progress in control and prevention. *Clin Infect Dis.* 1995;**21**:489–505.
57. Sotir MJ, Parrott P, Metchock B, et al. Tuberculosis in the inner city: impact of a continuing epidemic in the 1990s. *Clin Infect Dis.* 1999;**29**:1138–1144.
58. Salinas JL, Mindra G, Haddad MB, Pratt R, Price SF, Langer AJ. Leveling of tuberculosis incidence – United States, 2013–2015. *MMWR Morbidity and Mortality Weekly Report.* 2016;**65**:273–278.
59. Maloney SA, Pearson ML, Gordon MT, Del Castillo R, Boyle JF, Jarvis WR. Efficacy of control measures in preventing nosocomial transmission of multidrug-resistant tuberculosis to patients and health care workers. *Ann Intern Med.* 1995;**122**:90–95.
60. Zellweger JP, Rieder HL. Serial screening for latent tuberculosis infection in healthcare workers in low-risk settings. *Am J Respir Crit Care Med.* 2014;**189**:3–4.
61. da Costa PA, Trajman A, Mello FC, et al. Administrative measures for preventing Mycobacterium tuberculosis infection among healthcare workers in a teaching hospital in Rio de Janeiro, Brazil. *J Hosp Infect.* 2009;**72**:57–64.
62. Adelman MW, Kurbatova E, Wang YF, et al. Cost analysis of a nucleic acid amplification test in the diagnosis of pulmonary tuberculosis at an urban hospital with a high prevalence of TB/HIV. *PloS One.* 2014;**9**:e100649.
63. Leonard MK, Egan KB, Kourbatova E, et al. Increased efficiency in evaluating patients with suspected tuberculosis by use of a dedicated airborne infection isolation unit. *Am J Infect Control.* 2006;**34**:69–72.
64. Leonard MK, Osterholt D, Kourbatova EV, Del Rio C, Wang W, Blumberg HM. How many sputum specimens are necessary to diagnose pulmonary tuberculosis? *Am J Infect Control.* 2005;**33**:58–61.
65. Division of Microbiology Devices OoIVD, Radiological Health CfD, Radiological Health F, Drug A, Centers for Disease C, Prevention. Revised device labeling for the Cepheid Xpert MTB/RIF assay for detecting Mycobacterium tuberculosis. *MMWR Morbidity and Mortality Weekly Report.* 2015;**64:**193.
66. Centers for Disease C, Prevention. Availability of an assay for detecting Mycobacterium tuberculosis, including rifampin-resistant strains, and considerations for its use – United States, 2013. *MMWR Morbidity and Mortality Weekly Report.* 2013;**62:** 821–827.
67. Iwata K, Smith BA, Santos E, Polsky B, Sordillo EM. Failure to implement respiratory isolation: why does it happen? *J Infect Control Hosp Epidemiol.* 2002;**23**:595–599.
68. Scott B, Schmid M, Nettleman MD. Early identification and isolation of inpatients at high risk for tuberculosis. *Arch Intern Med.* 1994;**154**:326–330.
69. Centers for Disease C, Prevention. Tuberculosis outbreak in a community hospital–District of Columbia, 2002. *MMWR Morbidity and Mortality Weekly Report.* 2004;**53:** 214–216.
70. Leonard MK, Jr., Kourbatova E, Blumberg HM. Re: how many sputum specimens are necessary to diagnose pulmonary tuberculosis. *Am J Infect Control.* 2006;**34**:328–329.
71. Mase SR, Ramsay A, Ng V, et al. Yield of serial sputum specimen examinations in the diagnosis of pulmonary tuberculosis: a systematic review. *Int J Tuberc Lung Dis.* 2007;**11**:485–495.
72. Chaisson LH, Roemer M, Cantu D, et al. Impact of GeneXpert MTB/RIF assay on triage of respiratory isolation rooms for inpatients with presumed tuberculosis: a hypothetical trial. *Clin Infect Dis.* 2014;**59**:1353–1360.
73. Boehme CC, Nabeta P, Hillemann D, et al. Rapid molecular detection of tuberculosis and rifampin resistance. *N Engl J Med.* 2010;**363**:1005–1015.
74. Luetkemeyer AF, Firnhaber C, Kendall MA, et al. Evaluation of Xpert MTB/RIF versus AFB smear and culture to identify pulmonary tuberculosis in patients with suspected

tuberculosis from low and higher prevalence settings. *Clin Infect Dis.* 2016;**62**:1081–1088.

75. Buregyeya E, Nuwaha F, Verver S, et al. Implementation of tuberculosis infection control in health facilities in Mukono and Wakiso districts, Uganda. *BMC Infect Dis.* 2013;**13**:360.
76. Mirtskhulava V, Whitaker JA, Kipiani M, et al. Determinants of tuberculosis infection control–related behaviors among healthcare workers in the country of Georgia. *J Infect Control Hosp Epidemiol.* 2015;**36**:522–528.
77. Tenna A, Stenehjem EA, Margoles L, Kacha E, Blumberg HM, Kempker RR. Infection control knowledge, attitudes, and practices among healthcare workers in Addis Ababa, Ethiopia. *J Infect Control Hosp Epidemiol.* 2013;**34**:1289–1296.
78. Farley JE, Tudor C, Mphahlele M, et al. A national infection control evaluation of drug-resistant tuberculosis hospitals in South Africa. *Int J Tuberc Lung Dis.* 2012;**16**:82–89.
79. Tudor C, Mphahlele M, Van der Walt M, Farley JE. Health care workers' fears associated with working in multidrug- and or extensively-resistant tuberculosis wards in South Africa. *Int J Tuberc Lung Dis.* 2013;**17**:22–29.
80. HM. B. *TB Infection Control in the US and Abroad IDWeek 2015*; 2015 October 7, 2015; San Diego, CA.: Infectious Diseases Society of America; 2015.
81. Mazurek GH, Jereb J, Vernon A, et al. Updated guidelines for using Interferon Gamma Release Assays to detect Mycobacterium tuberculosis infection – United States, 2010. *MMWR Recomm Rep.* 2010;**59**:1–25.
82. Zwerling A, Benedetti A, Cojocariu M, et al. Repeat IGRA testing in Canadian health workers: conversions or unexplained variability? *PloS one* 2013;**8**:e54748.
83. Joshi M, Monson TP, Joshi A, Woods GL. IFN-gamma release assay conversions and reversions; hallenges with serial testing in U.S. health care workers. *Ann Am Thorac Soc.* 2014;**11**:296–302.
84. Fong KS, Tomford JW, Teixeira L, et al. Challenges of interferon-gamma release assay conversions in serial testing of healthcare workers in a TB control program. *Chest.* 2012;**142**:55–62.
85. Pai M, Denkinger CM, Kik SV, et al. Gamma interferon release assays for detection of Mycobacterium tuberculosis infection. *Clin Microbiol Rev.* 2014;**27**:3–20.
86. Targeted tuberculin testing and treatment of latent tuberculosis infection. This official statement of the American Thoracic Society was adopted by the ATS Board of Directors, July 1999. This is a Joint Statement of the American Thoracic Society (ATS) and the Centers for Disease Control and Prevention (CDC). This statement was endorsed by the Council of the Infectious Diseases Society of America. (IDSA), September 1999, and the sections of this statement. *Am J Respir Crit Care Med.* 2000;**161**:221–247.
87. Getahun H, Matteelli A, Chaisson RE, Raviglione M. Latent Mycobacterium tuberculosis infection. *N Engl J Med.* 2015;**372**:2127–2135.
88. Gillenwater KA, Sapp SC, Pearce K, Siberry GK. Increase in tuberculin skin test converters among health care workers after a change from Tubersol to Aplisol. *Am J Infect Control.* 2006;**34**:651–654.
89. Blumberg HM, White N, Parrott P, Gordon W, Hunter M, Ray S. False-positive tuberculin skin test results among health care workers. *JAMA.* 2000;**283**:2793.
90. Villarino ME, Burman W, Wang YC, et al. Comparable specificity of 2 commercial tuberculin reagents in persons at low risk for tuberculous infection. *JAMA.* 1999;**281**:169–171.
91. Bailey TC, Fraser VJ, Spitznagel EL, Dunagan WC. Risk factors for a positive tuberculin skin test among employees of an urban, Midwestern teaching hospital. *Ann Intern Med.* 1995;**122**:580–585.
92. Driver CR, Stricof RL, Granville K, et al. Tuberculosis in health care workers during declining tuberculosis incidence in New York State. *Am J Infect Control.* 2005;**33**:519–526.
93. Thrupp L, Bradley S, Smith P, et al. Tuberculosis prevention and control in long-term-care facilities for older adults. *J Infect Control Hosp Epidemiol.* 2004;**25**:1097–1108.
94. Ijaz K, Dillaha JA, Yang Z, Cave MD, Bates JH. Unrecognized tuberculosis in a nursing home causing death with spread of tuberculosis to the community. *J Am Geriatr Soc.* 2002;**50**:1213–1218.
95. Verma G, Chuck AW, Jacobs P. Tuberculosis screening for long-term care: a cost-effectiveness analysis. *Int J Tuberc Lung Dis.* 2013;**17**:1170–1177.
96. American Society of Heating RaA-CEA. *ASHRAE Position Document on Airborne Infectious Diseases*. Atlanta, GA: American Society of Heating, Refrigerating and Air-Conditioning Engineers, Inc.; 2014:1–22.
97. (ACGIH). *ACoGIH. Industrial Ventilation: A Manual of Recommended Practice for Design*, 28th ed. Cincinnati, Oh.: ACGIH; 2013.
98. American Society of Heating RaA-CE, Inc *Standard 170–2013 – Ventilation of Health Care Facilities*. Atlanta, Ga.: ASHRAE; 2013.
99. Abdul Salam ZH, Karlin RB, Ling ML, Yang KS. The impact of portable high-efficiency particulate air filters on the incidence of invasive aspergillosis in a large acute tertiary-care hospital. *Am J Infect Control.* 2010;**38**:e1–e7.
100. Rutala WA, Jones SM, Worthington JM, Reist PC, Weber DJ. Efficacy of portable filtration units in reducing aerosolized particles in the size range of Mycobacterium tuberculosis. *J Infect Control Hosp Epidemiol.* 1995;**16**:391–398.
101. Health. NIfOSa. *Environmental Control for Tuberculosis: Basic Upper-Room Ultraviolet Germicidal Irradiation Guidelines for Health care Settings*. Cincinnati, Ohio: DHHS/ CDC/NIOSH; 2009.
102. Nardell EA. Indoor environmental control of tuberculosis and other airborne infections. Indoor Air 2015.
103. Nardell EA. Transmission and institutional infection control of tuberculosis. *Cold Spring Harb Perspect Med.* 2015;**6**(2):a018192.
104. Mphaphlele M, Dharmadhikari AS, Jensen PA, et al. Institutional tuberculosis transmission. controlled trial of upper room ultraviolet air disinfection: a basis for new dosing guidelines. *Am J Respir Crit Care Med.* 2015;**192**:477–484.
105. Escombe AR, Moore DA, Gilman RH, et al. Upper-room ultraviolet light and negative air ionization to prevent tuberculosis transmission. *PLoS Medicine.* 2009;**6**:e43.
106. ASHRAE. *Standard 55–2013 – Thermal Environmental Conditions for Human Occupancy*. Atlanta, Ga.: ASHRAE; 2013.
107. Nardell E, Vincent R, Sliney DH. Upper-room ultraviolet germicidal irradiation (UVGI) for air disinfection: a symposium in print. *Photochem Photobiol.* 2013;**89**:764–769.

108. MacIntyre CR, Chughtai AA. Facemasks for the prevention of infection in healthcare and community settings. *BMJ.* 2015;**350**: h694.

109. Adal KA, Anglim AM, Palumbo CL, Titus MG, Coyner BJ, Farr BM. The use of high-efficiency particulate air-filter respirators to protect hospital workers from tuberculosis: a cost-effectiveness analysis. *N Engl J Med*. 1994;**331**:169–173.

110. Nettleman MD, Fredrickson M, Good NL, Hunter SA. Tuberculosis control strategies: the cost of particulate respirators. *Ann Intern Med.* 1994;**121**:37–40.

111. Department of Labor OSaHA. Occupational exposure to tuberculosis: proposed rule. Federal Register1997:54159–54308.

112. Prevention. CfDCa. Guidelines for preventing the transmission of Mycobacterium tuberculosis in healthcare settings, 1994. *MMWR Morbidity and Mortality Weekly Report.* 1994;**43**(RR-13):1–132.

113. Department of Labor OSaHAO. occupational exposure to tuberculosis; proposed rule; termination of rulemaking respiratory protection for M. tuberculosis; final rule; revocation. Federal Register 2003:75767–75775.

114. Department of Labor OSaHAO. Respiratory protection for M. tuberculosis. 29 CFR Part 1910 [Docket No. H–371]. Federal Register2003:75776–75780.

115. Tuberculosis and Respiratory Protection Enforcement. OSHA Letter of Interpretation (March 24, 2008). Resumes full enforcement of the entire Respiratory Protection standard, including 29 CFR 1910.134(f)(2). Occupational Safety and Health Administration (OSHA), 2008. (Accessed December 31, 2015, at www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=INTERPRETATIONS&p_id=26013.

116. Coffey CC, Campbell DL, Zhuang Z. Simulated workplace performance of N95 respirators. *Am Ind Hyg Assoc J.* 1999;**60**:618–624.

117. Coffey CC, Lawrence RB, Zhuang Z, Campbell DL, Jensen PA, Myers WR. Comparison of five methods for fit-testing N95 filtering-facepiece respirators. *Appl Occup Environ Hyg.* 2002;**17**:723–730.

118. Coffey CC, Lawrence RB, Campbell DL, Zhuang Z, Calvert CA, Jensen PA. Fitting characteristics of eighteen N95 filtering-facepiece respirators. *J Occup Environ Hyg.* 2004;**1**:262–271.

119. NIOSH-Approved N95 Particulate Filtering Facepiece Respirators. CDC/NIOSH, 2015. Available at: www.cdc.gov/niosh/npptl/topics/respirators/disp_part/n95list1.html. Accessed December 31, 2015.

120. Zhuang Z, Coffey CC, Ann RB. The effect of subject characteristics and respirator features on respirator fit. *J Occup Environ Hyg.* 2005;**2**:641–649.

121. Coffey CC, Lawrence RB, Zhuang Z, Duling MG, Campbell DL. Errors associated with three methods of assessing respirator fit. *J Occup Environ Hyg.* 2006;**3**:44–52.

122. Zhuang Z, Liu Y, Coffey CC, Miller C, Szalajda J. Inward Leakage Variability between respirator fit-test panels – Part I. deterministic approach. *J Occup Environ Hyg*. 2015;**12**:753–760.

123. U.S. Department of Health and Human Services. Centers for Disease Control and Prevention and National Institutes of Health. *Biosafety in Microbiological and Biomedical Laboratories*, 5th ed.: U.S. Department of Health and Human Services; 2009:1–438.

124. Fennelly KP, Nardell EA. The relative efficacy of respirators and room ventilation in preventing occupational tuberculosis. *J Infect Control Hosp Epidemiol.* 1998;**19**:754–759.

125. U.S. Department of Health and Human Serivces PHS, Centers for Disease Control and Prevention/National Institute for Occupational Safety and Health. TB Respiratory Protection Program in Health Care Facilities: Administrator's Guide. Cincinnati, Ohio: NIOSH; 1999:1–112.

126. Blumberg HM, Burman WJ, Chaisson RE, et al. American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America. Treatment of tuberculosis. *Am J Respir Crit Care Med.* 2003;**167**:603–662.

127. Parrish NM, Carroll KC. Role of the clinical mycobacteriology laboratory in diagnosis and management of tuberculosis in low-prevalence settings. *J Clin Microbiol.* 2011;**49**:772–776.

128. Lawn SD. Advances in diagnostic assays for tuberculosis. *Cold Spring Harb Perspect Med.* 2015;**5**:a017806

129. Taylor Z, Nolan CM, Blumberg HM, et al. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR Recomm Rep.* 2005;**54**:1–81.

130. Denkinger CM, Schumacher SG, Boehme CC, Dendukuri N, Pai M, Steingart KR. Xpert MTB/RIF assay for the diagnosis of extrapulmonary tuberculosis: a systematic review and meta-analysis. *Eur Respir J.* 2014;**44**:435–446.

131. Steingart KR, Schiller I, Horne DJ, Pai M, Boehme CC, Dendukuri N. Xpert(R) MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. *Cochrane Database of Systematic Reviews.* 2014;**1**:CD009593.

132. Wang JY, Lee MC, Chang JH, et al. Mycobacterium tuberculosis nucleic acid amplification tests reduce nosocomial tuberculosis exposure in intensive care units: a nationwide cohort study. *Respirology.* 2015;**20**:1233–1240.

133. Kipiani M, Mirtskhulava V, Tukvadze N, Magee M, Blumberg HM, Kempker RR. Significant clinical impact of a rapid molecular diagnostic test (Genotype MTBDRplus assay) to detect multidrug-resistant tuberculosis. *Clin Infect Dis.* 2014;**59**:1559–1566.

134. *Automated Real-Time Nucleic Acid Amplification Technology for Rapid and Simultaneous Detection of Tuberculosis and Rifampicin Resistance: Xpert MTB/RIF Assay for the Diagnosis of Pulmonary and Extrapulmonary TB in Adults and Children*: Policy Update. Geneva: 2013.

135. Gupta RK, Lawn SD, Booth H, Morris-Jones S. What is the role for Xpert(R) MTB/RIF in high-resource settings? Experience from a central London hospital. *Int J Tuberc Lung Dis.* 2014;**18**:1323–1326.

136. Diagnostic Standards and Classification of Tuberculosis in Adults and Children. This official statement of the American Thoracic Society and the Centers for Disease Control and Prevention was adopted by the ATS Board of Directors, July 1999. This statement was endorsed by the Council of the Infectious Disease Society of America, September 1999. *Am J Respir Crit Care Med.* 2000;**161**: 1376–1395.

137. Horsburgh CR, Jr., Barry CE, 3rd, Lange C. Treatment of tuberculosis. *N Engl J Med.* 2015;**373**:2149–2160.
138. Chaulk CP, Kazandjian VA. Directly observed therapy for treatment completion of pulmonary tuberculosis: Consensus Statement of the Public Health Tuberculosis Guidelines Panel. *JAMA.* 1998;**279**:943–948.
139. Chaulk CP, Moore-Rice K, Rizzo R, Chaisson RE. Eleven years of community-based directly observed therapy for tuberculosis. *JAMA.* 1995;**274**:945–951.
140. Getahun H, Matteelli A, Abubakar I, et al. Management of latent Mycobacterium tuberculosis infection: WHO guidelines for low tuberculosis burden countries. *Eur Respir J.* 2015;**46**:1563–1576.
141. Lonnroth K, Migliori GB, Abubakar I, et al. Towards tuberculosis elimination: an action framework for low-incidence countries. *Eur Respir J.* 2015;**45**:928–952.
142. Centers for Disease C, Prevention, American Thoracic S. Update: adverse event data and revised American Thoracic Society/CDC recommendations against the use of rifampin and pyrazinamide for treatment of latent tuberculosis infection–United States, 2003. *MMWR Morbidity and Mortality Weekly Report.* 2003;**52:** 735–739.
143. Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. *MMWR Recomm Rep.* 2000;**49:** 1–51.
144. Centers for Disease C, Prevention. Recommendations for use of an isoniazid-rifapentine regimen with direct observation to treat latent Mycobacterium tuberculosis infection. *MMWR Morbidity and Mortality Weekly Report.* 2011;**60:** 1650–1653.
145. Prevention CfDCa. Latent Tuberculosis Infection: A Guide for Primary Healthcare Providers. *Treatment of Latent TB Infection*. Atlanta, Ga.: Centers for Disease Control and Prevention; 2013:36.
146. Treatment of Latent TB Infection. Centers for Disease Control and Prevention (CDC), 2015. Available at www.cdc.gov/tb/topic/treatment/ltbi.htm. Accessed January 1, 2016.
147. Fraser VJ, Kilo CM, Bailey TC, Medoff G, Dunagan WC. Screening of physicians for tuberculosis. *J Infect Control Hosp Epidemiol.* 1994;**15**:95–100.
148. Barrett-Connor E. The epidemiology of tuberculosis in physicians. *JAMA.* 1979;**241**:33–38.
149. Geiseler PJ, Nelson KE, Crispen RG. Tuberculosis in physicians: compliance with preventive measures. *Am Rev Respir Dis.* 1987;**135**:3–9.
150. Camins BC, Bock N, Watkins DL, Blumberg HM. Acceptance of isoniazid preventive therapy by health care workers after tuberculin skin test conversion. *JAMA.* 1996;**275**:1013–1015.
151. Shukla SJ, Warren DK, Woeltje KF, Gruber CA, Fraser VJ. Factors associated with the treatment of latent tuberculosis infection among healthcare workers at a Midwestern teaching hospital. *Chest.* 2002;**122**:1609–1614.
152. Blumberg HM, Kempker RR. Interferon-gamma release assays for the evaluation of tuberculosis infection. *JAMA.* 2014;**312**:1460–1461.
153. Sahni R, Miranda C, Yen-Lieberman B, et al. Does the implementation of an interferon-gamma release assay in lieu of a tuberculin skin test increase acceptance of preventive therapy for latent tuberculosis among healthcare workers? *J Infect Control Hosp Epidemiol.* 2009;**30**:197–199.
154. Young KH, Ehman M, Reves R, et al. Tuberculosis contact investigations–United States, 2003–2012. *MMWR Morbidity and Mortality Weekly Report.* 2016;**64**:1369–1374.

Chapter

28

Patient Safety

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There is a strong and continually growing interest in patient safety in the United States. Fortunately, for healthcare epidemiologists, the practice of infection prevention is already a patient safety effort: surveillance for adverse events and interventions to prevent harm to patients in the future. In this chapter, we discuss the history and importance of patient safety, terms and techniques unique to the field, and the role of infection prevention and control.

Space Shuttle Disasters: The Importance of System Errors

The crash of the *Challenger* space shuttle in 1986 resulted in an investigation that found substantial problems with how the National Aeronautics and Space Administration (NASA) managed significant safety threats in the space shuttle program. In particular, it was found that problems with the O-rings that led to the crash had been known but ignored by NASA for years preceding the disaster.[1]

On February 1, 2003, the *Columbia* became the second space shuttle to be destroyed in flight, killing all on board. This is one of a number of prominent disasters that highlights the complex nature of the problems that affect safety. An investigation found that a falling foam chunk from another part of the shuttle damaged the heat-resistant surface of the left wing, allowing superheated air into the structure of the damaged wing, which eventually led to the destruction of the shuttle. Foam debris was known to have fallen in a similar manner from the space shuttle on multiple earlier flights, but the problem was never adequately addressed. During the flight, after the foam debris was spotted on video of the shuttle's takeoff, engineers repeatedly asked for photographs of the shuttle wing to be obtained so they could assess for damage. Because of lack of communication and a culture of downplaying potential risks, NASA management did not allow the photographs to be taken.

Errors in management and politics also predated the last flight of the *Columbia*. The NASA safety program personnel reported to managers who ran the program that was being assessed, which created a lack of independence in those evaluating and reporting on safety issues. There was a lack of strategic planning by NASA and the executive branch of the federal government. The space shuttle was originally designed as part of a broader (American) space station plan that was rejected; a large amount of money and effort was funneled into a space shuttle program that had little reason to exist. The budget approved by Congress, however, was insufficient to allow for a robust safety program. In summary, the *Columbia* disaster was primarily the result of multiple preexisting errors in the system for how the space shuttle program was run by NASA and the US government.[2]

Many poor infection prevention outcomes apparently "caused" by individual healthcare workers can similarly be traced back to latent system errors. For instance, inadequate sterile technique during placement of a central venous catheter (an individual error) that leads to a catheter-associated bloodstream infection (an adverse event) may actually be attributed to factors such as inadequate training, missing or incorrect equipment parts or additions to central-line insertion kits, and understaffing (such that there is no assistant and/or a fatigued staff member performing the line insertion), which are all potential latent system errors.

Introduction to Patient Safety

While the field of safety has been an active source of investigation and planning in nonmedical fields since the 1960s, it was only recently that the issue gained national attention in the medical industry. In 1999, the Institute of Medicine (IOM) released a report that estimated that 44,000–98,000 inpatients die each year from medical errors.[3] Even the lower estimate would make medical errors the eighth-leading cause of death in the United States, ahead of motor vehicle accidents and breast cancer. The cost of adverse events due to medical errors is estimated to be between $17 billion and $29 billion per year; the lower estimate is 2 percent of US annual healthcare expenditures.[3] Clearly, medical errors lead to substantial mortality and cost. The well-publicized IOM report[3] brought a renewed focus on patient safety, as well as an outpouring of studies and reviews addressing the topic. However, the response of the healthcare industry to introduce patient safety practices was slow, leading to external pressures on healthcare organizations to examine and improve the safety of patients. Regulation came in the form of patient safety requirements for healthcare organizations from the Joint Commission (formerly the Joint Commission on Accreditation of Healthcare Organizations, or JCAHO).[4] In addition, many states now mandate public reporting of healthcare-associated infections.[5] Businesses have also joined in the fray: the Leapfrog Group, a consortium of large businesses that purchase healthcare for their employees, recommends that its patients be cared for in hospitals that have taken particular patient safety measures, such as using computerized physician-order entry.[6]

Table 28.1 Patient-safety terminology

Term	Definition	Example
Error	The failure of a planned action to be completed as intended (i.e., error of execution) or the use of a wrong plan to achieve an aim (i.e., error of planning)	Error of execution: right medication administered to the wrong patient by a nurse
		Error of planning: wrong medication ordered by a physician
Active error	An error by an individual at the "front line" of a complex process	Nurse administers a toxic dose of an aminoglycoside (that was incorrectly ordered and dispensed)
Slip Mistake	An error of implementation (i.e., failure to perform a semiautomatic, low-level behavior)	Failure to order contact isolation for an inpatient with a new culture growing vancomycin-resistant *Enterococcus*
Latent error	An error of higher functioning during a nonstereotypic behavior	Physician made the wrong diagnosis although the right diagnosis was evident
Adverse event	A system error that leads to adverse events if combined with another factor or factors	Chronic understaffing of nursing, which may increase the risk of subsequent active errors by overworked nurses
	An unexpected negative outcome of a process; in the case of healthcare, the processes are medical interventions	Postoperative pneumonia in an otherwise healthy patient
Preventable adverse event	An adverse event caused by an error	Postoperative wound infection after failure to administer appropriate perioperative antibiotic prophylaxis
Sentinel event	An adverse event that is serious and unexpected	Death from postoperative pneumonia in an otherwise healthy patient
Near miss	An error that does not result in a preventable adverse event but could if the error were repeated in the future	Use of inadequately sterilized surgical instruments that does not lead to a subsequent infection in the patient

NOTE: Information is from Kohn et al.[3] and Reason.[26]

Compared with the healthcare industry, other industries have a far better safety record. For instance, for air travel, the fatality rate is 0.43 deaths per million opportunities, and the baggage mishandling rate is approximately 1 instance per 100 opportunities. The accuracy of inpatient medication delivery and the adequate use of postmyocardial infarction medication are compromised in more than1 opportunity in 10. These differences were noted in the IOM report.[3] The report suggested that significant improvements in patient safety were needed and would require large changes in the paradigm of how safety is addressed in healthcare organizations.

Patient safety is more than the use of computer physician-order entry or other interventions to prevent errors. It is a fundamental change in the way errors and adverse events are viewed. Previously, individuals have been singled out as the cause of an adverse event, leading to an organizational culture that emphasized blame and resulted in silence by healthcare workers when errors or adverse events were made. In the newer paradigm for patient safety, it is assumed that most workers are trying to do good work within the constraints of their job and that problems with the system are often the cause of adverse events. Optimally, a nonpunitive culture should emphasize reporting of problems and improving the design of systems so that adverse events in patients will be prevented.[7]

Patient Safety Terminology

To further understand errors and their consequences, a basic understanding of terms used in the safety field is necessary. Examples and definitions are given in Table 28.1.

Although errors may lead to adverse events, each can occur without the other. The failure to give appropriate perioperative antibiotics is an error that does not invariably lead to a postoperative surgical site infection (an adverse event). This error is then a near miss. Conversely, surgical site infection can occur even in the absence of errors. But, if an infection is due to an error, it is a preventable adverse event.

Postsurgical Wound Infection Outbreak: A Medical Adverse Event

An example of an adverse event relating to infection control was reported by the Agency for Healthcare Research and Quality in its online morbidity and mortality forum.[8] The case vignette describes an increase in postoperative sternal wound infections. An investigation by the infection prevention team determined that the outbreak was occurring in patients operated on by one surgeon and his team. When observed during surgery, this team used "sloppy" technique, including

having loose hair and jewelry while performing surgery. Although contamination of surgical wounds by the operating room personnel was not proven in this case, studies have suggested that bacteria shed from surgical personnel – including from skin and hair[9,10] – is common and has led to outbreaks of postoperative infection.[11,12] Although the operating room staff committed active errors (e.g., not properly covering their hair and not removing jewelry), these were likely related to errors in the system. For instance, the culture of the operating room (i.e., the entire surgical team) and leadership of the operating room (i.e., the individual surgeon and surgical chief) permitted sloppy personal surgical attire. Other potential system errors may have included lack of sleep and rest by surgical team members, a rushed schedule that compromised safe practices in order to facilitate rapid patient turnover, lack of access to properly fitting head coverings, and inadequate training of the operating room staff in infection control procedures.

Latent System Errors

In both examples given above, one individual did not act in error alone. Instead, there were multiple active errors because there were several latent errors in the system. For instance, in the *Columbia* disaster, there were many faulty decisions made before and during the flight. However, these decisions were made in a system of poor communication (between engineers and managers) and a culture that downplayed risks instead of actively exploring potential problems. The investigation concluded that the disaster was primarily the result of NASA's "culture," not the act of any one individual.[2] In the instance of the outbreak of sternal wound infections, bacteria shed from the hair of multiple individuals likely caused the wound contamination. These errors could only occur because of latent errors in training, leadership, group culture, and/or patient scheduling.

Adverse events are usually preceded by an active error by an individual. However, these errors are typically the result of latent errors that both increase the risk of the active error (e.g., understaffing) and allow the error(s) to progress to adverse events (e.g., lack of engineering or procedural safety checks). Thus, system errors are thought to account for most adverse events.[7]

Multiple errors usually need to occur together for major adverse events to occur. James Reason's "Swiss cheese" model analogizes the multiple errors that precede an adverse event to holes in slices of Swiss cheese lined up like dominoes.[13] The layers of cheese represent multiple barriers and safeguards for preventing adverse events from taking place. The holes in the cheese are active and latent errors. A hole in any one slice does not lead to an adverse event. Only when the holes in multiple layers momentarily line up (i.e., when multiple active and latent errors occur together) do adverse events happen.

Techniques for Detecting and Investigating Adverse Events

Since sentinel events represent severe adverse events, they are worthy of investigation, to prevent further injuries or deaths. Two techniques used to investigate past and potential future adverse events are root cause analysis (RCA) and failure modes and effects analysis (FMEA). Infection prevention programs have traditionally used surveillance to compare infection rates against past rates ("benchmarks") at a single institution or from other medical centers, such as those available through the National Healthcare Safety Network (NHSN) program at the Centers for Disease Control and Prevention (CDC).[14,15] After a discussion of RCAs and FMEAs, we contrast these methods with "benchmarking," and describe how the three approaches are complementary. While full instruction on how to perform an RCA and a FMEA is beyond the scope of this chapter, we provide a conceptual overview of the techniques, illustrated with theoretical examples that may be encountered in infection control.

RCA

RCA is used to investigate a sentinel event in order to determine and correct its causes, and thus to prevent the event or decrease the likelihood that the event will recur. An RCA starts with creation of a flow diagram of events that led to the adverse event. Next, a separate cause and effect diagram is made. Starting with the adverse event, the RCA team traces the causes of the event backward sequentially, elaborating the "roots of the tree" to determine underlying root causes of the event. Causal statements are then constructed to describe how a root cause(s) led to the adverse event(s), with emphasis on latent system errors. Finally, recommendations are made for how to correct the root causes to prevent the adverse event from recurring. It is important that the investigators both review the medical record and interview people involved in the process or event under study.[15]

An investigation of an unexpected death from a postsurgical wound infection could be performed using an RCA. In fact, the Joint Commission mandates that an RCA be performed for all such sentinel events (whether the event is infection related or not). The flow of events is mapped, starting with the need for surgery, through the details of the infection control practices and perioperative antibiotic prophylaxis used, and concluding with the postoperative diagnosis and the management of the infection up through the time of death. A causal diagram would elaborate the root cause of the infection-related death; for example: death from infection, *caused by* (1) wound contamination, *caused by* lack of hospital guidelines mandating that surgical attire cover all head and face hair; and (another branch) *caused by* (2) preoperative administration of antibiotics that was started after the skin incision, *caused by* a schedule that did not allow time for preoperative administration of antibiotics. Causal statements and recommendations may include the following: "Death from wound infection was caused by lack of adequate procedures for protection from wound contamination and lack of proper timing of preoperative antibiotics. Recommendation will be for use of a surgical checklist prior to skin incision that includes checking for proper surgical attire by entire surgical team and completion of preoperative antibiotic administration prior to skin incision."

FMEA

In general terms, FMEA is a systematic method of identifying and preventing product, equipment, and process problems before they occur. Each way a system can fail is called a "failure mode." Each failure mode has a potential "effect" (adverse event). As with an RCA, the first step is creating a flow chart of the system. Next, the FMEA team brainstorms to think of failure modes for each step and their potential effect(s). As with an RCA, people involved with the process under study should be interviewed (and/or included on the team). The "severity" of the effect, risk of "occurrence," and ease of "detection" are then assessed on a scale (e.g., a scale of 1 to 10, where 10 is the worst). Each effect is then assigned a risk priority number (RPN) which is the product of the 3 scores (the severity score multiplied by the occurrence score multiplied by the detection score). In our example, the RPN (or "criticality") of the effect will be on a scale from 1 to 1,000. The potential effects of a system are then ranked from highest to lowest RPN score. The effects with the highest RPN – and all effects with an absolutely high RPN – are targeted for corrective action. After the intervention(s), the RPNs of the effects are recalculated; these are referred to as the "resulting RPNs." Corrective actions should continue until the RPN or resulting RPN for all potential effects is at an acceptable level. An acceptable RPN level is not a number set in stone. The team performing the FMEA has to decide what an acceptable level of risk is in the system they are evaluating.

An example of an FMEA is the evaluation of a hospital's system for sterilizing surgical instruments. There are many steps in the process, including cleaning, sterilization, and the evaluation of sterilization using biological tests (i.e., determining if the sterilizer properly killed a standard test sample of bacteria). Failure to list all sterilized instruments in a log may be a common occurrence (occurrence score, 7), but it is easily detected (detection score, 2) and does not lead to a severe effect (severity score, 2), giving a low RPN of 28 (i.e., $7 \times 2 \times 2$). Failure to exchange the ethylene oxide canister in the ethylene oxide sterilizer during a sterilizer run may be an uncommon occurrence (occurrence score, 3), but it may be difficult to detect without an automatic alarm system (detection score, 8), and operating with nonsterile instruments is likely to have a severe effect (severity score, 8), leading to a relatively higher RPN of 192 (i.e., $3 \times 8 \times 8$). An FMEA of this system would first target the latter step for corrective action.

Contrasting RCA, FMEA, and Benchmarking

The advantages and disadvantages of using these three investigative techniques are listed in Table 28.2. Surveillance with benchmarking detects trends in infection rates even without an unexpected death or disability (i.e., without a sentinel event). An RCA can uncover system errors that may not be explored in an outbreak case-control study that focuses on patient-level risk factors. Since it can be triggered by a single sentinel event, an RCA investigation can also be initiated sooner, before a benchmarking-based system would have detected the new problem. Finally, an FMEA investigates the potential for adverse events that have not yet occurred, preventing

Table 28.2 Comparison of techniques for detecting and investigating adverse events

Method	Advantages	Disadvantages
Surveillance and benchmarking (and outbreak investigation)	• Detects trends in adverse events that are not sentinel events • Detects patient-level risk factors • Yields quantitative results	• Requires multiple events to trigger an investigation, with harm to those patients • May not detect system-level errors • Time-consuming and costly
Root cause analysis	• Can initiate after one sentinel event • Detects system errors	• Requires waiting until sentinel event occurs, such that at least 1 patient is harmed • Qualitative results may be susceptible to hindsight bias • May not detect patient-level risk factors
Failure modes and effects analysis	• Can be initiated prior to an adverse or sentinel event • Detects system errors	• Time-consuming and costly • Risk of potential events may not be anticipated until errors occur • Qualitative results may be susceptible to hindsight bias • May not detect patient-level risk factors • Time-consuming and costly

patient harm before it happens. Thus, the three techniques are complementary.

Healthcare-associated infections have traditionally been tracked using surveillance with benchmarking, then investigated with a retrospective cohort study or a case control study. An outcome is (at least in part) attributed to or "caused by" a risk factor if the probability of finding the observed association between risk factor by chance alone is less than 0.05 (i.e., if the *P* value is less than .05).[16] This quantitative approach can be contrasted with the qualitative techniques of RCA and FMEA, which base decisions on the consensus of an investigative team. However, the determination of the actual "causality" is done on the basis of the sum of the available evidence using Hill's classic criteria,[17] and it is not typically established by a single study. Furthermore, the results of any investigation need to be interpreted in the context of the study methods. While epidemiologists may be more comfortable with the results of a quantitative study, both qualitative and quantitative techniques have a useful role in investigating healthcare-associated infections.

Other Approaches to Improving Safety

In addition to the use of FMEAs and RCAs, there are multiple other quality improvement systems that have been adapted for use in the medical setting. For example, "Six Sigma" is an approach focused on reducing the error rate to less than 3.4 errors per 1 million events (i.e., 6 standard deviations [sigma] from the mean) by "design, measure, analyze and improving" processes (for ongoing processes); in one study, Six Sigma methodology improved hospital hand hygiene compliance[18] Another example is Toyota Production Systems (TPS), which seeks to reduce "overburden" and "inconsistency" in order to decrease waste and thus improve the efficiency of a process. TPS and real-time error reporting across a large healthcare system was used by the Pittsburgh Regional Healthcare Initiatives to decrease infection rates.[19] Another example is Positive Deviance, which identifies individuals in a group with an uncommon approach that leads to a better solution or outcome without using more resources. Along with TPS, Positive Deviance was utilized by selected Veterans Affairs hospital sites as part of a national Veterans Affairs collaborative to decrease the incidence of methicillin-resistant *Staphylococcus aureus* transmission and infections (personal observation, D.R.L.). These approaches represent potential systems of improvement or cultural change that can be learned and potentially adapted to improve hospital patient safety with respect to infections.

Infection Control and Patient Safety

The field of infection control is already working toward improving patient safety by focusing on the prevention of healthcare-associated infections. The Joint Commission's National Patient Safety Goal "7" is to "Prevent (healthcare-associated) Infection(s)" (through adherence to "proven guidelines").[4] Reviewers have emphasized the role of infection control as a critical component of patient safety.[21,22] The following list gives examples of infection control activities that promote patient safety by decreasing the risk of healthcare-associated infections.

1. Surveillance for healthcare-associated infections with feedback of data on infection rates to clinicians
2. Investigating and controlling outbreaks
3. Ensuring proper sterilization or disinfection of equipment for procedures and surgeries
4. Vaccination of vulnerable patients against preventable infectious diseases
5. Evaluating and improving infection control practices that protect patients
   - A. Fostering adherence to hand hygiene recommendations
   - B. Ensuring proper placement and care of invasive devices (e.g., central venous catheters)
   - C. Using contact isolation precautions for patients with infectious diseases that are spread by healthcare workers
   - D. Ensuring proper adherence to environmental infection control procedures by operating room staff (e.g., complete coverage of head and face hair)
   - E. Administering perioperative antibiotic prophylaxis when indicated
   - F. Ensuring judicious use of antimicrobials
   - G. Vaccination of staff against influenza

Joint Commission Regulations Addressing Infection Control

The Joint Commission is the major source of accreditation and stands at the intersection of patient safety and infection control. It first published 6 National Patient Safety Goals that became effective on January 1, 2003. For 2010, there are now 16 goals, of which 2 directly address issues in infection prevention.[4] Goal 7 is "*Reduce the risk of healthcare-associated infections.*" There are 5 requirements to this goal, 2 of which we review here in detail. Requirement 07.01.01 is "*Meeting hand hygiene guidelines*." Compliance with either CDC or World Health Organization hand hygiene guidelines by the hospital will be assessed by interviews and observations of hospital staff. If there is more than a "sporadic" miss in compliance by staff, the hospital will be scored as noncompliant. The hand hygiene recommendations of the most recent World Health Organization guidelines (published in 2009) are discussed and summarized in Chapter 9 of this book.

The second requirement (07.02.01) is *"Manage as sentinel events all identified cases of unanticipated death or major permanent loss of function associated with a healthcare-acquired infection."* In their regulations, the Joint Commission specifies that all sentinel events must be evaluated with an RCA. The Joint Commission emphasizes that this requirement is not new; it simply clarifies that an unanticipated death or loss of function should be reported even if

it is due to a healthcare-associated infection. Whether a death is "unanticipated" depends on the patient's condition on admission. The death of an otherwise healthy adult admitted for an elective procedure would be unanticipated. If the patient was not likely to survive the hospitalization because of their medical conditions at baseline and at admission, then their death would not be a sentinel event. Importantly, the Joint Commission emphasizes that this requirement should not increase the surveillance already being performed (by infection preventionists and/or other hospital personnel). Thus, a hospital's current sentinel event reporting system should clearly include events due to healthcare-associated infections. Another potential source of surveillance for these types of sentinel events is for infection preventionists to report whether infections discovered through surveillance activities are related to subsequent patient deaths.

The second National Patient Safety Goal that directly addresses issues in infection prevention is Goal 10, which is *"Reduce the risk of influenza and pneumococcal disease in institutionalized older adults."* This goal has two requirements: the first (10.01.01) is to develop protocols to identify whether to administer vaccine and to vaccinate patients at "high risk" for influenza and for pneumococcal disease, and the second (10.02.01) is to develop protocols to identify new cases of influenza and manage an outbreak.

Information Technology and Sentinel Event Reporting

The role of technology in improving the quality and safety of patient care in general has been emphasized in recent reviews and reports publications.[7,23] One example is electronic reporting of adverse events by healthcare workers to the hospitals. This approach provides several advantages over alternatives (e.g., paper-based reports). The hospital's internal computer network can be readily accessed at computer workstations, and the information is quickly transmitted to administrators (including healthcare epidemiologists) who can respond to the events. The reports can also be transmitted directly into a database. Thus, single sentinel events as well as trends in adverse events can be communicated efficiently, allowing for rapid response by the hospital administration and infection control team. Another example is infection control surveillance software that allow for real-time alerts based on electronically available data.[24]

Getting Started: Patient Safety and Infection Control at Your Healthcare Institution

1. By performing surveillance for healthcare-associated infections, investigating outbreaks, and promoting good infection control practices, you are already contributing to patient safety.
2. Ensure that a mechanism for reporting and investigating healthcare-associated infection sentinel events is in place at your hospital. Various mechanisms are possible, including passive surveillance by healthcare workers (through a telephone hotline, paper form, or computer-based form) or active surveillance by the infection control team or other hospital-based personnel, potentially with the assistance of surveillance software. Other administrators may primarily run sentinelevent reporting, but input from infection control will be vital. The infection control team should also become familiar with RCA and FMEA techniques and may be called upon by the hospital to lead or at least participate on teams performing these investigations.
3. Establish a nonpunitive culture with regard to medical errors. Healthcare workers do not report to work with the intention of making mistakes. However, they routinely perform complex tasks under less-than-ideal conditions (e.g., with inadequate training or as part of an understaffed department). Active errors by healthcare workers that led to adverse events were likely caused by (or allowed to happen by) system errors in how care is delivered. Although active errors should be evaluated and corrected with improvements in systems, including retraining of staff, they should not result in punitive action against the healthcare worker. Only in such a nonpunitive culture will errors and adverse events be reported, allowing for investigation and system corrections to protect future patients.[6]

Conversely, there are blameworthy behaviors that merit action by healthcare organizations (personal communication, James Bagian). The behaviors include errors by healthcare workers that occur because the worker is impaired by alcohol or other drugs, because the worker is working outside the scope of their responsibility, because of reckless behavior, or because of intentionally harmful behavior. A nonpunitive environment does not mean that people are not responsible for their actions but that staff who commit errors will be encouraged to report mistakes and slips rather than hide them for fear of reprisal and with the assurance that they will be valued for their reporting.

Other Resources for FMEA and RCA

The review article by Spath,[25] "Using failure mode and effects analysis to improve patient safety," summarizes the history and methodology of FMEA using simple language and concepts.

The Veterans Affairs Patient Safety Web site[26] has explanations and instructions for performing RCAs and FMEAs, as well as links to other resources. The site describes a trademarked FMEA methodology referred to as a Healthcare FMEA.

The chapter "Making Health Care Safer: A Critical Analysis of Patient Safety Practices," in the report on patient safety from the Agency for Healthcare Research and Quality,[27] describes the RCA process, then critically evaluates the evidence supporting its use as a tool to investigate medical sentinel events and to improve patient safety.

References

1. GPOAccess. Selected congressional hearings and report from the Challenger space shuttle accident. Available at : www.gpo.gov/help/about_challenger_space_shuttle_accident_selected_congressional_hearings_and_reports.htm. Accessed October 30, 2015.
2. Columbia accident investigation board. Report. Available at : http://history.nasa.gov/columbia/CAIB.html. Accessed October 30, 2015.
3. Kohn LT, Corrigan JM, Donaldson MS, eds. Committee on Quality Health Care in America, Institute of Medicine. *To Err Is Human: Building a Safer Health system*. Report 0309068371. Washington, DC: National Academy Press; 1999.
4. The Joint Commission. National Patient Safety Goals (NPSG): hospital. Available at: www.jointcommission.org/standards_information/npsgs.aspx. Accessed October 30, 2015.
5. The Centers for Disease Control and Prevention. 2015. Available at: www.cdc.gov/HAI/state-based/index.html. Accessed October 27, 2015.
6. Eikel C, Delbanco S. The Leapfrog Group for patient safety: rewarding higher standards. *Jt Comm J Qual Saf.* 2003;**29**(12):634–639.
7. Committee on Quality Health Care in America, Institute of Medicine. *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, DC: National Academy Press; 2001. Available at: www.iom.edu/Reports.aspx. Accessed October 12, 2009.
8. Agency for Healthcare Research and Quality (AHRQ). AHRQ Web M&M: Morbidity and Mortality Rounds on the Web. Environmental Safety in the OR. Available at : https://psnet.ahrq.gov/webmm/case/47/environmental-safety-in-the-or. Accessed October 30, 2015.
9. Bitkover CY, Marcusson E, Ransjo U. Spread of coagulasenegative staphylococci during cardiac operations in a modern operating room. *Ann Thorac Surg.* 2000;**69**(4): 1110–1115.
10. Hubble MJ, Weale AE, Perez JV, Bowker KE, MacGowan AP, Bannister GC. Clothing in laminar-flow operating theatres. *J Hosp Infect.* 1996;**32**(1):1–7.
11. Mastro TD, Farley TA, Elliott JA, et al. An outbreak of surgical-wound infections due to group A *Streptococcus* carried on the scalp. *N Engl J Med.* 1990;**323**(14):968–972.
12. Dineen P, Drusin L. Epidemics of postoperative wound infections associated with hair carriers. *Lancet.* 1973;**2**(7839):1157–1159.
13. Reason J. Human error: models and management. *BMJ.* 2000;**320** (7237):768–770.
14. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 to June 2002, issued August 2002. *Am J Infect Control.* 2002;**30**(8): 458–475.
15. Hidron AI, Edwards JR, Patel J, et al.; National Healthcare Safety Network Team; Participating National Healthcare Safety Network Facilities. Antimicrobial-resistant pathogens associated with healthcare-associated infections: annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007 [published correction appears in *Infect Control Hosp Epidemiol*. 2009;**30**(1):107]. *Infect Control Hosp Epidemiol.* 2008;**29** (11):996–1011.
16. Vincent C. Understanding and responding to adverse events. *N Engl J Med.* 2003;**348**(11):1051–1056.
17. Rosner B. *Fundamentals of Biostatistics*. 6th ed. Pacific Grove, Calif.: Duxbury Press; 2005.
18. Hill AB. The environment and disease: association or causation? *Proc R Soc Med.* 1965; **58**:295–300.
19. Eldridge NE, Woods SS, Bonello RS, et al. Using the Six Sigma process to implement the Centers for Disease Control and Prevention guideline for hand hygiene in 4 intensive care units. *J Gen Intern Med.* 2006;**21**(Suppl 2): S35–S42.
20. Sirio CA, Segel KT, Keyser DJ, et al. Pittsburgh Regional Healthcare Initiative: a systems approach for achieving perfect patient care. *Health Aff (Millwood).* 2003;**22**(5):157–165.
21. Burke JP. Patient safety: infection control: a problem for patient safety. *N Engl J Med.* 2003;**348**(7):651–656.
22. Gerberding JL. Hospital-onset infections: a patient safety issue. *Ann Intern Med.* 2002;**137**(8):665–670.
23. Bates DW, Gawande AA. Improving safety with information technology. *N Engl J Med.* 2003;**348**(25):2526–2534.
24. Masnick M, Morgan DJ, Wright MO, Lin MY, Pineles L, Harris AD, and the SHEA Research Network. *Infect Control Hosp Epidemiol.* 2014;**35**(7):891–893.
25. Spath PL. Using failure mode and effects analysis to improve patient safety. *Aorn J.* 2003;**78**(1):16–37.
26. Patient Safety Web site. Veterans Affairs National Center for Patient Safety. Available at: www.patientsafety.va.gov/index.asp. Accessed October 30, 2015.
27. Shojania KG, Duncan BW, McDonald KM, Wachter RM, Markowitz AJ. Agency for Healthcare Research and Quality. Making health care safer: a critical analysis of patient safety practices. *Evid Rep Technol Assess (Summ).* 2001;**43**:i–x, 1–668.

Chapter

29 Infection Prevention in Design, Renovation, and Construction

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Construction, renovation, and maintenance in healthcare facilities challenge infection prevention personnel. These activities can increase the risk of healthcare-associated infections. Obviously these activities increase the risk to patients, but the construction activity itself is not the only consideration. Construction and renovation projects in healthcare facilities must meet guidelines and regulations established by the local (i.e., city and county) governments and state governments, as well as those established by the federal government and by regulatory and accreditation agencies. The infection preventionist must collaborate with engineers, architects, administrators, nurse managers, physicians, construction personnel, and maintenance staff before, during, and after the project.

During maintenance, renovation, and construction, bacterial or fungal microorganisms in the dust and dirt can contaminate air handling or water systems, which can transmit these organisms to susceptible persons. Seemingly benign activities or changes in the healthcare environment can increase the risk of infection for these patients. While bigger construction and renovation projects usually receive the most attention, infection prevention staff should not forget that simple daily activities that may be considered general maintenance, can also put patients at risk for healthcare-associated infections. For example, moving a ceiling tile to replace a telephone line or pulling up an old carpet can release *Aspergillus* spores into the air and ventilation system. Activities such as cutting into walls may disturb mold growing in areas where the plumbing or the windows leaked. Capping off a plumbing line or shutting down the water system for repairs can create dead spaces in the system, leading to the growth of *Legionella* species.

When important systems such as plumbing or air handling are nonfunctional, routine prevention measures, such as hand washing, may be difficult to maintain. Restarting these systems after maintenance or renovations also may increase the risk of infections such as legionnaire's disease. Furthermore, routine clinical practice and traffic patterns may need to be substantially modified during construction projects to ensure that basic infection prevention precautions are maintained. Current patient populations in hospitals, clinics, and care centers are sicker than those in the past. The numbers of elderly patients, immunocompromised patients, and patients with significant underlying illnesses have increased, and these patients are at high risk of acquiring infections associated with maintenance, renovation, and construction. Thus, the infection prevention staff, especially the infection preventionist, have a tremendous opportunity and responsibility to protect patients, visitors, and staff members during such projects. This chapter identifies the potential risks involved in maintenance, renovation, and construction activities and provides practical solutions to decrease these risks. Although not specifically discussed in this chapter, excavation and demolition projects near patient-care areas create similar infection prevention issues. Infection prevention personnel who must deal with such projects should read the article on demolition issues by Streifel et al.[1]

Role of the Infection Prevention Team

The primary goal of the infection prevention team during maintenance, renovation, or construction in healthcare facilities is to protect susceptible patients, visitors, and healthcare workers from acquiring infections. The 2014 Facilities Guidelines Institute (FGI) Guidelines for Design & Construction of Hospitals and Outpatient Facilities and the Residential Guideline, as well as the 2015 APIC Construction and Renovation Manual,[2] all excellent resources, suggest that the role of the infection prevention team is to provide infection prevention expertise throughout a project (i.e., from predesign until the area is commissioned and ready for occupation and use). Thus, infection prevention personnel should participate in construction projects from the inception, so that they can identify potential infection prevention problems created by the project and can design solutions prospectively. In addition, infection prevention personnel should understand the purpose of the project (which should be described within the functional program), so they can assess whether or not the design will facilitate good infection prevention practice.

The infection prevention team must collaborate with the architects, engineers, and maintenance staff to develop comprehensive maintenance, renovation, and construction policies that define the procedures necessary to maintain a safe environment. An infection control risk assessment (ICRA) is an essential part of these policies.[2,3] The ICRA helps infection prevention personnel and other members of a multidisciplinary planning team determine the infectious risks associated with each project. By forcing the team to identify the patient populations at risk and the magnitude of the project, the ICRA helps the team identify important preventive strategies such as which type of barriers are necessary, whether workers need to wear protective attire and use special entrances and exits, and whether obtaining particle counts is necessary.

During construction projects, infection prevention personnel will be asked to evaluate numerous designs and products.

Table 29.1 Examples of design and construction omissions or errors that affect infection prevention

• No All rooms in a unit likely to provide care for patients with airborne diseases
• Entrance to dirty utility room is through clean utility room
• Air intakes placed too close to exhausts
• Incorrect number of air exchanges
• Air-handling system functions only during the week or on particular days of the week
• No redundancy built in for critical air-flow areas (e.g., ORs, BMT)
• Air vents not re-opened after construction completed
• Carpet placed in areas where spills likely to occur
• Wet-vacuum system in the operating suite pulls water up one floor into a holding tank rather than down one floor
• Aerators on faucets
• Sinks too small or shallow
• Sinks located in inaccessible places
• Patient rooms or treatment rooms without sinks
• Alcohol hand rub locations not included in room layout
• No forced air available in endoscope processing area

Often, they will be asked to determine how much space is necessary for a certain function, which products should be used (e.g., vinyl floor covering or carpet), and what air handling requirements must be met, and any of a number of other questions. To avoid costly mistakes, infection prevention personnel must ask many questions to determine core issues; how the product, equipment, room, or clinic will be used; what possible solutions are available; what the budgetary limitations are; and what infection prevention principles or external regulations apply. In addition, infection prevention personnel may need to review the medical literature, governmental codes, guidelines from architectural and engineering societies and accrediting agencies, and product descriptions to determine which of the products or designs are within the project's budget and also balances the infection prevention requirements with patient and employee safety and satisfaction.

As healthcare budgets shrink, the expertise of infection prevention personnel will become more important during construction and renovation projects. Simultaneously, infection prevention personnel will feel increasing pressure to choose the least expensive products or design. Despite the pressures, they must remember their primary goals and recommend the products or design that will achieve these goals most effectively. The appropriate products or designs may be more expensive initially, but, in the long run, they probably will be less costly, as they may prevent outbreaks or may last longer and require less maintenance.

Infection prevention personnel often are the only clinical personnel who work on all construction and renovation projects. Thus, they may have to be the watchdogs for the entire project to make sure that the design and the construction meets the appropriate standards.

Many of the comments above are based on common sense. However, our experience and the medical literature testify that common sense answers often are not chosen during construction projects (4–34). Table 29.1 lists design and construction errors that the authors of this chapter have encountered in the practice of infection prevention.

Risks Associated with Maintenance, Renovation, and Construction

Persons at Risk of Acquiring Construction-Related Infections

In a healthcare setting, special precautions are needed to protect susceptible or immunocompromised patients from acquiring infections related to maintenance, renovation, or construction. The persons who are most susceptible to these infections have immunologic disorders (infection with human immunodeficiency virus or congenital immune deficiency syndromes) or are receiving immunosuppressive therapy (radiation, chemotherapy, steroids, anti–organ rejection drugs, antitumor necrosis factor antibodies). Patients with severe neutropenia (defined as an absolute neutrophil count of 500 cells/mL or less), such as patients who have undergone allogeneic or autologous hematopoietic stem cell transplant or patients with leukemia who are receiving intensive chemotherapy, are at highest risk of these infections.[35] However, patients with underlying diseases such as chronic obstructive pulmonary disease, cancer, cardiac failure, or diabetes are also at increased risk, compared with healthy individuals.[6]

Organisms That Cause Construction-Related Infections

The two microorganisms that are often noted with outbreaks of healthcare-associated infection during construction-type activities are *Legionella* species[4–7] and *Aspergillus* species.[6–34] *Legionella* species are ubiquitous aquatic microorganisms that can be isolated from 20 to 40 percent of freshwater environments and from soil and dust.

There are 42 species of *Legionella* and 54 serogroups. *Legionella pneumophila* serogroup 1 causes 90 percent of the 10,000–20,000 cases of legionnaire's disease. Common sources of *Legionella* associated with outbreaks include heating and air-conditioning systems, cooling towers, and plumbing systems contaminated with *Legionella* species. These organisms are most commonly transmitted by inhaled aerosols. During construction, *Legionella* organisms can be introduced directly into the water when pipes are disrupted and become contaminated with soil. If a water system is already contaminated, organisms in the biofilm can be released into the water by changes in water pressure (e.g., when a plumbing system is repressurized).

Legionella can multiply rapidly in stagnant water. Therefore, pipes that have not been used for a considerable period of time should be flushed for more than 5 minutes before the water is used.[37] In general, outbreaks of legionellosis have been related to contaminated water. However, one outbreak was associated with the installation of a lawn sprinkler system; investigators postulated that *L. pneumophila* was aerosolized during excavation and inhaled by susceptible people, who developed legionnaire's disease.[6]

Fungi are ubiquitous in both indoor and outdoor environments. There are approximately 900 fungal species that cause mycosis,[38] but *Aspergillus fumigatus* and *Aspergillus flavus* are the species that cause invasive disease most frequently. *Aspergillus* species can be found anywhere in a hospital; however, during construction activities, dust, dirt, and debris that harbor these organisms can be released into the air in quantities that can be harmful to susceptible patients. In general, healthy persons are not susceptible to *Aspergillus* infection, but immunocompromised patients may become severely ill and may die from it. Case fatality rates from a literature review show that cerebral Aspergillosis has a 99 percent mortality rate, whereas pulmonary Aspergillosis has an 86 percent mortality rate and sinus Aspergillosis has a 66 percent mortality rate.[57]

Additional Construction-Related Health Risks

There are other problems with fungi and mold that can occur during maintenance and renovation of healthcare facilities. Fungi may be growing behind walls, above false ceilings, or in any area that may have had water leaks or high humidity. Mold grows quickly and can contaminate water-soaked building materials within 48 hours.[58] Organisms such as *Penicillium*,[39] *Fusarium, Trichoderma*, and *Memnoniella* species and *Stachybotrys chartarum* can produce potent mycotoxins that are harmful to persons who inhale them or touch them with bare skin. Mold-related illness can range from mild allergic rhinitis symptoms – with symptoms such as runny nose, sneezing, and itchy eyes to hypersensitivity pneumonitis, an allergic reaction to mold that becomes worse with repeated exposures and can cause permanent lung damage. Toxins produced by molds can cause a severe illness called "organic dust toxic syndrome," which can start after exposure to a single heavy dose of allergen. The signs and symptoms are abrupt onset of fever, influenza- like symptoms, and respiratory difficulty within hours after exposure.

If employees discover discoloration or a musty odor in an area that is undergoing maintenance or is being renovated, the area needs to be assessed, and mold remediation must be done before the project is finished. The workers should tape a tight barrier of plastic around the affected area and report it immediately to the project manager. Only persons trained in mold remediation should clean the area. If the area is small, trained maintenance or housekeeping staff wearing goggles without venting holes, N-95 respirators, and gloves can clean the area with a mild detergent or a 10 percent solution of bleach (sodium hypochlorite). Large areas of mold may need to be addressed by a professional mold remediation contractor who uses protective attire and engineering controls, such as barriers and high efficiency particulate air (HEPA)–filtered, negative-airflow machines. Organizational policies should define when these special precautions are needed.[40]

Overview of Guidelines, Standards, and Regulations

A number of agencies have produced important resources for infection prevention personnel who are helping with maintenance, renovation, and construction projects. The most important documents are provided by the organizations listed in Tables 29.2 29.3, and 29.4. When reviewing these resources, facility design or means/methods of construction must be considered within the context of requirements by the local authority having jurisdiction (local or state building authority).

Facility Guidelines Institute

The Facilities Guidelines Institute (FGI), with assistance from the American Society of Health Care Engineering and ASHRAE, has developed guidelines on the design and construction of inpatient, ambulatory, long-term care, residential health, and support care facilities.[3] These documents, published every four years by the FGI, are used by more than 42 states and several federal agencies, including the Joint

Table 29.2 Organizations that provide important resources for infection prevention personnel who are helping with maintenance, renovation, and construction projects

Organization	URL
Facilities Guidelines Institute	www.fgiguidelines.org/
Association of Professionals in Infection Control and Epidemiology	www.apic.org/
American Society for Healthcare Engineering of the American Hospital Association	www.ashe.org
American Society of Heating, Refrigeration, and Air- Conditioning Engineers	www.ashrae.org
AORN	www.aorn.org/
Centers for Disease Control and Prevention	www.cdc.gov/
The Joint Commission	www.jointcommission.org/
Occupational Safety and Health Agency	www.osha.gov/
The Center for Health Design Knowledge Repository, (Citations related to healthcare built environments and Key Point Summaries):	www.healthdesign.org/knowledge-repository
Center for Health Design Toolboxes:	www.healthdesign.org/topics

Table 29.3 Guidelines, recommendations, and standards

SOURCE	Key points	Summary/information
AIA Guidelines	Infection control risk assessment (ICRA)	AIA Guidelines (Sect. 1.5–2.1.1).
	Toilet rooms	Patient access without entering a hallway (Sect. 2.1–2.2.1) Staff toilets (Sect. 2.1–2.4.2)
	Hand-washing stations	Required in all patient bathrooms (Sect 2.1–2.1.2) In nursing locations, hand-washing stations shall be conveniently accessible to the nurse station, medication station, and nourishment area. (Sect 2.1–3.1.5.5).
	Emergency department	At least one airborne infection isolation (AII) room (Sect. 2.1–5.1.2.6).
	Finishes	Floor materials shall be readily cleanable and appropriately wear-resistant for the location (Sect. 2.1–7.2.3.2). Wall finishes shall be washable and, in the proximity of plumbing fixtures, shall be smooth and moisture-resistant. (Sect. 2.1–7.2.3.3).
	Ventilation requirements	Table 2.1–5 lists all the special requirements needed for room ventilation.
	Clean and soiled workrooms	Such rooms shall be separate from and have no direct connection with clean work rooms or clean supply rooms. (Sect. 2.1–2.3.8).
	Housekeeping rooms	Housekeeping rooms shall be directly accessible from the unit or floor they serve and may serve more than one nursing unit on a floor. (Sect 2.1–2.3.10.1).
	Airborne infection isolation room(s) and protective environment rooms	The ICRA shall address number, location, and type of airborne infection isolation and protective environment rooms. (Sect. 1.5–2.2.1.1).
	Protective environment rooms	Each protective environment room shall have an area for hand-washing, gowning, and storage of clean and soiled materials located directly outside or immediately inside the entry door to the room. (Sect. 2.1–3.2.3.50).
	Clean linen storage	Location of the designated area within the clean workroom, a separate closet, or an approved distribution system on each floor shall be permitted. If a closed cart system is used, storage of clean linen carts in an alcove shall be permitted. This cart storage must be out of the path of normal traffic and under staff control. (Sect. 2.1–2.3.9.1).
CDC Guidelines for Environmental Infection Control in Healthcare Facilities: Recommendations – Air Section II	ICRA	Convene a multidisciplinary team including infection prevention to coordinate the project.
	Education	Educate the construction team about dispersal of fungal spores
	Mandatory adherence agreements	Written in to the contract or contractor safety policy.
	Infection prevention surveillance	Review microbiologic data and other means of surveillance for fungal infections.
	Control measures	Define scope of activity; determine barrier/infection prevention requirements; relocate patients/staff; conduct measures to prevent contamination through HVAC systems; create negative air pressure in work zones and monitor barriers.
	Monitor the construction environment	Infection prevention professional should make rounds on a routine basis.

Table 29.3 (cont.)

SOURCE	Key points	Summary/information
	Conduct epidemiologic investigations in cases of healthcare acquired *Aspergillus* infections or other fungal disease	Use airborne particle sampling to evaluate barrier integrity; conduct an environmental assessment as indicated; perform conductive measures to eliminate fungal contamination.
CDC Guidelines: Recommendations Water Section VII Cooling Towers & Evaporative Condensers	Planning construction of new healthcare facilities	Locate cooling towers so that drift is directed away from air-intake system; design to minimize the volume of aerosol drift
CDC Guidelines: Recommendations – Environmental Services	Construction activities	Develop strategies for pest control
The Joint Commission 2004 Standard: EC.7.10 The hospital plans for managing utilities	Promote a safe, controlled environment of care Reduce the potential for hospital-acquired illness	Develop a process for designing, installing, and maintaining appropriate utility systems – e.g., domestic water, cooling towers, and ventilation systems including pressure relationships, air exchanges, air filtration efficiencies. Control of elements used in healthcare: biological agents, gases, fumes, dust.
The Joint Commission 2004 Standard: EC.8.30 The organization manages the design and building of the environment when it is renovated, altered or newly created	This standard refers to the AIA Guidelines, state and county regulations and codes or standards that provide equivalent design standards, ICRA Identify hazards that could compromise patient care	Follow AIA Guidelines for Design and Construction of Hospital and Healthcare Facilities and local rules and regulations. Development of an ICRA to address the effect of construction activities on air quality, infection prevention and control, utility requirements, noise, vibration and emergency. procedures.

Table 29.4 HVAC and water guidelines

Design element	Facility type	Guidelines or other references
HVAC Systems	Hospital	Part 4 (ASHRAE 170)
	Outpatient facilities	Part 4 (ASHRAE 170)
Water / Plumbing Systems		**FGI Guidelines**
Potable Water System	Hospital	2.1–8.4.2.3
	Outpatient facilities	3.1–8.4.2.3
Heated potable water distribution system	Hospital	2.1–8.4.2.5, Table 2.1–3
	Outpatient facilities	3.1–8.4.2.5
Dialysis	Hospital	2.1–8.4.2.2 2.2–3 10.6.15
	Outpatient facilities	3.10–8.4.1.2
Drainage systems / condensate/ floor drains	Hospital	2.1–8.4.2.6 2.1–8.4.2.7

Table 29.4 (cont.)

Design element	Facility type	Guidelines or other references
	Outpatient facilities	3.1–8.4.2.6 3.1–8.4.2.7
Emergency eyewash and emergency shower stations	Hospital	2.1–8.4.3.8
	Outpatient facilities	3.1–8.4.3.8
Hand-washing stations (plumbed sinks) and hand sanitation dispensers	Hospital	2.1–2.6.8, 2.1–8.4.3.4 2.2–2.2.6.8 2.1–7.2.2.8 2.1–8.4.3.2
	Nursing Units	2.2–2.2.2.5, 2.2–2.2.6.5, 2.2–2.6.2.5
	NICU/Nursery	2.2–2.10.2.5, 2.2–2.12.2.4
	Cancer treatment / infusion therapy	2.2–3.10.2.5
	Imaging	2.2–3.4.4.5, 2.2–3.4.5.3
	Outpatient treatment / exam rooms	3.1–3.2.2.3 3.1–3.2.3.3
	Mobile units	3.13–3.1.5
Hand scrub facilities (scrub sinks)	Hospital	2.1–3.3 2.1–8.4.3.6
	Outpatient facilities	3.1–3.3 3.1–8.4.3.6
Ice machines	Hospital	2.1–2.6.8, 2.1–8.4.3.4
	Outpatient facilities	3.1–8.4.3.4
Sinks – clinical	Hospital	2.1–8.4.3.5
	Outpatient facilities	3.1–8.4.3.5
Showers/bathing facilities	Hospital	2.1–8.4.3.3
	Outpatient facilities	3.1–8.4.3.3
Surfaces and Furnishings		
Surfaces	Hospital	2.1–7.2.3
	Outpatient facilities	3.1–7.2.3
Furnishings	Hospital	2.1–7.2.4
	Outpatient facilities	3.1–7.2.4

Commission, to regulate healthcare facility design and construction within the United States (see the 2015 APIC Infection Prevention Manual for Construction and Renovation for a listing of state authorities having jurisdiction and the status of adoption of the FGI Guidelines).

The Hospital and Outpatient Facilities document addresses general acute care hospitals, critical access hospitals, psychiatric hospitals, rehabilitation hospitals, primary outpatient care centers, freestanding diagnostic and treatment facilities, ambulatory surgery centers, office surgical facilities, cancer treatment centers, endoscopy facilities, and dialysis facilities.

This document provides requirements for design of features that are of specific interest to infection prevention, including but not limited to requirements for the design of hand hygiene sinks, guidance on the selection of surfaces, requirements for design of operating rooms (including hybrid) and procedure rooms, requirements for the design of protective environment and airborne infection isolation rooms.

The Residential Health, Care and Support Facilities Guideline provides minimum requirements for the design and construction of nursing homes, hospice facilities, assisted living facilities, independent living settings, adult day care facilities, wellness centers and outpatient rehabilitation centers. This document provides excellent guidance on supporting person-centered care while maintaining infection prevention practices.

Both documents incorporate the ANSI/ASHRAE/ASHE Standard 170 "Ventilation of Healthcare Facilities" into the guidelines.

CDC/HICPAC Guideline

The Centers for Disease Control and Prevention (CDC) and the Healthcare Infection Control Practices Advisory Committee (HICPAC) published a guideline on environmental infection control in healthcare facilities in 2003, an extensive document that describes environmental infection prevention strategies and engineering controls to help prevent transmission of infectious agents.[41] Discussions of construction issues are interspersed throughout the document, but most of the recommendations regarding construction are in the section "Recommendations – Air: Section II, Construction, Renovation, Remediation, Repair, and Demolition" (see Table 29.3).

The Joint Commission Standard

The Joint Commission (formerly the Joint Commission on Accreditation for Healthcare Organizations [JCAHO]) evaluates and accredits nearly 17,000 healthcare organizations and programs in the United States. The Joint Commission cites the FGI Guidelines in their standard on management of the environment of care[42] and recommends that healthcare organizations follow the guidelines when planning to renovate existing space or construct new facilities. The Joint Commission's surveyors assess whether healthcare facilities comply with the Environment of Care Standard,[42] the FGI Guidelines,[3] and the CDC's recommendations[41] for protecting patients, visitors, and healthcare workers during maintenance, renovation, and construction projects (see Table 29.3).

Infection Control Risk Assessment (ICRA)

Team Development

Whether the project involves remodeling an existing area or building a new one, the staff members must complete an ICRA before the project begins. A multidisciplinary team that includes individuals with expertise in infection prevention, risk management, facility design, construction, heating, ventilating, and air-conditioning (HVAC), and safety (Figure 29.1) should complete the ICRA to ensure that the project meets all the standards and codes.[3] Infection prevention personnel should help complete the ICRA and should participate in projects from their inception so that they can identify infection prevention issues early and they can make suggestions prospectively, rather than after the design is complete.

Notification of Team Members

Infection prevention personnel should be notified of all major and/or high-risk projects so that they can determine which precautions are needed. However, infection prevention personnel must be available to consult on any project.[2] Maintenance personnel can do minor maintenance and renovation projects that have low risk for patients without direct input from the infection prevention team, if policies have been previously developed describing how to manage the infection prevention risks created by these projects and if education on ICRA expectations has been provided to maintenance personnel who will do these minor projects. Barnes- Jewish Hospital, St. Louis, Missouri, requires that an ICRA be completed for all projects, regardless of size. Additionally, the facility maintenance department has been educated about ICRAs and the infection prevention requirements needed for each project.

It is a common misconception that infection prevention considerations only apply to the construction phase of a project. However, the design of a project can have significant bearing on infection prevention practices and infection transmission. Infection prevention considerations should also be included during commissioning. The FGI Guidelines specifically recommend performing a Safety Risk Assessment (SRA) in the earliest stages of project planning. The SRA includes several safety considerations, including infection prevention. Each facility needs a mechanism whereby infection prevention personnel are engaged in the SRA process during early planning phases of a project. In small hospitals, the person responsible for renovation and construction could simply call the infection preventionist and invite him or her to the first meeting or could notify the infection preventionist and other persons who should be on the team at a meeting of another committee such as the Environment of Care, Risk or Safety Committee. Large hospitals that have many projects under way at the same time should develop a more formal process for notifying infection prevention personnel and other ICRA team members to ensure that they can participate. To facilitate planning, some healthcare facilities hold regularly scheduled meetings at which new projects are discussed and updates are provided on current projects. Project managers should be educated as to the importance of having infection prevention input early in the process. After all, design changes are much cheaper before construction begins.

The multidisciplinary team must address the following key points when completing the ICRA:[2,9]

1. The team must assess the type of patients treated in the affected area (i.e., their risk factors for infection) and the services that are provided there. In particular, the team should ask whether the area or facility cares for patients who are highly immunocompromised.
2. The team should assess whether essential services, such as power, medical gas, water, sewer, and fire protection, might be disrupted, and it should develop a contingency plan to provide these services if one or more of them are affected by the project.

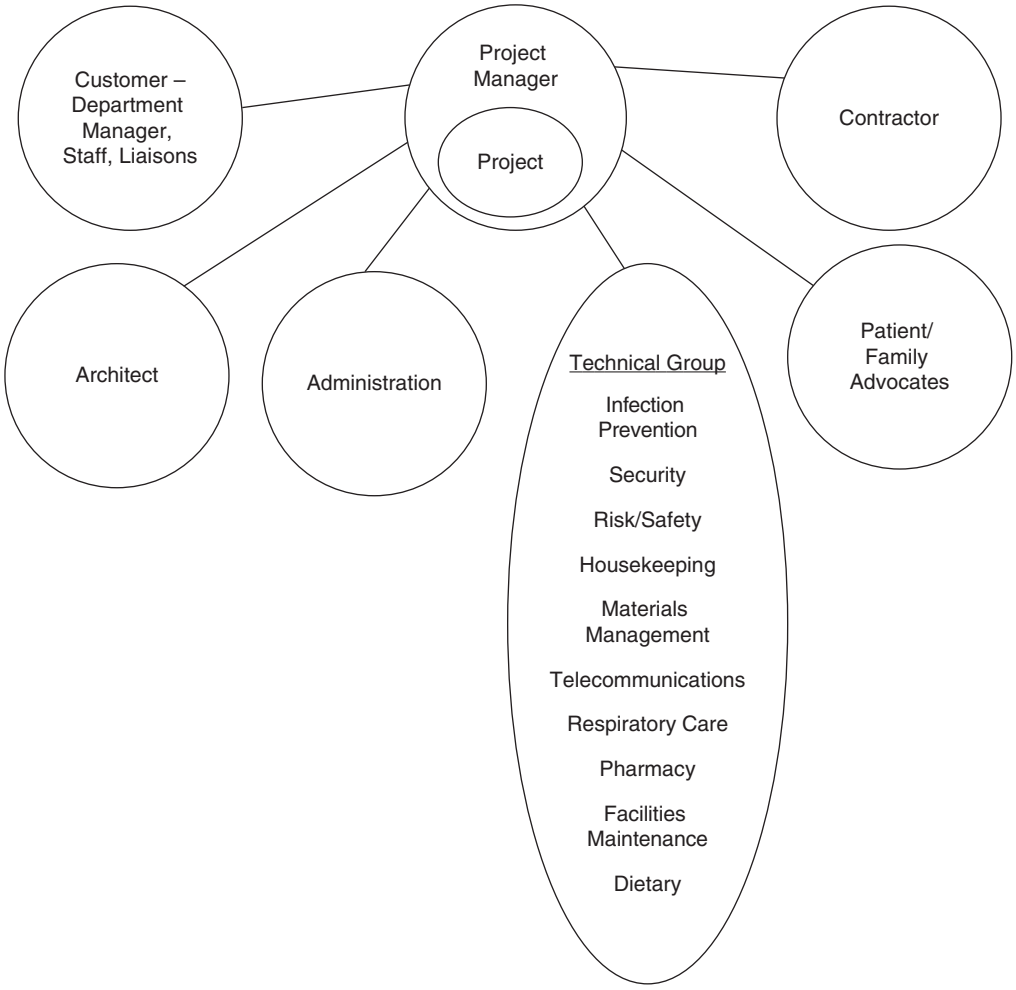

Figure 29.1 Infection Control Risk Assessment

3. The team should evaluate areas that are above, below, and adjacent to the affected area and determine whether any phase of the project will affect these areas adversely. The team must develop a plan to minimize problems and infection risks on the other units.
4. The team must determine whether the patients on the affected or nearby units need to be relocated during the project to protect them from possible infectious risks or to provide an environment conducive to healing (e.g., to limit noise). Also consider if essential environmental controls (e.g., changes to the HVAC system to control pressurization in the construction area) will affect adjacent spaces. Any disruption of key operational spaces (e.g., soiled utility, EVS closets, clean storage, linen storage) must have alternative plans for provision if the unit is to remain operational during construction.
5. The team must decide what types of barriers are necessary to decrease the risk of infection and should assign responsibility for inspecting the barriers and the cleanliness of both the work area and the area immediately adjacent. The barriers and detailed descriptions of other infection control measures should be included in the project specifications so that the costs of these measures can be included in the cost of the project.
6. The team must discuss how the ventilation system will be affected by the project and must determine what measures should be taken to protect the ventilation system and to maintain good quality air in the surrounding areas. For example, the team should determine whether the supply and return ducts need to be sealed. They should also ensure that the ventilation system around the affected area is balanced and that appropriate pressure relationships are maintained. On the basis of the types of patients or activities (e.g., lab, pharmacy) in adjacent areas, the team should decide whether to obtain particle counts before and during the project. The most critical measure during construction activity is for pressurization, if the risk assessment determines the construction zone must be negatively pressurized during the high-dust phases of construction work.

These questions are formalized in the ICRA matrix. This is a tool that can help infection prevention personnel and other members of the multidisciplinary team systematically identify

Step One:
Using the following table, *identify* the Type of Construction Project Activity (Type A-D)

TYPE A	**Inspection and Noninvasive Activities.** Includes, but is not limited to: ▪ Removing ceiling tiles for visual inspection limited to 1 tile per 50 square feet ▪ Painting (but not sanding) ▪ Working on wall coverings, electrical trim work, minor plumbing, and activities that do not generate dust or require cutting into walls or access to ceilings other than for visual inspection.
TYPE B	**Small scale, short duration activities that create minimal dust** Includes, but is not limited to: ▪ Installing telephone and computer cabling ▪ Accessing chase spaces ▪ Cutting into walls or ceilings where dust migration can be controlled.
TYPE C	**Work that generates a moderate to high level of dust or requires demolition or removal of any fixed building components or assemblies** Includes, but is not limited to: ▪ Sanding walls for painting or wall covering ▪ Removing floorcoverings, ceiling tiles, and casework ▪ Constructing new walls ▪ Working on ducts or electrical wiring above ceilings (minor) ▪ Moving or placing cables (major) ▪ Any activity that cannot be completed within a single workshift.
TYPE D	**Major demolition and construction projects** Includes, but is not limited to: ▪ Activities that require consecutive work shifts ▪ Activities that require heavy demolition or removal of a complete cabling system ▪ New construction.

Step 1 _____

Steps 1–3 Adapted with permission of CHI Baylor St. Luke's Medical Center, Houston TX.
Steps 4–14 Adapted with permission Fairview University Medical Center, Minneapolis MN.
Forms modified and provided courtesy of Judene Bartley, ECSI Inc. Beverly Hills MI.

Figure 29.2 Infection Control Risk Assessment Matrix of Precautions for Construction and Renovation.

the infection precautions needed for the project. In one style of ICRA matrix (Figure 29.2), the first task is to identify the type of construction project activity. There are four types (A–D) that range from noninvasive procedures or simple inspection to major demolition and construction projects. Next (step 2) the team must identify the areas (locations) affected by the project and thereby determine how susceptible the patients in these areas are to construction-related infections (i.e., determine the patients' level of risk). These locations should be customized for each facility. Subsequently, (step 3), the team uses the information about the project type and the patients' risk group to determine the class of precautions necessary for the project. The matrix specifies the precautions necessary for each classification. Again, although the matrix may include usual precautions, each risk assessment should be customized to include or exclude requirements based on the scope, location, and risks within the area. The matrix requires the team to answer questions about the project that will help them prospectively identify the most important infection prevention issues.

Appendix: Identify and communicate the responsibility for project monitoring that includes infection control concerns and risks. The ICRA may be modified throughout the project. Revisions must be communicated to the Project Manager.

Some institutions may allow an ICRA to be performed without infection prevention involvement if the scope of work is small (e.g., typical maintenance and renovation work). Figure 29.3 provides an example of another type of ICRA matrix that is tailored to the institution but allows nonclinical personnel to assess the potential risks for the specified task.

Step Two:
Using the following table, ***identify*** **the Patient Risk Groups** that will be affected.
If more than one risk group will be affected, select the higher risk group:

Low risk	Medium risk	High risk	Highest risk
▪ Office areas	▪ Cardiology ▪ Echocardiography ▪ Endoscopy ▪ Nuclear Medicine ▪ Physical Therapy ▪ Radiology/MRI ▪ Respiratory Therapy ▪ Other patient care areas not identified in **High Risk** or **Highest Risk** categories	▪ Cardiac Care Unit ▪ Emergency Room ▪ Labor & Delivery ▪ Laboratories (specimen) ▪ Newborn Nursery ▪ Outpatient Surgery ▪ Pediatrics ▪ Pharmacy ▪ Post-Anesthesia Care Unit ▪ Surgical Units	▪ Any area caring for immunocompromised patients ▪ Burn Unit ▪ Cardiac Catheter Lab ▪ Central Sterile Supply ▪ Intensive Care Units ▪ Medical Unit ▪ Negative pressure isolation rooms ▪ Oncology ▪ Operating rooms including C-section rooms

Step 2_____

Step Three: Match the

Patient Risk Group (***Low, Medium, High, Highest***) with the planned **…**
Construction Project Type (***A, B, C, D***) on the following matrix, to find the **…**
Class of Precautions (***I, II, III or IV***) or level of infection control activities required.

Class I–IV Precautions are delineated on the following page.

IC Matrix – Class of Precautions: Construction Project by Patient Risk

	Construction project type			
Patient risk group	**TYPE A**	**TYPE B**	**TYPE C**	**TYPE D**
LOW risk group	**I**	**II**	**II**	**III/IV**
MEDIUM risk group	**I**	**II**	**III**	**IV**
HIGH risk group	**I**	**II**	**III/IV**	**IV**
HIGHEST risk group	**II**	**III/IV**	**III/IV**	**IV**

Note: Infection Control approval will be required when the Construction Activity and Risk Level indicate that **Class III** or **Class IV** control procedures are necessary.

Figure 29.2 (cont.)

The ICRA matrix is only a guide. The team must assess each project individually and must flexibly apply the principles in the matrix. Not all projects fit exactly into the parameters listed in the matrix. Thus, infection prevention personnel and the team must use their best judgment when their project falls between classifications. Additionally, the ICRA may be a fluid document, changing with the different stages of the project. Unit staff, architects, engineers, maintenance personnel, and construction workers must be educated about infection risks associated with construction and about appropriate methods for minimizing these risks. Education is a continual process, because different hospital staff members will be involved in each project and because many people involved with maintenance, renovation, and construction are contract workers. Educational materials in multiple languages may be developed to discuss basic infection prevention issues in construction. Another helpful tool may be to develop a checklist that itemizes infection prevention essentials, to answer particular questions and prevent problems that occur frequently (e.g., the number and location of sinks, the type of ceiling tiles to use, and the types of flooring and wall coverings to use).

Healthcare facilities should include the infection prevention requirements in the written contract for the project, so the contractors know what they are expected to do. Note that while the requirements will likely need tailoring once the contractor is selected for the project, inclusion in the construction documents provides expectations for fair bidding. If the construction team consistently ignores infection prevention policies, the hospital should levy a fine and/or the contractors should not be allowed to do other projects in the hospital.

Step 3

Description of Required Infection Control Precautions by Class

	During construction project	Upon completion of project
CLASS I	1. Use methods that minimize dust. 2. Immediately replace a ceiling tile displaced for visual inspection.	1. Clean work area when task is completed.
CLASS II	1. Prevent dust from dispersing into air. 2. Use mist (water) on work surfaces to control dust while cutting. 3. Seal unused doors with duct tape. 4. Block off and seal air vents. 5. Place dust mat at entrance and exit of work area 6. Remove or isolate HVAC system in work areas. 7. Contain construction waste in tightly covered containers before transport.	1. Wipe work surfaces with disinfectant. 2. Wet mop and/or vacuum area with HEPA filtered vacuum before leaving. 3. Re-integrate HVAC system.
CLASS III	1. Isolate HVAC system in area where work is being done to prevent contamination. 2. Complete all critical barriers, ie., sheetrock, plywood, plastic, to seal work area from non-work area or use control cube method before construction begins. 3. Maintain negative air pressure within work site; use HEPA equipped air filtration units. 4. Contain construction waste in tightly covered containers before transport. Cover transport receptacles or carts.	1. Do not remove barriers from work area until completed project is inspected by the owner's Safety Department and Infection Control Department and thoroughly cleaned by the owner's Environmental Services Department. 2. Remove barrier materials carefully to minimize spreading dirt and debris created by construction. 3. Vacuum work area with HEPA filtered vacuums. 4. Wet mop area with disinfectant. Do not sweep. 5. Re-integrate HVAC system.
CLASS IV	1. Isolate HVAC system in area where work is being done to prevent contamination of duct system. 2. Complete all critical barriers, ie., sheetrock, plywood, plastic, to seal area from non-work area or implement control cube method before construction begins. 3. Maintain negative air pressure within work site; use HEPA-equipped air filtration units. 4. Seal holes, pipes, conduits, and punctures. 5. Construct anteroom. All personnel must use anteroom so they can be vacuumed using a HEPA vacuum cleaner before leaving work site or they can wear cloth or paper coveralls that are removed each time they leave the work site. 6. All personnel entering work site are required to wear shoe covers and change them each time they exit the work area. 7. Contain construction waste before transport in tightly covered containers. Cover transport receptacles or carts.	1. Do not remove barriers from work area until completed project is inspected by the owner's Safety Department and Infection Control Department and thoroughly cleaned by the owner's Environmental Services Department. 2. Remove barrier material carefully to minimize spreading dirt and debris created by construction. 3. Vacuum work area with HEPA-filtered vacuums. 4. Wet mop area with disinfectant. Do not sweep. 5. Re-integrate HVAC system.

Figure 29.2 (cont.)

Additionally, contractors need to be aware that if proper infection prevention requirements are not followed and there is a clear patient safety risk, the infection preventionist may halt work on the project.

Infection Prevention Construction Permit

Infection prevention expectations that have been determined during risk assessment should be clearly documented and provided as part of the construction documents for bidding. Some organizations refer to this documentation as an Infection Prevention Construction Permit (example provided in Figure 29.4). The permit identifies the project's location, start and end date, project manager, the type of construction activity, the patient risk group, the class selected for the particular project, and the necessary precautions. Complex projects are likely to require multiple permits throughout various phases, as plans must be tailored to specific locations and scope of work. Either the infection prevention team or the project manager should keep this permit on file, and the contractor should maintain a copy at the job site.

Construction Site Monitoring Tool

Both the Owner (or the Owner's representative) and the contractor should inspect the work site to make sure that the construction workers are following the requirements of the ICRA permit. An example of a Construction Site Monitoring

Step 4. **Identify the areas surrounding the project area, assessing potential impact**

Unit below	Unit above	Lateral	Lateral	Behind	Front
risk group	risk group	risk group	risk group	risk group	risk group

Step 5. **Identify specific site of activity, e.g., patient rooms, medication room, etc.**

_____

Step 6. **Identify issues related to ventilation, plumbing, electrical systems (e.g., Are outages likely to occur during the project?).**

_____

Step 7. **Identify necessary containment measures based on the classification of the project. What types of barriers (e.g., solids wall barriers) are needed? Is HEPA filtration required?**

_____

(Note: Renovation/construction area shall be isolated from the occupied areas during construction and shall be at negative pressure with respect to surrounding areas.)

Step 8. **Consider potential risk of water damage. Is there a risk due to compromising structural integrity (e.g., wall, ceiling, roof) ?**

Step 9. **Work hours: Can or will the work be done during non-patient care hours?**

Step 10. **Do plans allow for adequate number of isolation/negative airflow rooms?**

Step 11. **Do the plans allow for the required number & type of handwashing sinks?**

Step 12. **Does the infection control staff agree with the minimum number of sinks for this project?**
(Verify against AIA Guidelines for types and area.)

Step 13. **Does the infection control staff agree with the plans relative to clean and soiled utility rooms?**

Step 14. **Plan to discuss the following containment issues with the project team: traffic flow, housekeeping, debris removal (how and when), etc.**

_____

_____

_____

Appendix: Identify and communicate the responsibility for project monitoring that includes infection control concerns and risks. The ICRA may be modified throughout the project. Revisions must be communicated to the Project Manager

Figure 29.2 (cont.)

Tool is provided in Figure 29.5. This documentation is useful for noting compliance with infection prevention expectations or lapses that could correlate with epidemiologic findings. If an infection occurs that is thought to be associated with construction activity, documentation of compliance with ICRA permit requirements will be essential, should legal action ensue.

Each facility should determine how often the site should be inspected and who will do the inspections. The hospital's size, the type of project, and the nature of surrounding patient-care areas will affect this decision. In a small hospital, daily monitoring may be feasible. In a larger hospital, weekly monitoring may be more feasible. However, if the project is done in a highly sensitive area, such as a bone marrow transplant unit or an operating suite, more frequent inspections may be necessary. The frequency and focus of inspections will also vary with the stages of a project. If staff on the surrounding units are taught which critical factors to report, they can assist in monitoring the site almost continuously and supplement the oversight effort. If the unit staff members note breaches in infection prevention practice, they can contact the Project Manager, who should immediately address the issue. If the issue is not addressed in a timely manner, Infection Prevention should be notified.

Commissioning

Commissioning a space assures that the area is appropriately functioning and ready for occupancy. A checklist such as the Unit/Area Opening Worksheet (Figure 29.6) is a basic checklist that can provide questions and inspection points for infection prevention personnel to use in determining whether a unit or area is ready for occupancy.

Date:

Project Name:
Project Location:

Step 1 - Choose work area:	
1 - Work Area	1 - Work Area
1 Office Areas	4 Endo/DDCC CSPD Pharmacy Main AND all satellites 4400, 7200 Dialysis ALL ORs Perfusion, Card Cath All ICUs and CCUs Chemo Center All nurseries 5300, 5400 14300 Radiation Oncology Gamma Knife 3200, 5900 6900, 7900 8100, 9400 89ICU & PICRU Bronch, MPC
2 Kitchens, cafeterias 2300 6300, 6400 7300, 7400, 7500 10100, 10200 11100, 11200 11400, 11500 12100, 12200 13100, 17400 14400, 14500 15300, 15400, 15500 17400	5 Outside near air intakes
3 Wound Center, CDL Admitting, ED Pulmonary Rehab Resp Care, Lab PACU, Shukar, SDSA All Radiology and CT Physical Therapy 5200, 6200, 6500 7100, 71OU Nuclear Medicine 9100, 9200 10100, 10200, 10500 4900 Ultrasound	6 Outside away from air intakes
NOTE: DAMAGED ASBESTOS FOUND WILL BE ABATED OR ENCAPSULATED PER ENVIRONMENTAL HEALTH AND SAFETY POLICY	

Step 2 - Choose type of work:
2 - Type of Work
A Non-invasive, inspection, wallcovering, electrical trim, minor plumbing NO sanding, wall cutting or dust generation at all
B Small scale, short duration, minimal dust generation. Including but not limited to; cables or wires above ceilings, accessing chase spaces, wall cutting, ceiling penetrations where dust can be controlled
C Work that generates moderate to high levels of dust, removal or demolition of fixed building components or assemblies, including but not limited to; sanding walls, removing floorcovering, ceiling tiles and casework, new wall construction, minor duct or electrical work above ceilings, major cabling or wiring activities, or anything that cannot be completed within a single work shift.
D Major demolition or construction. Including but not limited to; activities which require consecutive work shifts, heavy demolition orremoval of complete cabling or wiring systems, new construction.
STEP 5
Date Contractor **I am aware of and will enforce Infection Control precautions required for this project.**

Step 3 - Find Precaution Level: **Step 4 - Color level of project:**
3 - Infection Control Precautions
GREEN **1A, 2A, 3A, 5A, 6A, 6B, 6C, 6D** *Ceiling tile sprayed with bleach prior to displacing, replaced immediately after visual inspection. * Visitor and patient traffic routes should avoid work area. * Clean supplies transported and stored away from contaminated materials. * Water interruption scheduled during times of low activity.
YELLOW **1B, 1C, 2B, 5B** In addition to GREEN precautions; * Mist work surfaces when cutting *Air vents or returns blocked and sealed - Facilities Engineering to evaluate - If air handler supplies construction area only, it should be shut down (monitor filters during construction and change if necessary) *1 room areas to have walls from floor to ceiling, door closed, frame and door duct taped. *Debris removed in covered, sealed or taped containers, use service elevators or non patient elevator. * Walk-off mats at entrance *Penetrations in walls not open for > 4 hours. Cover w plastic and tape if more. *Ceiling tiles replaced ASAP, if open >4 hours, must be covered.

Step 5 -Sign and authorize risk assessment below **Step 6 - Return to Infection Control - Addresses below**
3 - Infection Control Precautions
ORANGE **4A, 3B, 2C, 5C** In addition to GREEN and YELLOW precautions; ***Infection Control consulted** * Dust minimized - partitions erected to deck above. * Optimal: Chute for debris removal, with HEPA filter or see YELLOW elevator guidelines. * Barriers - dampers closed, assure adjacent air filters functioning, airtight plastic or drywall barriers from floor to ceiling, seams sealed with duct tape or ECUs - **NOTE** barriers must be removed carefully to minimize dust generation. Barriers to be disposed of with other debris. *Negative pressure in const. area with HEPA filters *Increase air filter changing. * Vents cleaned prior to occupancy * Water lines at site and adjacent areas flushed prior to occupancy *Outside demolition >75 feet from air intakes.
RED **4B, 3C, 4C, 1D, 2D, 3D, 4D, 5D** In addition to GREEN, YELLOW and ORANGE precautions; ***Infection Control consulted** *Patients relocated to remote area away from construction.
STEP 6 **Please send to Infection Control**

Figure 29.3 Infection control risk assessment (ICRA) matrix tailored to the specific institution that can be used to identify the infection precautions needed for a construction and renovation project

INFECTION CONTROL CONSTRUCTION PERMIT

					Permit No:
Location of Construction:				Project Start Date:	
Project Coordinator:				Estimated Duration:	
Contractor Performing Work				Permit Expiration Date:	
Supervisor:				Telephone:	
YES	NO	CONSTRUCTION ACTIVITY	YES	NO	INFECTION CONTROL RISK GROUP
		TYPE A: Inspection, non-invasive activity			GROUP 1: Low Risk
		TYPE B: Small scale, short duration, moderate to high levels			GROUP 2: Medium Risk
		TYPE C: Activity generates moderate to high levels of dust, requires greater 1 work shift for completion			GROUP 3: Medium/High Risk
		TYPE D: Extended duration and major construction activities requiring consecutive work shifts			GROUP 4: Highest Risk

	During Construction	Upon Completion of Construction
CLASS I	1. Use methods that minimize dust. 2. Immediately replace any ceiling tile displaced for visual inspection.	1. Clean work area when task is completed.
CLASS II	1. Prevent dust from dispersing into air. 2. Use mist (water) on work surfaces to control dust while cutting. 3. Seal unused doors with duct tape. 4. Block off and seal air vents. 5. Place dust mat at entrance and exit of work area. 6. Remove or isolate HVAC system in work areas. 7. Contain construction waste in tightly covered containers before transport.	1. Wipe work surfaces with disinfectant. 2. Wet mop and/or vacuum with HEPA filtered vacuum before leaving work area. 3. Re-integrate HVAC system.
CLASS III **Date** **Initial**	1. Isolate HVAC system in area where work is being done to prevent contamination of the duct system. 2. Complete all critical barriers or implement control cube method before construction begins. 3. Maintain negative air pressure within work site; use HEPA equipped air filtration units. 4. Contain construction waste in tightly covered containers before transport. Cover transport receptacles or carts.	1. Don't remove barriers until project is inspected and thoroughly cleaned. 2. Remove barrier materials carefully to minimize spreading dirt and debris created by construction. 3. Vacuum work area with HEPA filtered vacuums. 4. Wet mop with disinfectant. Do not sweep. 5. Re-integrate HVAC system.
CLASS IV **Date** **Initial**	1. Isolate HVAC system in area where work is being done to prevent contamination of duct system. 2. Complete all critical barriers or implement control cube method before construction begins. 3. Maintain negative air pressure within work site; use HEPA equipped air filtration units. 4. Seal holes, pipes, conduits, and punctures appropriately. 5. Construct anteroom. All personnel must go through ante-room and be vacuumed with a HEPA vacuum cleaner before leaving work site or they can wear cloth or paper coveralls that are removed each time they leave the work site. 6. All personnel entering work site are required to wear shoe covers and change them each time they exit the work site. 7. Contain construction waste before transport in tightly covered containers. Cover transport receptacles or carts.	1. Do not remove barriers from work area until completed project is inspected and thoroughly cleaned. 2. Remove barrier materials carefully to minimize spreading dirt and debris created by construction. 3. Vacuum work area with HEPA filtered vacuums. 4. Wet mop with disinfectant. 5. Re-integrate HVAC system.

Additional Requirements:

_____ Date Initials	_____Exceptions/Additions to this permit Date Initials are noted by attached memoranda
Permit Request By:	Permit Authorized By:
Date:	Date:

Figure 29.4 Sample infection control construction permit

CONSTRUCTION SITE SURVEY TOOL

Date:_____ **Time:**_____ **Time:**_____

Barriers		
Construction signs posted for the area	☐ Yes ☐ No	☐ Yes ☐ No
Doors properly closed and sealed	☐ Yes ☐ No	☐ Yes ☐ No
Floor area clean, no dust tracked	☐ Yes ☐ No	☐ Yes ☐ No
Air handling		
All windows closed behind barrier	☐ Yes ☐ No	☐ Yes ☐ No
Negative air at barrier entrance	☐ Yes ☐ No	☐ Yes ☐ No
Negative air machine running	☐ Yes ☐ No	☐ Yes ☐ No
Project area		
Debris removed in covered container daily	☐ Yes ☐ No	☐ Yes ☐ No
Designated route used for debris removal	☐ Yes ☐ No	☐ Yes ☐ No
Trash in appropriate container	☐ Yes ☐ No	☐ Yes ☐ No
Routine cleaning done on job site	☐ Yes ☐ No	☐ Yes ☐ No
Traffic control		
Restricted to construction workers and necessary staff only	☐ Yes ☐ No	☐ Yes ☐ No
All doors and exits free of debris	☐ Yes ☐ No	☐ Yes ☐ No
Dress code		
Appropriate for the area (OR, CSS, OB, BMTU)	☐ Yes ☐ No	☐ Yes ☐ No
Required to enter	☐ Yes ☐ No	☐ Yes ☐ No
Required to leave	☐ Yes ☐ No	☐ Yes ☐ No

OR = operating room; CSS = central sterile supply; OB = obstetrics; BMTU = bone marrow transplant unit

Comments:

Surveyor:_____

Figure 29.5 Construction site survey tool

Be aware, however, that it is not the responsibility of infection prevention to commission a space; professionals should be contracted to evaluate the expected functioning and safety of all utility systems.

Major Infection Prevention Issues to Consider During Planning of Projects

Air Handling Systems

Generally, air handling systems do not transmit nosocomial pathogens. However, at times these systems can transmit pathogens such as *Mycobacterium tuberculosis, Aspergillus* species, *Legionella pneumophila*, and Varicella zoster virus. Air handling systems can increase the risk of infection in other ways. For example, if the humidity level is high and the number of air exchanges is inadequate, mold growth may develop, or walls, ceilings, and vents may drip water onto sterile supplies or clean surfaces. Thus, infection prevention personnel should make sure that the air handling systems planned for new or renovated buildings will meet basic infection prevention requirements.

There is a new challenge to healthcare organizations in the HVAC realm. There have been a series of conflicting and vague standards and guidelines issued from different organizations. The guidance from ASHRAE (American Society of Heating, Refrigerating and Air-Conditioning Engineers) suggests that design requirements are not the same as clinical practice requirements. A joint HVAC task force has been created to address these concerns and will issue clarifying guidance for both healthcare organizations as well as surveying organizations. At the time of this writing, this guidance is not yet available.

During the schematic design phase infection prevention personnel and the HVAC Design Engineer should ensure that the air handling systems will be adequate to provide the

INFECTION CONTROL UNIT/AREA OPENING WORKSHEET

Area Surveyed_____ Date_____

Surveyors are to check yes, no, or N/A for each criteria. A satisfactory review is required prior to reopening any unit/department.

Criteria	Yes	No	N/A	Comments
I. Contractor Final Cleanup				
a. Horizontal surfaces free of residual construction dust				
b. Installed equipment and cabinets properly cleaned				
c. Barriers cleaned and removed				
II. HVAC System				
a. HVAC system cleaned if not isolated				
b. New filters in place and operational				
c. HVAC system balanced as specified				
III. Plumbing System				
a. No visible leaks				
b. Plumbing system flushed within 24 hours prior to occupancy				
c. Sinks functional				
IV. Equipment				
a. Soap/towel dispensers/hand sanitizers installed and filled				
b. Refrigerators – checklist for temperature control				
c. Ice machine cleaned and flushed				
V. Final Cleaning				
a. Housekeeping final cleaning completed				
VI. Environmental Rounds				
a. Completion of Environmental Rounds				

Surveyors – Additional Comments:

Date_____

☐ Satisfactory Review
☐ Unsatisfactory Review

Unit Administrator_____
Infection Control_____
Facilities Management_____
Housekeeping_____

Figure 29.6 Infection control unit/area opening worksheet

ventilation required for that area.[3] Exact requirements can vary by state, and may change with updates in guidelines, so the latest guidance should be sought before finalizing requirements. In general, patient rooms should have 6 air changes per hour (ACH), of which 2 ACH must be outside air. Operating rooms and cesarean section delivery rooms require 15 ACH with 3 ACH of outside air. The relative humidity in operating rooms should be 30–60 percent, and the airflow should move from the operating room to adjacent areas. Airborne Infection Isolation (AII) rooms require 12 ACH with 2 ACH of outside air and negative airflow with respect to adjacent areas (i.e., air flows to the adjacent areas). Air from these rooms should be exhausted to the outside away from air intakes or be recirculated after passing through HEPA filters. In addition, rooms in which high- risk procedures (such as bronchoscopy and aerosolized pentamidine treatments) are performed should have negative air-pressure with respect to adjacent areas. Bronchoscopy suites are required to have 12 ACH with outside air comprising 2 ACH. If a room that has special ventilation is renovated, the engineers should measure the number of air changes per hour and the pressure relationships before and after the renovation to ensure that the renovation did not disrupt the air handling system within the room.[43]

Code requirements should ensure that exterior air intakes are placed in appropriate locations in relation to exhaust outlets. Intakes should be located away from cooling towers, trash compactors, loading docks, heliports, exhaust from biological

safety hoods,[44] ethylene oxide sterilizers, aerators, and incinerators. Personnel from infection prevention and engineering should evaluate the design and operation of ventilation systems carefully to ensure that potentially contaminated air is discharged safely, to prevent airborne disease transmission.[45] The commissioning agent should tour the air intake and exhaust sites to ensure filters are properly fitted and the system is functioning as designed.

Isolation Rooms

Given the resurgence of tuberculosis and the emergence of multidrug-resistant bacterial pathogens and new viral pathogens, infection prevention personnel must ensure that the number, type, and placement of isolation rooms is adequate. The advent of new syndromes such as Severe Acute Respiratory Syndrome (SARS) or Middle Eastern Respiratory Syndrome (MERS) suggests that healthcare facilities may need more AII rooms than previously indicated. In the past, some facilities have transferred patients with tuberculosis rather than create a sufficient number of new AII rooms. However, it may not be possible (or safe) to transport patients with SARS or MERS from one facility to another, and each facility may need AII rooms to accommodate such patients.

As of 2010, single bed rooms are a minimum standard in the FGI Guidelines. Infection prevention personnel should assess the community population served by the facility to determine how many AII rooms are necessary. Typically, a hospital should have 1 isolation bed for every 30 acute care beds.[3] In general, isolation rooms for patients with nonrespiratory diseases do not require special ventilation features. If the isolation room has an anteroom, both the room and the anteroom should have hand washing sinks. Nurse-server cabinets or isolation carts may be helpful design considerations to store necessary supplies, such as gowns, masks, and gloves.

Patients who have infectious diseases that are spread by respiratory droplets or droplet nuclei often are seen first in the emergency department or an outpatient clinic. Thus, appropriate isolation rooms in waiting areas would be beneficial in these settings. The FGI Guidelines[3] state that emergency departments need at least 1 AII isolation room for patient care.

Some hospitals use flexible ventilation systems that allow patient-care rooms to have either neutral or negative air-pressure. For such rooms, care must be taken to ensure the airflow is appropriate for the patient in the room. The FGI Guidelines no longer allow switchable air pressurization. Each AII room must have a hand washing station and storage area for clean and soiled material located directly outside or immediately inside the entry door. Each room must have a separate toilet room with a tub or shower and a hand washing station. The door must have a self-closing device, and penetrations in walls, ceilings, and floors must be tightly sealed so that room is maintained at negative air-pressure with respect to the surrounding environment.[45,47] A permanent monitor must assess the air pressure status of the room continuously, and when the room is in use for airborne precautions the negative pressure must be verified daily. This may be achieved manually or through building automation. Anterooms are not required for AII rooms, except for those intended for immunosuppressed patients who need AII. Infection prevention personnel must evaluate proposed AII isolation rooms during the design phase, because retrofitting regular patient rooms to meet the requirements of AII isolation rooms can be very costly.

Protective Environments

Protective environments include operating rooms and bone marrow transplant rooms. These areas must remain as free of airborne infectious agents as possible. The airflow within these areas must flow from clean to less-clean (positive pressure).[43]

Hand Washing Facilities

Each patient-care room, procedure room, and toilet room needs at least 1 hand washing sink, which should be located as close to the room's exit as possible. Sinks should be large enough to prevent splashing. The FGI Guidelines provide specific parameters for sink design. All sinks must have an associated soap dispenser (built-in stainless steel soap dispensers should not be used) and a method to dry hands located at a level that is comfortable for the user. If disposable towels are used, a trash receptacle should be placed near the sink, so paper towels can be discarded properly. Alcohol-based hand rub dispensers should be located away from electrical outlets and switches.[48] Consistency of placement of hand hygiene stations and gel dispensers can facilitate use. Also, when designing a space, place hand hygiene facilities so they are visible and convenient for use, not hidden behind doors or curtains.

A variety of mechanisms exist to control water flow. Conventional hand controls are the least expensive but may not be appropriate for all areas. Foot, knee, or electric-eye controls allow staff members to wash their hands or scrub without touching the sink ("no-touch" methods). Such sinks would be appropriate in operating suites, isolation rooms, and critical-care units. The electric-eye devices are more expensive than the foot or knee controls. In addition, consider automated flushing features for electronic faucets that may be in locations of infrequent use; otherwise, stagnant water will develop biofilm within the faucet. Infection prevention personnel should help unit staff and architects select the best equipment for the location and purpose.

Water Supply and Plumbing

Occasionally, the hospital's water supply will be disrupted intentionally or accidentally during construction projects. Hospitals should have emergency plans that are activated if the water supply to the hospital is disrupted or contaminated. Infection prevention personnel should help develop this plan, because water is crucial to many infection prevention practices and because contaminated water can spread pathogenic organisms. During the summer of 1993, the University of Iowa Hospitals and Clinics, in Iowa City, was faced with the possibility of losing its water supply because the Iowa River was flooding. The hospital's contingency plan included water conservation measures, such as shutting down drinking fountains and ice machines, replacing showers and full-tub or bed baths

with partial baths, using alcohol-based hand cleaners rather than soap and water, and serving meals on disposable dishes. The alternative water system was a well, which was tested for coliform organisms, nitrates, and iron. The hospital's plant operations department was prepared to adjust the plumbing system in order to use the well water. Hospitals that do not have wells must design alternative plans. If the water supply will be disrupted only for a short time, staff can fill large plastic containers with water to be used while the water system is turned off. If the water supply will be off for a longer period of time, the hospital may need to have a company deliver bottled water. During emergencies, agencies such as the US National Guard may be able to provide water. If, during a construction project, the water supply will be turned off for more than 4 hours, the contractor should do this work during times of nonpeak water use, such as evenings, nights, or weekends.

Space for Personal Protective Equipment

All patient-care areas should store personal protective equipment, such as gloves, gowns, masks, and face shields in areas where they are readily accessible. A container for disposal of sharp devices (sharps) must be accessible to workers who use, maintain, or dispose of sharps. The number of containers must be adequate, the size must be large enough for the sharps that will be disposed in that area, and healthcare workers must be able to safely access the opening when they need to discard a sharp. The opening in the sharps containers should be 132–142 cm (52–56 inches) above the floor for use by healthcare workers who are standing, or 96–107 cm (38–42 inches) above the floor for use by healthcare workers who are sitting.[49]

Waste

Infection prevention personnel should help clinical staff plan how urine and feces will be discarded in patient care areas, clinics, and laboratories. Consideration should be made for storage of waste collection devices such as bedpans and urinals, if not single-use disposable. A variety of bedpan flushing devices are available, such as spray hoses and spray arms. Some of these options create splash hazards, clean poorly, or allow water to pool in hoses or nozzles. Alternatives such as disposable pulp bedpan liners can be quite expensive. Soiled utility rooms should contain a clinical sink or a flushing-rim fixture and also a separate hand washing sink. Additionally, containers must be available for biohazardous and nonbiohazardous waste. There may be local regulatory agency requirements relating to biohazardous waste. A nonbiohazardous waste container must be large enough to prevent overfilling and must be located so it is easily accessible to both staff who generate the waste and staff who remove the waste.

Finishes

General Considerations

During the design development phase, infection prevention personnel should help the clinicians and architects choose the finishes: for example, flooring, wall coverings, and ceiling tiles. Ideal finishes are those that are washable and easy to clean.[3] Porous or textured materials can be difficult to clean and thus may allow bacteria and fungi to grow. The finishes should be durable and able to withstand repeated cleaning. In addition, counter tops, backsplashes, and floors should have as few joints as possible, so they are easy to clean.

Ceilings

Ceiling tiles should be appropriate for the areas in which they are being placed. Acoustical tiles may be used in hallways, waiting rooms, and standard patient rooms. Ceilings in semi-restricted areas, such as central sterile supply, radiology procedure rooms, minor surgical procedure rooms, and clean corridors in operating suites, should not be perforated or have crevices where mold and bacteria could grow. The ceiling must be made of smooth, nonabsorptive material that can be washed and is capable of withstanding cleaning with chemicals. Perforated, serrated, cut, or highly textured ceilings are not permitted. In restricted areas, such as operating rooms, all ceilings should be capable of withstanding cleaning chemicals.[3] Cracks and perforations are not allowed. Ceilings in protective isolation rooms should also be cleanable.

Floors

Floors should be easy to clean and should resist wear. Floors where food is prepared should be water-resistant, and floors that are walked on while wet should have a nonslip surface. The housekeeping department should use their cleaning procedures on samples of flooring to determine whether the materials can withstand cleaning and disinfection with germicidal cleaning solutions. Floors in operating rooms and delivery rooms used for cesarean section delivery should be monolithic and should not have joints. Floors in kitchens, soiled work rooms and other areas that are frequently washed with water should have tightly sealed joints.

Carpets decrease noise and have become popular in healthcare facilities. There is no conclusive evidence that links carpet to illness, but carpets can harbor microorganisms. Additionally, the vacuuming of the carpet can create microbursts of dust and potentially put patients at risk. Carpets should not be used in isolation rooms, protective environments, operating rooms, critical care units, kitchens, laboratories, autopsy rooms, or dialysis units. The CDC recommends that carpet should not be used in any high traffic areas or in areas where people might spill liquids.[41,56]

Walls

Walls should be washable and the finish should be smooth. Wall finishes in areas where blood or body fluids could splatter (e.g., operating rooms and cardiac catheterization laboratories) should be fluid resistant and easy to clean. Wall finishes around plumbing fixtures should be smooth and water resistant.[3] Wall bases and floors, especially around small pipes, should not have joints or should have joints that are sealed tightly.[3] In food preparation areas, walls should be free

of spaces that harbor insects and rodents. In operating rooms, cesarean section delivery rooms, and sterile processing rooms, walls should not have fissures, open joints, or crevices that permit dirt particles to enter the room.

Counter Tops

Counter tops should typically be composed of a nonporous solid material, such as thermoset polymer or stainless steel. Laminate, even with a protective sealant, can easily absorb water, resulting in mold growth, discoloration, and warping.

Minimizing the Risk of Infection During Projects

Air Handling Systems

Infection prevention personnel should collaborate with the facility's HVAC specialist to decide whether the HVAC system needs to be isolated during construction. During renovation or construction projects, selected air intakes (particularly those near excavation sites) and air ducts in the construction area need to be protected from dust by 1 of 3 methods: shutting them down, equipping them with additional filters, or covering them with plastic. Engineering or maintenance personnel also should check air filters frequently and change them when necessary. Air handling units in areas that care for highly immunocompromised patients should contain HEPA filters, to decrease the amount of particulate matter and the number of microbes in the air.

For most high-risk projects in Class III or Class IV, according to the ICRA matrix, the airflow should move from outside the construction site into the site, because air should flow from a clean area into a dirty area. Negative air pressure, or airflow into the construction site, can be achieved by placing a HEPA-filtered negative-airflow machine within the work zone. Ideally, the air from this machine would be exhausted directly to the outside. If this is not possible, the air can be exhausted into a dedicated exhaust vent of the existing air system. Do not exhaust construction air into the building return air system. A pressure monitor should be placed within the work zone to ensure that this area is maintained at negative air pressure with respect to the adjacent areas. A simple visual monitor, such as a flutter strip, is adequate and can be used by area staff as well as the contractor to monitor the space. The contractor is responsible to monitor the airflow and to make sure the HEPA filters are clean and working properly.

A HEPA-filtered negative-airflow machine may be required for other projects. For example, such machines would be necessary during work on the ceilings within patient-care areas in Group 3 (i.e., medium high risk) or Group 4 (highest risk) of the ICRA matrix for Class I or Class II construction activities. For lower-risk projects that may not produce much dust or are located in lower-risk areas, HEPA machines can be used to "scrub" the air in a construction zone without the requirement of negative pressurization. Each contractor should own one or more of these machines, and healthcare maintenance departments should have at least one machine that they can use during maintenance activities that generate dust. It is vital that these machines be maintained and their filtration verified using a particle counter.

The air quality must be maintained and monitored carefully in areas where immunocompromised patients are cared for, including patients receiving treatment for malignancies, patients with bone marrow or solid organ transplants, and premature neonates. We recommend that infection prevention personnel work with staff in the appropriate departments to develop policies that describe in detail what must be done when any modifications, renovations, demolition, or construction are done in their areas of the facility. Activities as seemingly minor as installing computer cables or conduits in the ceiling space could stir up *Aspergillus*-laden dust that would be hazardous for immunocompromised patients. When work is being done in areas that house immunocompromised patients, some precautions are needed in addition to those used in all patient care areas (see the subsection on barriers, below). For example, existing air ducts and the space above the ceiling tiles must be cleaned with a HEPA-filtered vacuum cleaner before undertaking any project that involves opening these areas. The area inside the barrier must be cleaned and vacuumed (with a HEPA-filtered vacuum cleaner) before the barrier is removed and again after the barrier is removed. In addition to these precautions, portable HEPA filters can be placed in patients' rooms to ensure that the air is as clean as possible ("air scrubbing"). Facilities that cannot implement appropriate precautions must close these units or move patients to other areas of the hospital that can provide an appropriate level of safety for the duration of the project.

Controlling Dust and Dirt

Construction and renovation projects create tremendous amounts of dust or debris that may carry microorganisms, such as *Aspergillus* spores.[55] Infection prevention personnel must collaborate with other staff to devise ways to prevent the dust and dirt from contaminating clean or sterile patient-care surfaces, supplies, and equipment. Some general measures to limit dust and dirt and to minimize the risk of fungal infections in healthcare facilities during maintenance, renovation, or construction include the following:

- Wet mop the area just outside the door to the construction site daily, or more often if necessary.
- Use a HEPA-filtered vacuum to clean adjacent carpeted areas daily, or more often if necessary.
- Shampoo carpets when the construction project is completed.
- Transport debris in containers with tight-fitting lids, or cover debris with a wet sheet.
- Remove debris as it is created; do not let it accumulate.
- Do not haul debris through patient-care areas, if possible.
- Remove debris through a window when construction occurs above the first (ground) floor, if possible.
- Remove debris after normal work hours, if possible, through an exit restricted to the construction crew.

- Designate an entrance, an elevator, and a hallway for use only by construction workers.
- If workers must traverse high-risk patient-care areas, they must remove dust from their bodies and clothes and then put on gowns, shoe covers, and head covers before walking through the unit. In particular areas of the hospital (e.g., the operating suite), workers may need to wear protective clothing while working in the construction site during times of heaviest contamination, then removing this garb prior to redonning to exit the construction zone to move through the patient care area.
- For small projects, the construction-tool carts should be cleaned before entering the unit and left at the exit through the barrier (see the subsection on barriers, below). For larger projects, the carts and equipment should go into the area and stay behind the barrier until the project is done. Before removing carts and equipment from inside the barrier, the construction crew should clean the items and cover them (e.g., with moist sheets) during times of heavy dust generation. They should be moved off the unit by the designated route. Ideally the path of debris should not be through a patient unit; if a window chute is feasible, this is preferable.

Barriers

Barriers are needed during maintenance, renovation, and construction projects to minimize the dispersion of dust. Commercially available, portable drop-down cubicle barriers can be used for small, quick jobs, such as removing ceiling tiles to install computer cables. These units are equipped with either small HEPA-filtered negative-airflow machines or connections for HEPA vacuums so that the space inside each cubicle is at negative air pressure with respect to the surrounding area. A closed door that is sealed with tape is an adequate barrier for enclosed short-term projects that generate minimal dust.

Plastic sheeting that is 3–8 mil (0.08–0.2 mm) thick or canvas barriers made specifically for dust control can be used for short- term projects that have minimal traffic and do not require fire rating. If plastic is used, contractors must inspect the integrity of the barrier several times during a work shift and they must repair holes, tears, or any defects in the plastic or canvas barrier immediately. A door can be created in the plastic barrier with a zipper or with an overlap of the plastic of 61 cm (2 feet). Anterooms, made of plastic, allow workers to don or remove protective attire or clean dust and debris off of their clothes and their carts before they leave the construction zone and enter a patient-care area. Solid drywall barriers that are taped and finished are required for longer, more extensive projects. If the area is a high-risk area (e.g., a bone marrow transplant unit or an operating suite), plastic barriers should be erected, and the drywall barriers should be built behind the plastic barriers. Plastic barriers should be wiped down with a moist cloth before they are removed.

Facilities that are undergoing construction or renovation in particularly sensitive areas (e.g., bone marrow transplant units if patients are on the unit) may want to document that the barriers are adequate. Particle counters that determine the number of particles suspended in the air can be used for this purpose. The infection prevention personnel on the multidisciplinary team should determine during the ICRA whether it is necessary to obtain particle counts. Particle counts should be obtained outdoors and compared with the indoor counts to ensure that the filters are functioning properly. Thereafter, particle counts should be obtained at intervals that are adequate for the scope and schedule of the project, such as in the areas adjacent to the work site before construction begins, during several days at the start of the project, and weekly until completion. Cultures of air samples are not as useful for this task and should be reserved for special circumstances (e.g., before opening a bone marrow transplant unit after construction) to document that the environment is not contaminated by fungi.

The work site should be kept as clean as possible to enhance the effectiveness of the barriers. HEPA-filtered vacuums should be used for cleaning the construction site and the workers' clothing before they leave the work site. If HEPA-filtered vacuums are not available, the site can be wet mopped, but it should never be swept, because sweeping disperses dust into the air. In addition, sticky "walk-off" mats should be placed just inside the entrance to the work site to clean shoes and the wheels of equipment. The dirty mats should be pulled frequently. Oftentimes these mats are inadequate during heavy demolition. Moist "walk-off" mats do not adequately remove dust from the wheels of carts as they exit a work site. For these circumstances, disposable wet blankets may be used to trap dust on wheels and feet. These should be changed and disposed of when tracking is noted.

Traffic Patterns

To reduce the amount of dust and dirt in the hospital and the risk of exposure to infectious agents, patients, visitors, and staff may need to traverse the hospital by alternate routes. Infection prevention personnel should help identify the appropriate detours before construction begins. Staff should design (and signal) these routes in a logical manner, so that they do not inadvertently increase the risk of nosocomial infection or of noninfectious hazards, such as falls. They also should consider whether housekeeping personnel can maintain the new route, whether the new route interferes with the work done in the area, and whether the route meets minimum aesthetic requirements. If construction is necessary in or near operating suites, surgical personnel must be able to move from place to place without contaminating their surgical attire (scrubs).

The routes by which inanimate items are transported throughout the hospital may need to be altered during construction. In general, all materials, including food, linens, medical supplies and equipment, and janitorial supplies and equipment, must be handled in a manner that minimizes the risk of contamination.[52] Before the construction project begins, infection prevention personnel should help the staff from the affected units plan the routes by which various supplies and equipment will be transported. Clean or sterile

supplies and equipment must be transported to storage areas by a route that minimizes contamination from the construction site and prevents contact with soiled or contaminated trash and linens. To prevent unnecessary contamination with dirt and dust, used supplies and equipment should be moved in enclosed containers from the point of use to the point at which they will be processed.

Traffic patterns in critical areas, such as the operating suite, labor and delivery rooms, nurseries, laboratories, and pharmacies, may not be easy to alter to meet these infection prevention requirements. In such circumstances, the construction crew may need to work during off hours and on weekends. If infection prevention requirements still cannot be met, some areas may need to relocated or closed temporarily.

Storage Areas

During construction, basic principles of infection prevention still apply. Thus, clinical areas must maintain appropriate storage areas, which may be difficult, because the allotted space may be small or may lack essential features. Before construction begins, infection prevention personnel should help the staff identify the locations in which they will store equipment and supplies. Temporary storage areas should allow staff to do the following:

- Easily monitor the supplies (e.g., look at expiration dates)
- Store sterile supplies and equipment away from soiled items (separate clean and dirty areas must be maintained)
- Store clean or sterile supplies at an appropriate distance from sinks to prevent the supplies from becoming wet
- Store contaminated wastes in a designated dirty area outside of direct patient-care areas
- Move items without placing them on the floor (have adequate work space)

In addition, the temporary storage space should be clean, have adequate temperature and humidity control, and should be free of insects and rodents.

An outbreak of 4 surgical and burn wound infections that occurred when a large tertiary-care hospital renovated its central inventory control area illustrates the importance of storing supplies properly during construction.[22] The investigators identified several *Aspergillus* species on the outside of packages of materials from the main floor of Inventory Control: on bags of intravenous preparations, the outsides of sterile paper wrappers, and storage bins in the pharmacy, which was adjacent to the area under construction; and on the outsides of packages containing burn dressings, elastic adhesive, Elastoplast (Beiersdorf AG), gloves, and disposable scissors that were stored on the burn unit and in the intensive care unit. The investigators postulated that the supply boxes were contaminated during construction. The outside of the packages became contaminated when the boxes were opened, and the fungus was inoculated directly into the patients' wounds when the packages were torn open during dressing changes.[53]

Final Check

After the project is completed, the area should be inspected to ensure that all requirements have been met. In some organizations, infection prevention personnel may be consulted to verify the following steps have been taken:

1. Check the location of soap, alcohol-based hand hygiene products, towel dispensers, the sharps disposal container, and the wastebasket. Aesthetics must be challenged if they don't support infection prevention best practices.
2. Check all areas to ensure that the appropriate flooring, ceiling tiles, and wall finishes have been installed.
3. Check all procedure rooms, kitchens, and utility rooms to ensure that they have the appropriate washable flooring and splash guards on sinks.
4. Inspect water faucets to ensure that they do not have aerators.
5. Check pressure and drainage in the water system.
6. Have personnel from maintenance or housekeeping run all faucets the day before patients occupy the unit to decrease the risk of infection from *Legionella* species.
7. Evaluate the direction of airflow in negative air pressure rooms and ensure that the air pressure monitors are placed and functioning properly.
8. Review the HVAC balance reports to ensure that the system meets the specification.

In sensitive areas, such as a bone marrow transplant unit or operating rooms, air sampling can be performed with an air sampling device, such as the SAS compact air sampler (PBI International), to check for contaminated air. Alternatively, sampling can be done by placing settle plates in various areas throughout the room for 30 minutes to 1 hour while the ventilation system is running and the room is vacant. The door should be closed and taped shut, so that persons do not enter the room while the settle plates are in place. If the ventilation system is running properly, the settle plates should be negative for pathogenic microbial growth.[44]

Cost of Construction-Related Infection Control Measures

There is no rule of thumb to determine the cost of the ICRA and the infection prevention measures. Douglas Erickson, a fellow of the American Society for Healthcare Engineering, estimated that when the ICRA was first introduced, costs per contract increased by 25 percent, but by last year this figure was down to 5 percent. He noted recently that some contractors were reporting that these measures actually reduced costs because they increased the pace of the project and prevented delays (D. Erickson, personal communication).

The most accurate way to determine the cost of infection prevention measures is to add the cost of all the components (i.e., the barriers, the HEPA-filtered negative- airflow machines, vacuums, "walk-off" mats, modifications to the HVAC system, cleaning of the work zone and surrounding

areas, monitoring of air pressure, and protective attire). Other costs to consider are special methods needed to minimize noise, vibration, and dust. For example, chipping masonry by hand rather than with a rotary hammer will take more time but will protect nearby patients from excessive noise and vibration. Generally, infection prevention precautions for large projects are best priced on the basis of a fixed set-up cost (i.e., the cost of barriers and duct work) plus the cost per day (i.e., the daily cost of renting negative-airflow machines, maintaining barriers, cleaning work zones, and replacing "walk-off" mats). The longer the project takes, the greater the cost. However, the cost of a project cannot be compared to the cost of a potentially fatal healthcare-acquired infection or the reputational cost that may ensue should infections occur and become public news.

Infection prevention precautions can make otherwise simple projects, such as carpet replacement and installing electrical wiring, more complicated and costly. For example, a project to replace 35,000 square feet (3,252 m^2) of flooring at the authors' hospital was bid at $ 147,000 without infection prevention measures and $ 180,000 once infection prevention precautions were included. The infection prevention measures added $ 33,000 to the cost of the project, which was about $ 1 extra per square foot, or an increase of 22 percent over the cost of conventional carpet replacement. At Barnes-Jewish Hospital (St. Louis, Missouri), a carpet replacement project on the bone marrow transplant unit was bid without taking infection prevention precautions into account. Fortunately, the project was discussed with the infection preventionist, and, after looking at all of the costs and options, staff decided to install new carpet over the old carpet. When the unit is renovated in the future, the patients will be moved and both layers of carpet can be removed safely.

Conclusion

Construction and renovation projects pose special challenges for infection prevention personnel. In many hospitals, they are the only clinical staff members who assist in all construction and renovation projects. We would encourage infection prevention personnel to be involved in all phases of these projects to avert outbreaks of infection and to ensure that newly constructed or renovated areas allow staff to follow good infection prevention practices. We would also encourage infection prevention personnel to maintain good relationships with the architects, contractors, facility maintenance personnel, and others involved in construction and renovation of healthcare facilities so that together they can ensure that the area is safe and well designed.

We think the role of infection prevention personnel in these projects will increase as the clinical complexity of hospitalized patients and the proportion with immunosuppression increase at the same time that hospitals are required to decrease their budgets drastically and regulatory and accrediting agencies are increasing the number of infection prevention guidelines. Infection prevention aspects of construction and renovation projects require large amounts of time and hard work. We would argue that the time and energy invested before and during the project will save hours of time, huge sums of money, and the lives of patients and healthcare workers after the project is finished.

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References

1. Streifel AJ, Lauer JL, Vesley B, Juni B, Rhame FS. *Aspergillus fumigatus* and other thermotolerant fungi generated by hospital building demolition. *Appl Environ Microbiol* 1983;**46**:375–378.
2. Association for Professionals in Infection Control and Epidemiology (APIC). *Infection Prevention Manual for Construction and Renovation*, 2015. 1st ed. Washington, DC; 2015:2–3.
3. *Facilities Guidelines Institute 2014 Guidelines for Design and Construction of Hospitals and Outpatient Facilities*. 2014 ed. Chicago, Ill., FGI; 2014. Available at: www.fgiguidelines.org/guidelines2014_HOP.php.
4. Mermel LA, Josephson S, Giorgio C, et al. Association of legionnaires' disease with construction: contamination of potable water? *Infect Control Hosp Epidemiol.* 1995;**16**:76–91.
5. Parry MF, Stampleman L, Hutchinson JH, et al. Waterborne *Legionella bozemanii* and nosocomial pneumonia in immuno-suppressed patients. *Ann Intern Med.* 1985;**103**:205–210.
6. Thacker SB, Bennett JV, Tsai TF, et al. An outbreak in 1965 of severe respiratory illness caused by legionnaires' disease bacterium. *J Infect Dis.* 1978;**138**:512–519.
7. Haley CE, Cohen ML, Halter J, et al. Nosocomial legionnaire's disease: a continuing common-source epidemic at Wadsworth Medical Center. *Ann Intern Med.* 1979;**90**:583–586.
8. Kistemann T, Huneburg H, Exner M, Vacata V, Engelhart S. Role of increased environmental aspergillus exposure for patients with chronic obstructive pulmonary disease (COPD) treated with corticosteroids in an intensive care unit. *Int J Hyg Environ Health.* 2002;**204**:347–351.
9. Oren I, Haddad N, Finkelstein R, Rowe JM. Invasive pulmonary aspergillosis in neutropenic patients during hospital construction: before and after chemoprophylaxis and institutions of HEPA filters. *Am J Hematol.* 2001;**66**(4): 257–262.
10. Bryce EA, Walker M, Scharf S, et al. An outbreak of cutaneous aspergillosis in a tertiary-care hospital. *Infect Control Hosp Epidemiol.* 1996;**17**:170–172.
11. Lueg EA, Ballagh RH, Forte V. Analysis of the recent cluster of invasive fungal sinusitis at the Toronto Hospital for Sick Children. *J Otolaryngol.* 1996;**25**:366–370.
12. Loo VG, Bertrand C, Dixon C, et al. Control of construction-associated nosocomial aspergillosis in an antiquated hematology unit. *Infect Control Hosp Epidemiol.* 1996;**17**:360–364.

13. Sessa A, Meroni M, Battini G, et al. Nosocomial outbreak of *Aspergillus fumigatus* infection among patients in a renal unit? *Nephrol Dial Transplant.* 1996;**11**:1322–1324.
14. Alvarez M, Lopez Ponga B, Raon C, et al. Nosocomial outbreak caused by *Scedosporium prolificans (inflatum)*: four fatal cases of leukemic patients. *J Clin Microbiol.* 1995;**33**: 3290–3295.
15. Berg R. Nosocomial aspergillosis during hospital remodel. In: Soule BM, Larson EL, Preston GA, eds. *Infections and Nursing Practice: Prevention and Control.* St. Louis: Mosby; 1995: 271–274.
16. American Health Consultants. Aspergillosis: a deadly dust may be in the wind during renovations. *Hosp Infect Control.* 1995;**22**:125–126.
17. American Health Consultants. Construction breaches tied to bone marrow infections. *Hosp Infect Control.* 1995;**22**:130–131.
18. Iwen PC, Davis JC, Reed EC, et al. Airborne fungal spore monitoring in a protective environment during construction and correlation with an outbreak of invasive aspergillosis. *Infect Control Hosp Epidemiol.* 1994;**15**:303–306.
19. Gerson SL, Parker P, Jacobs MR, et al. Aspergillosis due to carpet contamination. *Infect Control Hosp Epidemiol.* 1994; **15**:221–223.
20. Flynn PM, Williams BG, Hethrington SV, Williams BF, Giannini MA, Pearson TA. *Aspergillus terreus* during hospital renovation [letter]. *Infect Control Hosp Epidemiol.* 1993;**14**: 363–365.
21. Dewhurst AG, Cooper MJ, Khan SM, et al. Invasive aspergillosis in immunosuppressed patients: potential hazard of hospital building work. *BMJ* 1990;**301**:802–804.
22. Jackson L, Klotz SA, Normand RE. A pseudoepidemic of *Sporothrix cyanescens* pneumonia occurring during renovation of a bronchoscopy suite. *J Med Vet Mycol.* 1990;**28**: 455–459.
23. Hospital Infection Control. APIC coverage: dust from construction site carries pathogen into unit. *Hosp Infect Control.* 1990;**17**:73.
24. Humphreys H, Johnson EM, Warnock DW, Willats SM, Winter RJ, Speller DC. An outbreak of aspergillosis in a general intensive therapy unit. *J Hosp Infect.* 1991;**18**:167–168.
25. Barnes RA, Rogers TR. Control of an outbreak of nosocomial aspergillosis by laminar air-flow isolation. *J Hosp Infect.* 1989; **14**:89–94.
26. Weems JJ, David, BJ, Tablan OC, et al. Construction activity: an independent risk factor for invasive aspergillosis and zygomycosis in patients with hematologic malignancy. *Infection Control* 1987;**8**:71–75.
27. Perraud M, Piens MA, Nicoloyannis N, Girard P, Sepetjan M, Garin JP. Invasive nosocomial pulmonary aspergillosis: risk factors and hospital building works. *Epidemiol Infect.* 1987;**99**:407–412.
28. Opal SM, Asp AA, Cannady PB Jr, Morse PL, Burton LJ, Hammer PG II. Efficacy of infection control measures during a nosocomial outbreak of disseminated aspergillosis associated with hospital construction. *J Infect Dis.* 1986;**153**:634–637.
29. Krasinski K, Holzman RS, Hanna B, Greco MA, Graff M, Bhogal M. Nosocomial fungal infection during hospital renovation. *Infect Control.* 1985;**6**(7):278–282.
30. Grossman ME, Fithian EC, Behrens C, et al. Primary cutaneous aspergillosis in six leukemic children. *J Am Acad Dermatol.* 1985;**12**(2 part 1):313–318.
31. Sarubbi FA, Kopf HB, Wilson MB, et al. Increased recovery of *Aspergillus flavus* from respiratory specimens during hospital construction. *Am Rev Respir Dis.* 1982;**125**:31–38.
32. Lentino JR, Rosenkranz MA, Michaels JA, Kurup VP, Rose HD, Rytel MW. Nosocomial aspergillosis: a retrospective review of air-borne disease secondary to road construction and contaminated air conditioners. *Am J Epidemiol.* 1982;**116**:430–437.
33. Arnow PM, Sadigh M, Costas C, et al. Endemic and epidemic aspergillosis associated with in-hospital replication of aspergillus organisms. *J Infect Dis.* 1991;**164**:998–1002.
34. Aisner J, Schimpff S, Bennett J, et al. *Aspergillus* infections in cancer patients. *JAMA.* 1976;**235**:411–412.
35. Centers for Disease Control and Prevention. Infectious Disease Society of America, American Society of Blood and Marrow Transplantation. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. *MMWR Recomm Rep.* 2000;**49**(RR-10):1–125.
36. Miscellaneous gram-negative bacilli. In: Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. *Medical Microbiology*. 4th ed. St. Louis: Mosby; 2002:325–333.
37. American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE). *Minimizing the Risk of Legionellosis Associated with Building Water Systems.* ASHRAE Guideline 12–2000. Atlanta, GA: ASHRAE; 2000. Available at: www .ashrae.org/publications/page/1285. Accessed September 16, 2009.
38. Opportunistic mycoses. In: Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. *Medical Microbiology*. 4th ed. St. Louis: Mosby; 2002:664–672.
39. Fox BC, Chamberlin L, Kulich P, et al. Heavy contamination of operating room air by *Penicillium* species: identification of the source and attempts at decontamination. *Am J Infect Control.* 1990;**18**:300–306.
40. D'Andrea C, New York City Department of Health and Mental Hygiene Bureau of Environmental and Occupational Disease and Epidemiology. *Guidelines on Assessment and Remediation of Fungi in Indoor Environments.* New York: 2000:1–17.
41. Centers for Disease Control and Prevention (CDC), Health- care Infection Control Practices Advisory Committee. Guide- lines for environmental infection control in healthcare facilities: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR Recomm Rep.* 2003;**52**(RR-10):1–44.
42. The Joint Commission. *Comprehensive Accreditation Manual for Hospitals: The Official Handbook*. Chicago: The Joint Commission;2015.
43. Streifel A. Healthcare IAQ guidance for infection control. *HPAC Engineering.* 2000;**72**(Apr-May):28–36.
44. Soule BM, ed. *The APIC Curriculum for Infection Control Practice, Vol II.* Dubuque, Ia.: Kendall/Hunt Publishing; 1983.
45. Neill HM. Isolation-room ventilation critical to control disease. *Health Facil Manage.* 1992;**5**:30–38.
46. Langley JM, Hanakowski M, Bortolussi R. Demand for isolation beds in a pediatric hospital. *Am J Infect Control.* 1994;**22**: 207–211.
47. Centers for Disease Control and Prevention. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health care facilities, 1994. *MMWR Recomm Rep.* 1994; **43** (RR-13):1–132.

48. Boyce JM, Pittet D, Healthcare Infection Control Practices Advisory Committee, HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Guideline for hand hygiene in healthcare settings. *MMWR Recomm Rep.* 2002;**51**(RR-16):1–45.
49. US Department of Health and Human Services (DHHS), National Institute for National Safety and Health (NIOSH). *Selecting, evaluating and using sharps disposal containers*. DHHS (NIOSH) publication 97–111. Cincinnati, OH: NIOSH; 1998.
50. Madden CS. Environmental considerations in critical care interiors. *Crit Care Nurs Q.* 1991;**14**(1):43–49.
51. Opal SM, Asp AA, Cannady PB Jr, Morse PL, Burton LJ, Hammer PG II. Efficacy of infection control measures during a nosocomial outbreak of disseminated aspergillosis associated with hospital construction. *J Infect Dis.* 1986; **153**:634–637.
52. Fitch H. Hospital and industry can benefit by sharing contamination control knowledge. *Clean Rooms.* 1993;7:8–9.
53. Bryce EA, Walker M, Scharf S, et al. An outbreak of cutaneous aspergillosis in a tertiary-care hospital. *Infect Control Hosp Epidemiol.* 1996;**17**:170–172.
54. Downs P. Infection control expert hosted by local architecture, engineering firms. *CNR News* 2003. Available at: www.stlconstruction.com.
55. Haiduven D. Nosocomial aspergillosis and building construction. *Med Mycol.* 2009;**47**(Suppl 1):S1–S6.
56. Noskin GA, Peterson LR. Engineering infection control through facility design. *Emerg Infect Dis.* 2001;**7**:354–357
57. Lin S, Schranz, J, Teutsch S. Aspergillosos case-fatality rate: systemic review of the literature. *Clinical Infectious Diseases* 2001;**32**:358–366.
58. FEMA brochure, Dealing with Mold & Mildew in Your Flood Damaged Home. Available at:www.fema.gov/pdf/rebuild/recover/fema_mold_brochure_english.pdf.

Chapter

30

Regulatory Issues Concerning Healthcare Epidemiology and Infection Prevention

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Introduction

With a growing appreciation of the toll and seriousness of healthcare-associated infections (HAI), key stakeholders have demanded a more strict and prescriptive approach to regulating the prevention and management of infections that complicate healthcare. As a result, there has been a growing degree of regulatory activism on the part of policy makers that has slowly but inexorably raised expectations for infection prevention leaders. Healthcare epidemiologists and infection prevention professionals find themselves in the challenging situation of advocating for patients and evidence-based practice while simultaneously navigating an increasingly complex regulatory landscape.

Leading an effective and compliant infection prevention program presents a series of complicated and sometimes conflicting questions to even the most seasoned expert. What are the federal, state, and local regulations and policies with which the program must be compliant? What are the reporting requirements for HAI, notifiable conditions, clusters, outbreaks, and sentinel events? How does performance with respect to processes and outcomes affect the likelihood for financial penalties and incentives in pay-for-performance and value-based programs? In the sections that follow, we discuss the history and background of infection prevention policies and introduce major policy makers to provide context for the sometimes arcane and overlapping alphabet soup of authorities with which the infection prevention provider must be familiar. In the subsequent section, we discuss how these different agencies and programs affect the work of hospital-based infection prevention, specifically expectations around accreditation compliance and site visits, public reporting, and progressively more rigorous performance standards. These sections are followed by a discussion of future trends in infection prevention policy and a discussion of advocacy and how healthcare epidemiologists and infection prevention professionals can and should contribute to the discourse that shapes policy.

For the most part, the discussion will focus on policies and practices in the United States, while recognizing that standards and expectations vary considerably in Europe and other parts of the world. Furthermore, in that so much of the regulatory activism around HAI has up until recently focused on acute care hospitals, the chapter similarly adopts this emphasis.

History: The Origins of Infection Prevention Regulation

The regulations and statutes around the prevention and management of HAI have a long history rooted in public health law, consumer protection, and healthcare regulation and oversight. One basic expectation of government and policy is to prevent undue and avoidable harm to individuals. That communicable disease represents one such harm is well established in case law and policy across most western societies. Historically, the premium placed on preventing contagion among citizens has been valued so highly that policy makers have favored interrupting transmission over expectations of freedom of movement and congregation. Examples of this include the approach to quarantine; whether in the context of medieval ships arriving in port to more contemporary examples of pathogens such as measles, smallpox, and most recently Ebola.

Analogous expectations to prevent infection are similarly placed on both public and private entities licensed by government to conduct business with the public. Food safety laws, whether applied at the level of producer, wholesaler, retailer, preparer, or server have been powerful motivators for improved methods and standards in service to consumers in both the United States and much of the developed world. While challenges in execution and enforcement persist, the precedent stands that individuals have a reasonable expectation to be protected from illness originating in the food they eat and the products and services they purchase.

With these established precedents in mind, it may be surprising to consider that prevention of HAI and multidrug-resistant organisms (MDRO) has emerged as a focus for regulators and lawmakers only in the past several decades. Of course, this contemporary focus reflects the relatively recent appreciation of the scope and consequences of these frequently morbid infections. A similarly recent understanding that many of these infections are preventable has further enabled contemporary activism.

The approach to regulating infection prevention has grown somewhat organically and reactively in the US through a variety of federal, state, or local sources and mechanisms. As a result, HAI regulations have at times left the practicing healthcare epidemiologist and infection prevention professional to reconcile an array of recommendations, standards, and laws that frequently vary among locales. The Centers for Disease Control and Prevention (CDC) has emerged with a primary charge around public health at the national level in the US and now is at the center of supporting innovative practice and policies for preventing HAI and MDRO. The Joint Commission (TJC) now has a principal enforcement arm in holding providers to rigorous standards as defined by the Centers for Medicare and Medicaid Services (CMS). The substantial impact that TJC, CMS, and other federal

agencies have on infection prevention practice will be discussed at length later in the chapter.

Beginning in the early 2000s, legislators at the state and local level became active in regulating and setting policies around infection prevention. This was in part prompted by the visibility given to HAI risks articulated by the media and patient advocacy groups, also discussed later in the chapter. Much of this early state legislative activity focused on transparency around the frequency of HAI and MDRO infections.

Finally, policymakers have continued to increase the pressure with measures that directly link provider reimbursement with performance in reducing HAI. With the Deficit Reduction Act of 2005, the first financial penalties were applied to hospitals that failed to prevent specific conditions that were not present or detected at the time of hospital admission. These pay-for-performance measures have proliferated and are a key driver as the US healthcare system moves from a model of reimbursement for volume to one that rewards value.

Oversight: Governmental and Related Agencies with Regulatory Authority

Overview

The healthcare epidemiologist and infection prevention professional must interact with a large number of government agencies and other nongovernmental entities on an ongoing basis. That said, the interface with these outside organizations is shared with multiple other institutional departments such as government affairs, regulatory compliance, risk management, human resources, finance, laboratory, occupational health, pharmacy, equipment and device sterilization and processing, and nutrition and food services. It is important that hospital-based infection prevention leaders establish and sustain a collaborative relationship with colleagues and leaders from these departments in order to ensure that the overall approach to the extramural agencies described below is coherent and integrated. These entities are introduced here and discussed in greater detail later in the section.

The Department of Health and Human Services (HHS) is the principal US governmental agency for protecting the health of all Americans and is the primary federal agency that affects infection prevention policy and practice. HHS oversees a broad portfolio related to human health: research, public health, food and drug safety, and reimbursement and regulations for federal insurance programs (including Medicare and Medicaid).[1] Key agencies within the HHS are the CDC, CMS, the Food and Drug Administration (FDA), the Agency for Healthcare Research and Quality (AHRQ), the National Institutes of Health (NIH), and the Health Resource Service Administration (HRSA). Occasionally, the Office of Inspector General (OIG) within HHS may influence the work of a healthcare epidemiologist through requests for information on how threats to public policy are addressed and integrity of billing and compliance as it relates to healthcare quality.

In addition to HHS, infection prevention leaders should become familiar with a number of other departments within the US government including the Department of Labor, which protects the health of the workforce including healthcare workers through the Occupational Safety and Health Administration (OSHA) and the Department of Veterans Affairs, which is responsible for the health and wellness of veterans of the US military services. The regulations and expectations of other federal agencies may occasionally come to bear on the leaders of infection prevention in specific circumstances. For example, the Environmental Protection Agency (EPA) is responsible for examining disinfectants used in healthcare, and the Department of Transportation governed the transportation of regulated medical waste during the Ebola epidemic in the US.

The official written record of all US federal statutes is the *United States Code* (USC).[2] The *Code of Federal Regulations* (CFR) is an annual codification of the general and permanent rules published in the Federal Register by the executive departments and agencies of the federal government.[3] Title 42 in USC or CFR is applicable to public health and welfare, and most regulations applicable to infection prevention are contained in this title.

The enforcement of federal policies and expectations around infection prevention is supported by the activities of a number of nongovernmental agencies, principal among them being TJC (formerly the Joint Commission for the Accreditation of Healthcare Organizations). CMS has authorized "deeming authority" to such groups and in doing so has assigned to them the responsibility for ensuring that US healthcare organizations maintain high standards of clinical care and operations that are in accord with CMS expectations. Maintenance of a favorable accreditation status is a condition for receipt of reimbursement from CMS and is therefore essential to the successful operation of any acute care facility.

In the following section, the specific roles and activities of these key agencies are examined in greater detail. In addition, an extensive list of these and other relevant agencies is provided in Table 30.1.

The Centers for Disease Control and Prevention (CDC)

Although the CDC does not have *direct* regulatory or enforcing authority on healthcare facilities and practice, there is a general expectation that CDC guidance be applied in the care of patients and in clinical operations in the US. Ultimately, it is CDC guidelines that drive regulations and accreditation standards around infection control as enforced by agencies such as CMS and TJC. The CDC also develops and employs surveillance definitions for HAI and MDRO, as well as approaches to outbreak investigation and control, public health preparedness regarding bioterrorism, communicable diseases such as tuberculosis and influenza, and pandemic infectious diseases and emerging pathogens such as H1N1 influenza, Ebola, Middle East Respiratory Syndrome (MERS) and Zika virus. Much of this work is articulated and codified by the CDC's Healthcare Infection Control Practices Advisory Committee (HICPAC).

Table 30.1 Key governmental agencies with oversight and authority over the practice of US–based infection control and prevention programs. Adopted from Judene Bartley (from prior edition)

Agency	Program(s) and/or jurisdiction	URL	Regulatory or voluntary oversight	Key areas of focus	Comments
HHS					
Food and Drug Admin. (FDA)[a]	Safe Medical Device Act (SMDA); Safe Blood Supply (both FDA and CDC); food safety for all but meat, poultry, and eggs; drugs; biologics	www.fda.gov	Regulatory: enforces SMDA and regulates germicides as antiseptics, medical devices, medical device systems, and blood products; investigates food contamination, vaccine-related adverse events	Interacts with safety enforcement and recalls, including infection issues; needle-device safety per health department, OSHA	Major focus on needles, surgical implants, latex issues, sterile gloves, and medical devices, including reuse of single-use devices
Health Resources and Services	Health Delivery Services	www.hrsa.gov	Regulatory: National Practitioner Data Bank; Organ procurement	Licensure; privileges; Federal and local conditions local funding for public health program development e.g., Ryan White program	Reports on adverse actions; may include infection-related events
Admin. (HRSA)			Transplant/funding aspects		
Centers for Medicare and Medicaid Services (CMS)[a]	Oversight for Medicare/ Medicaid Conditions of Participation for reimbursement; includes Hospital Acquired Conditions, Healthcare Associated Infections and Infection Control, Antimicrobial stewardship, Interpretative Guidelines Web page; CLIA standards *(See the State level, below, for inspection and enforcement)*	www.cms.gov (access to Medicare/Medicaid data-bases for all sites) www.cms.hhs.gov/HospitalAcqCond/01_Overview.aspwww.cms.hhs.gov/SurveyCertificationGenInfo/PMSR/list.asp#TopOfPagewww.cdc.gov/clia/	Regulatory: hospital certificate and licensure; quality screens; infection control and quality assurance standards; hospital-acquired conditions and healthcare-associated infections; Infection Control Interpretative Guidelines; CLIA standards; Gives deeming authority to accreditation agencies	Enforces "Safe and Sanitary" facility in Infection Control standards; CLIA standards for laboratories and offices, hospital-acquired conditions and healthcare-associated infections for inpatient and future outpatient settings	CMS rules; Conditions of Participation for all applicable standards; infection control standards and Interpretive Guidelines for acute care; ambulatory surgical centers; long-term care
Environmental Protection Agency[a]	Regulated medical waste; disinfectants for hard surfaces; antimicrobial pesticides	www.epa.govwww.epa.gov/osw/nonhaz/industrial/medical/mwfaqs.htm	Regulatory: environmental chemicals; disinfectants and cleaners; regulates disinfectants and antimicrobials as pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act	Regulation of medical waste and incinerators, chemical cleaners and disinfectants; has a hotline for antimicrobial pesticides	Major impact on programs for waste disposal; claims for chemical cleaners and disinfectant; and label checks. Approves disinfectants as "hospital use"

Table 30.1 (cont.)

Agency	Program(s) and/or jurisdiction	URL	Regulatory or voluntary oversight	Key areas of focus	Comments
Dept. of Labor					
Occupational Health and Safety Admin. (OSHA)[a]	OSHA standards: general safety and health standards	www.osha.gov www.osha.gov/SLTC/bloodbornepathogens/index.html	Regulatory: bloodborne pathogens, also environmental chemical germicides for blood spills	Enforces standard precautions; hepatitis B vaccination and vaccination offered to all workers; Exposure follow-up	Enforced by federal OSHA or by states with state-plan OSHA agencies
[same]	OSHA standards: respiratory protection: Standard 1910.134, General Industry Respiratory Protection Standard (GIRPS)	www.osha.gov/SLTC/tuberculosis/	Regulatory: enforces under the General Duty Clause9; the GIRPS includes medical evaluation, annual fit-testing of respirators, training, and record keeping	Enforces 2005 CDC tuberculosis guideline with a compliance survey document based on the General Duty Clause	Enforced in states through state plan OSHA agencies; 24 states have their own plan
Dept. of Transportation	Research and Special Programs	www.dot.gov	Regulatory: regulates hazardous and medical waste crossing state lines	Regulates infectious substances; impacts state medical waste regulations.	Enforces regulated medical waste crossing state lines. Issue for facilities is the training of workers and availability of the waste manifest
US Dept. of Agriculture	Food Safety Inspection Service	www.fsis.usda.gov/	Regulatory: food inspections for commercial food providers	Recall of food products; enforcement	Healthcare facility cafeterias inspected if open to public; enforced by local health departments.
Dept. of Homeland Security	Emergency preparedness and response	www.dhs.gov/index.shtm	Regulatory	Interacts with Federal Emergency Management Admin. and bioterrorism planning; pandemic influenza plan	Created by Public Law 110–53, Aug 3, 2007
Voluntary organizations Nongovernmental accreditation The Joint Commission (TJC)	TJC Committee of leading medical professional societies	www.jointcommission.org/	Voluntary: major organization providing deemed status for Medicare/Medicaid in lieu of CMS agent	Accredits healthcare organizations for CMS Medicare and Medicaid reimbursement through "deemed status"; core measures: enforces government regulations and the organizations' policies	TJC core indicators include National Patient Safety Goals: device-related infection, infection due to multidrug-resistant organisms, and surgical site infection

American Osteopathic Association	Healthcare Facilities Accreditation Program	www.osteopathic.org/	Same as above	Same as above	. . .
Det Norske Veritas Healthcare	National Integrated Accreditation for Healthcare OrganizaTions	www.dnv.us	Same as above	Same as above	. . .
HMO					
National Committee on Quality Assurance	Accredits HMO and outpatient settings; as of 1998, collaborates with TJC and the American Medical Accreditation Program for quality and measurement	www.ncqa.org	Voluntary: provides for reimbursement agreements for private and possibly government funding	Accredits organization for CMS reimbursement; HEDIS provides measurement set used for HMO reimbursement	Indicators such as immunization rates; infection control input critical
College of American Pathologists	Certifies laboratories; recognized as having "deemed status"	www.cap.org	Voluntary: sets standards for laboratory tests	Third-party payer reimbursement requires TJC, CAP, or COLA; must meet CLIA standards	Requirement for meeting basic of laboratory safety and infection control; asepsis; medical waste
Commission on Office Laboratory Accreditation	Certifies laboratories; recognized as having "deemed status"	www.cola.org	Voluntary: sets standards for laboratory tests	Third-party payer reimbursement requires TJC, CAP, or COLA; must meet CLIA standards	Requirement for meeting basic of laboratory safety and infection control; asepsis; medical waste
State					
Dept. of public or community health; disease control; laboratory services	Infectious disease control services; e.g., Communicable Disease Control	URL is state-specific	Regulatory: CDC reporting AIDS/HIV or HIV infection; MRSA, VRE infection	Tuberculosis testing; DNA typing; HIV reporting	Communicable disease reporting; immunization issues; state guidelines
State agencies charged with health facility enforcementa	State licensing bureau: construction codes; Office of Fire Safety	URL is state-specific	Regulatory: enforce ventilation codes; authority for clinical and physical plant surveys	Enforce CMS Conditions of Participation for Medicare/Medicaid, CLIA standards, and state codes and standards. Follow up with validation surveys after accreditation surveys as part of validating "deemed status"	CMS and Certificate of Need; facility construction review; state codes based on American Institute of Architects guidelines1; enforces CLIA standards
Agency charged to enforce medical wasteprogram and/or incinerators[a]	State plan: environmental quality agency, such as Department of Natural Resources	URL is state-specific	Regulatory: medical waste, hazardous materials and chemical waste, and incinerators	Incinerators and medical waste are controversial issues	Major impact on medical waste program; safety programs

Table 30.1 (cont.)

Agency	Program(s) and/or jurisdiction	URL	Regulatory or voluntary oversight	Key areas of focus	Comments
State occupational health dept.; radiation health	State plan: 24 states have state plan enforcement; remaining states have enforcement by federal OSHA	URL is state-specific	Regulatory: Bloodborne Pathogen Standard enforcement; tuberculosis enforcement	Major enforcer of CDC guidelines; Bloodborne Pathogen Standard and tuberculosis; focus is on healthcare personnel	Enforces negative air pressure for tuberculosis control; regulated medical waste occupational injury for healthcare personnel
State Labor dept.: general safety program[a]	State plan: general safety program is within the Labor division, but refer to Occupational Health as needed	URL is state-specific	Regulatory: safety programs, workers compensation; levies fines	Labor inspections, wall-to-wall surveys every 3–5 years, involves infection control; frequently calls in Occupational Health Division	Includes barrier-free hallways, trip hazards etc.; impacts on isolation; traffic
Local					
Public health dept.; jurisdiction may be separate from state health depts.[a]	Local public health dept. communicable disease agency	URL is state-specific and may have local links	Regulatory: communicable disease reporting and follow-up	Laboratory: infection prevention and control interaction	Reporting of communicable diseases according to local rules and regulations
City or municipality dept. of public health[a] or local jurisdiction for safety	Local public health codes and inspection for food, water, waste regulations	URL is state-specific and may have local links	Regulatory: inspections for food safety, water department for effluent, etc.	Infection control and interaction with dietary, facility services, environmental services, etc.	Concerned with spills of hazardous materials and/or chemicals (eg, mercury or formaldehyde) into waste water

NOTE: CDC, Centers for Disease Control and Prevention; CLIA, Clinical Laboratory Improvement Amendments; HEDIS, Healthcare Effectiveness Data and Information Set; HHS, US Department of Health and Human Services; HIV, human immunodeficiency virus; HMO, health maintenance organization; MRSA, methicillin-resistant *Staphylococcus aureus*; URL, uniform resource locator; VRE, vancomycin-resistant *Enterococcus*. HHS designations based on the HHS organizational chart, available at http://www.hhs.gov/about/agencies/orgchart/index.html (accessed 2/13/2016).

[a] Survey agency.

Accrediting agencies generally expect hospitals and providers to incorporate CDC guidelines (e.g., hand hygiene, MDRO control, isolation precautions, and bloodborne pathogen exposure prevention) and National Health Safety Network (NHSN) surveillance definitions into local policies within healthcare systems and explain deviations from the CDC guidance where they exist. The CDC has influence with state and local public health departments; with whom the healthcare epidemiologist should establish positive working relationships.[4]

In addition, the CDC also has several initiatives to improve the health of the public, including the antimicrobial stewardship core elements for acute care hospitals and nursing homes and the 6/18 Initiative targeting six common and costly health conditions (including HAI) with 18 proven specific interventions. Familiarity with these initiatives may help in program planning to advance the infection prevention policies and practices of a hospital or healthcare system.

The Centers for Medicare and Medicaid Services (CMS)

Much of the authority and influence of CMS is leveraged by the agency's oversight of reimbursement for Medicare and Medicaid programs through its 10 regional offices. The regional offices maintain close working relationships with state health departments. Ultimately, in the case of a CMS site visit, it is frequently surveyors from the state agency who arrive to conduct the formal accreditation visit.

CMS develops "Conditions of Participation (CoP)" and "Conditions for Coverage," which are minimum health and safety standards that healthcare organizations must meet in order to be CMS-certified and receive reimbursement. CMS also maintains standards for infection prevention and control in hospitals, ambulatory surgical centers, long-term care facilities, and home care agencies and enforces compliance with these as conditions for payment. An Infection Control Condition citation can risk a hospital's CMS standing and/or closure to new patient admissions, a possibility that carries considerable implications even for financially sound organizations. Recently, CMS proposed a major revision, a CoP for Infection Prevention and Control and Antimicrobial Stewardship for acute care hospitals, as well as an Infection Control CoP for long-term care facilities. The updates to the CMS regulations are published in the Federal Register and on the CMS website.[5]

CMS may grant deeming status to accrediting organizations as long as they have and enforce standards that meet the federal CoP. TJC remains the most recognizable accrediting agency in the US and is discussed in the following section. Others with deeming authority include the American Osteopathic Association's Healthcare Facilities Accreditation Program and National Integrated Accreditation for Healthcare Organizations, the Center for Improvement in Healthcare Quality and the accreditation program of *Det Norske Veritas* Healthcare, which is the first accrediting agency to integrate the International Organization for Standards' ISO 9001 quality management system standards with CMS CoP.

In addition to accreditation and compliance with best practices through the CoP, CMS makes policies to govern mandatory reporting, public reporting, and financial reimbursement rules under its inpatient prospective payment system (IPPS). From time to time, CMS also announces Request for Proposals for innovation projects and administers government programs such as the state 1115 waiver program (also called the Delivery System Reform Incentive Payment [DSRIP] program) that offer opportunities to voluntarily undertake large-scale transformation projects related to quality improvement.

The Joint Commission (TJC)

TJC is an independent, not-for-profit organization founded in 1951. It evaluates, accredits, and certifies more than 20,500 healthcare organizations and programs in the United States. TJC sets specific standards for infection prevention and control. The standards are revised and published annually in the Comprehensive Accreditation Manual for Hospitals, which can be purchased in paper or electronic format.[6] The infection prevention and control team must be familiar with the standards and collaborate with other hospital departments to adjust policies and procedures in an ongoing manner. Standards impacting the infection prevention and control program are not limited to the section designated "Infection Prevention and Control." Sections on patient rights, information management, environment, emergency management, leadership, and others often involve infection prevention and control program activities.

TJC established the National Patient Safety Goals in 2002 to stimulate organizational improvement activities for the most pressing patient safety issues. The National Patient Safety Goals are updated at least once annually by TJC and include specific patient safety indicators and requirements that are typically later incorporated into Infection Control Standards. Many of the goals have impact on the infection prevention and control program, such as those pertaining to hand hygiene compliance and the prevention of device-associated infections, infections with MDRO, and surgical site infections.

Occupational Safety and Health Administration (OSHA)

OSHA is the federal agency authorized to conduct workplace inspections in order to determine whether employers are complying with the agency's safety and health standards. The General Duty Clause of the Occupational Safety and Health Act of 1970 requires that employers provide every worker with a safe and healthful workplace. OSHA may adopt a specific standard or regulation, such as the Bloodborne Pathogens standard, on which it bases all its inspections and enforcement actions. OSHA also has the authority to inspect work sites for occupational risks of tuberculosis. All standards are easily accessed from the OSHA Internet site.[7] Additional details are discussed under the section on OSHA survey.

State Government and Public Health Departments

The state administrative code is a compilation of all state agency rules passed by the state legislature. The applicable state rules and regulations vary widely from state to state and are published in the State Register. The agencies, including state health departments, that pass these rules are responsible for enforcing them. Rules applicable to infection prevention may include mandatory state reporting of HAI, notifiable conditions, healthcare worker vaccinations, rules governing informed consent prior to obtaining specimens from a person who was a source of bloodborne pathogen exposure, and detention of a person who could potentially be a source of communicable disease. For example, California has recently mandated antimicrobial stewardship programs in hospitals, while many other states compel active surveillance for methicillin-resistant *Staphylococcus aureus* (MRSA) and other MDRO.

State rules also govern building codes that inform infection prevention practices in healthcare facilities (e.g., minimum number of air changes per hour in specially engineered areas like airborne infective isolation rooms) as well as infection control pre-construction risk assessment before renovation, remodeling or new hospital construction.

Local Departments of Public Health

The infection prevention department often serves as the liaison between the health system and local public health authorities. Applicable federal and state public health requirements are usually channeled via the local public health department. The relationships between the local and the state department of health are variable, and the infection prevention leader is advised to learn the relationship between these entities.

Interested Parties: Other Key Stakeholders in Shaping Infection Prevention Policy

While a clear understanding of the key federal and state policies and policymakers is essential, this knowledge alone does not offer a full perspective on just how policies come into being. Ultimately, the regulations that govern infection prevention practices are the result of a complex interplay between scientific knowledge, clinical experience, politics, and advocacy. It is essential to understand this environment and the context from which these policies and regulations emerge, both in order to appreciate the nuance and intent of expectations, and also to allow for meaningful engagement in influencing future policy (see end of this chapter). A good starting point in this understanding is a review of some of the other key stakeholders in the process.

Over the past 20 years, the role of *grassroots patient advocacy groups* in the development of new policies related to infection prevention has grown significantly. Often, these efforts are prompted by the personal experience of a single individual or groups of individuals who have been affected by the specific infection. For example, a group that has been highly visible in advocating for more aggressive control strategies for MRSA in the US has been the MRSA Survivor's Network. Recently, social media has facilitated the efforts for such movements.

Over the past several years, such grassroots activism has been accelerated through more formal organization and support from *regional and national advocacy groups*. The distinction between consumer and patient advocacy has been blurred with respect to the crisis of HAI. Chief among these organizations is the Consumer's Union (CU). Founded in 1936 with a primary focus on product safety and consumer rights, the CU became involved in HAI through their Safe Patient Project.[8] This initiative aims to help patients find the highest-quality healthcare by promoting disclosure of infection rates and harm events. Through high profile awareness programs, direct activism with policy makers and by mobilizing and energizing a broad base of consumer support, CU has emerged as an important influence on US infection prevention policies and regulations.

A sometimes-uncomfortable reality of policy making in healthcare is the interposition of *commercial interests* in the development of policy and regulations. While much of the sometimes critical attention at the interface of commerce and care delivery has been focused on large pharmaceutical companies and device manufacturers, there is a growing number of service, industrial, and engineering firms that specialize in developing products that intend to support the work of prevention of HAI and MDRO. There are numerous examples including manufacturers and distributors of disinfectants, textiles, screening assays, and devices to reduce the risk of cross-contamination. In addition, as the financial impact of poor performance in infection prevention is magnified, a cottage industry of consultants and advisors has become available to health system leaders.

On balance, the commercial sector has helped produce some of the pioneering tools to innovate and advance the cause of eliminating HAI and MDRO. However, with the real pressures of sustaining a financial margin, in service to shareholders in the case of publicly held companies, there is also a pressing motivation to drive returns and ultimately increase market share. One of the most powerful shortcuts to these objectives is the enactment of public policy or regulations that compel the use of a particular product or specific practice that in essence creates instant market leadership. For products or firms at the vanguard of technology or innovation, and especially where intellectual property laws protect the technology, the windfall can be extraordinary. Investments in lobbying and political activism correspond to these interests.

Understanding this influence of industry on policy and practice renders it especially important for healthcare epidemiologists to carefully manage relationships with commercial entities and to ensure that real or perceived conflicts of interest are handled both cautiously and transparently. Gifts, favors, and promotions, while ostensibly aligned to the common goals of safety and improved outcomes, should be avoided diligently. Failure to do so damages credibility and may ultimately stand as a barrier to the adoption of rational and evidence-based practices.

Of course, the impact of commercial interests on the US healthcare system goes far beyond those who manufacture drugs and technology. Indeed, with at least 18 percent of the US gross domestic product spent on healthcare, the focus of nearly every industry is on reducing healthcare costs as a means of improving the bottom line. In some cases, such as for the commercial insurance industry, the challenge is direct. Reimbursement reform has pressured insurance companies to not only become more efficient and effective but also to reconsider their entire business model. In some ways, the distinction between provider and payer organizations has blurred. Part and parcel of this have been changes to contracting that puts more pressure on delivering value by reducing expenses while improving outcomes. A patient readmitted for HAI is enormously costly to an insurance provider. In risk-based contracting, this expense is passed on to the provider, and ultimately the infection prevention team to ensure that such events are rare.

This concern for expense applies not only to payers, but also to those who pay the payers. Large employers who maintain insurance plans for their employees demand the best return on their investment. Incorporating high expectations for performance can be the difference between a profitable and an unsuccessful quarter for even the largest industrial entities. It was for this reason that a number of large employers have collaborated to support and sustain the Leapfrog Group, a well-recognized arbiter of expectations and ratings of healthcare providers.[9] With so much at stake, that both insurance providers and large employers are among the strongest advocates for improved quality in healthcare comes as no surprise.

Practically speaking, there is a final, but often forgotten, group of stakeholders that strongly influence infection prevention regulations, and indeed all of public policy. It is essential for those who wish to shape and influence infection prevention policy to appreciate the important role played by the personal priorities and perspective of *individual policy makers and their teams*. In their efforts to advance their individual agenda and aspirations, politicians, legislators, their appointees, and aides endeavor to identify issues that resonate with their constituencies. They gravitate to personal stories and experiences, from their own lives or those that they represent, that can drive a narrative of concern, responsiveness, and activism. They are influenced by the experience of their peers, often informed by meetings of national and regional societies of legislators and legislative aides. In this environment, HAI and MDRO prevention has emerged as a hot topic in many jurisdictions. With so much at stake, and with so many regulatory agencies and powerful interests aligned to drive high performance in infection prevention, it is important to consider how these pressures and expectations impact the day-to-day work of hospital-based infection prevention.

The Impact of Public Policy on the Work of Hospital-Based Infection Prevention

There exists a set of foundational activities that serves as the basis of an effective infection prevention program, including but not limited to hand hygiene promotion, other transmission control programs, and occupational health and safety and training and education. It is these practices and policies, adhered to with high reliability by trained providers, that are most tightly governed and scrutinized by regulations and public health policy. With this in mind, the role of the accreditation survey or site visit, when these procedures and standards are closely examined, assumes special significance and serves as the most tangible interface between practice and regulations for most hospitals and health systems. In this section we will focus on preparation and readiness for surveys and site visits. First, a general approach is introduced. Then, specific observations about the survey practices and expectations for specific groups are discussed. This section ends with a discussion of the impact of regulation on a variety of infection prevention activities outside of the context of an accreditation visit, including surveillance and performance improvement.

General Approach to Surveys and Site Visits

The best way to prepare for any regulatory survey is to fully understand the rules and regulations, include these elements in annual and ongoing infection control risk assessment and plans, and to implement them regardless of whether a survey is imminent. Having an active program of "continual readiness" greatly reduces the sometimes frenetic just-in-time preparation that marks such visits at too many hospitals and health systems. Generally, every health system has a department and personnel that oversee regulatory activities and continual readiness for site visits. It is helpful for the infection prevention leader to maintain an active relationship with this department in order to stay informed about the full spectrum of regulatory activities in the organization. It is also helpful to maintain a strong collaborative relationship with departments such as environmental services, occupational health, sterile processing, kitchen and nutrition services, and antimicrobial stewardship programs because a violation in any of these could potentially be cited directly under infection control. Reviewing previous survey findings for the health system or comparable health systems is helpful for shaping continual readiness efforts.

For any site visit or survey, the infection prevention program documentation and the minutes and records of the organization's infection control committee need to reflect that the program encompasses all areas of the health system, that all key stakeholders are engaged and providing input into policies, that there is follow through on all issues identified, that the health system leadership is fully engaged and supportive, and that the infection prevention department has the necessary resources for the responsibilities assigned. Examples of infection prevention practices the surveyors would observe and evaluate are hand hygiene, appropriate use of personal protective equipment (PPE), appropriate storage and disinfection and/or sterilization of medical equipment, vaccination of staff and licensed independent practitioners, management of infected employees and patients who are potentially contagious, and preparedness for an influx of potentially infectious patients, including coordination with the

community and the communications plan. Hand hygiene standards are frequently difficult to meet and document. In addition to reviewing policies and data, surveyors will tour patient care areas to identify episodes of noncompliance. If personnel are observed to omit appropriate hand hygiene practices, then the surveyor may score the hospital as noncompliant with that element. Although this seems like a simple issue, this is one of the more common citations. The surveyors take a similar approach to proper use of PPE. The best approach is to have a program that evaluates and promotes appropriate hand hygiene and proper use of PPE on a continuous basis. A continuous monitoring process should include some "secret shopper" observers who are unlikely to be recognized by employees.

It is important that infection prevention leaders highlight their best projects to the surveyors even if there were no directly related questions. Accrediting agencies require the hospital to follow its own policies. Therefore, infection prevention policies need to be practical and implementable. The surveyors also focus on how infection prevention requirements are disseminated throughout the organization, and they may call on frontline clinicians to ask how they would handle a particular situation like cleaning up a blood spill or when they were last screened for tuberculosis. The surveyors also focus on how healthcare personnel are educated and continually trained.

Last but not the least, it is helpful to remember that surveyors bring their experiences and personalities with them. They spend a great deal of time away from home and frequently endure stressful, even hostile, situations. Courtesy and hospitality will create a good working environment. Most surveyors appreciate time at the end of the day to summarize their work and begin written reports. Meetings and tours should begin on time. Committee minutes and policies should be organized and easy to access. Presentations should be concise and given by knowledgeable individuals.

CMS Survey

Although CMS confers "deeming authority" to accrediting agencies and accepts their accreditation recommendations, it will conduct inspections in hospitals for a variety of reasons. Random *validation surveys* are carried out in 5 percent of organizations after an accrediting agency (e.g., TJC) survey. These are full, comprehensive surveys that may involve many surveyors and can last a full week, depending on the size of the facility.

State surveyors will conduct a *full survey* if a hospital does not participate in a survey of an accrediting agency, "for cause" as a follow-up on a complaint to CMS or the state, or before restoring full licensure and/or certification if the hospital has lost them following any survey. A *partial survey* is done as a follow-up to complaint investigations and focuses on specific standard(s).

The key to preparation is being familiar with the Infection Control Conditions and Standards and ensuring that all aspects of the condition are accounted for in the written program of the institution's infection prevention program. The Infection Control CoP states that "the hospital must provide a sanitary environment to avoid sources and transmission of infections and communicable diseases." It further specifies that there must be an active program for the prevention, control, and investigation of infections and communicable diseases. Policy standards state that an individual must be designated as infection control officer to develop and implement policies around infection prevention. There is also a standard related to responsibilities of the chief executive officer, medical staff, and director of nursing services that they must ensure that the hospital-wide quality assurance program and training programs address problems identified by the infection control officer or officers, and be responsible for the implementation of successful corrective action plans in affected problem areas.

"Interpretive Guidelines" is a guidance document intended to assist the surveyor. It is immensely helpful for healthcare epidemiologists and infection prevention departments to serve as a checklist for preparation and continual readiness for a CMS survey. It is important to recognize that the expectations are mostly qualitative or categorical. CMS also requires linking the Infection Control Standards to the Quality Assurance and Performance Improvements standards. CMS puts a great deal of focus on surveyors' observations as they move through the facility as well as the documentation, particularly on any action taken for an identified problem. Therefore, impressions matter a great deal.

It is helpful to know the CMS regulatory terminology so that the survey reports are more understandable. For example, the Infection Control CoP is filed in the CFR under Title 42 (relates to Public Health) Chapter IV (relates to CMS) 482.42 (482 relates to acute care hospitals, and 42 under 482 relates to infection control). While the CoP represents the entire expectation, specific parts of the condition are called standards. The CMS term for noncompliance is *deficiency*, which may be a condition-level deficiency, a standard-level deficiency, or immediate jeopardy if there is an immediate threat to health and safety. Extreme noncompliance in one standard can be cited as a condition-level deficiency or even immediate jeopardy. Tags are a reference for CoP items in the summary report of survey completed by the CMS. An A-tag is a Federal/CMS tag (e.g., A-tags for infection prevention may be A-0747, A-0749, A-0750, A-0756). An X-tag is a state tag to identify findings a CMS surveyor may find as a violation of the State Administrative Code.

Upon meeting the CoP, CMS usually transfers the deeming authority to TJC, which is discussed in detail in the next section.

Joint Commission Survey

Surveys for maintaining hospital accreditation are unannounced and occur approximately every three years. The survey team usually includes a physician, a nurse, and a life safety code specialist or hospital administrator who has senior management experience. Prior to the on-site visit, the survey team reviews multiple sets of information from the institution such as the data on "core" measures submitted to TJC through its

ORYX® initiative, interim reports from the hospital based on the results of the institution's quality improvement program and the previous TJC survey, information on the facility's programs, and reported sentinel events.

TJC surveyors tour patient care areas to observe compliance with the facility's policies and procedures, TJC standards for Infection Control and Antimicrobial Stewardship, and pertinent National Patient Safety Goals. Surveyors use "patient tracers" who follow the patient through all of the facility's care processes, to assess whether staff understand and follow infection prevention standards and comply with policies such as hand hygiene and isolation requirements. Surveyors will review the annual infection control risk assessment and plan, and also review medical records and interview patients. Surveyors tend to prefer measurable goals for the program and quantitative evaluation annually.

During the "infection control tracer," which occurs near the end of the survey, surveyors will interview the infection prevention staff about issues they have uncovered regarding employee knowledge or policy and procedure breaches. At the end of the visit, surveyors meet with the hospital leadership team to summarize their findings and provide a preliminary report. TJC has a central committee that issues formal notices of noncompliance and determines the accreditation status of the hospital.

In general, surveyors score performance on a standard as either "compliant" or "not compliant." Standards are made up of individual elements of performance, each of which is also scored. Elements that are not applicable to an institution are not scored. Each element of performance is scored as an "A" standard (Yes or No for compliance) or as a "C" standard for which multiple observations are required for a score of noncompliance. Some standards require a "measurement of success." Two components are scored for each element of performance: compliance with the standard and the track record of compliance. The track record of compliance refers to the underlying processes and program design that support performance. Elements of performance may be scored as satisfactory, partial, or insufficient compliance. Partial or insufficient compliance will result in a "Requirement for Improvement" (usually referred to as an "RFI"). Standards are weighted on the basis of how critical the issue is to the safety of patients. There are two levels of "criticality": immediate impact requirements and less immediate impact requirements.

Each Requirement for Improvement must be addressed by submission of "Evidence of Standards Compliance." Immediate impact requirements must be addressed within 45 days, whereas less immediate impact requirements must be addressed within 60 days. Failure to submit an acceptable Evidence of Standards Compliance within the specified time frame will lead to an unfavorable accreditation decision. A second site visit may be required for hospitals that have a large number of citations or that have citations in highly critical areas.

Ultimately, TJC will use the information obtained from the site visit and the organization's response and corrective actions to determine which accreditation category the institution should receive: Accreditation, Preliminary Accreditation, Provisional Accreditation, Conditional Accreditation, Preliminary Denial of Accreditation, or Denial of Accreditation. The decision process takes into account the size and complexity of the organization and the institution's response to deficiencies identified by TJC. If the institution receives a Denial of Accreditation, this will result in an independent CMS review. TJC does have an appeal process if the organization disputes the survey findings.

Case Study: Parkland Health and Hospital System, Dallas, Texas; 2011–2013

Parkland Health and Hospital System in Dallas, Texas is a public tertiary care academic health system with a 784-bed hospital with six intensive care units, a busy emergency department with 200,000 visits annually, and a level I trauma center. Physician services are provided by faculty from the University of Texas Southwestern Medical Center. When the health system was surveyed by the CMS in 2011, the health system's accreditation had been previously renewed by TJC for three years in 2010, and there had been no concerning findings related to infection prevention at that time. Following a "for cause" survey at Parkland, an unannounced full hospital survey was conducted on July 11–21, 2011. The hospital was notified on August 10, 2011, that the conditions in the hospital represented "Immediate Jeopardy" and placed patients at risk for severe infection and possibly subsequent death. In the Tag 42 CFR 482.42 Infection Control A747 of the CMS report, the surveyors stated that infection prevention practices were not adhered to by physicians, nursing staff, and other personnel. Specific findings included lack of hand hygiene after use of gloves, leaving masks hanging on the neck in the perioperative areas, lack of standardization in operating room attire, personal food items in the nursing stations, instances of improperly disposed infectious waste in patient rooms, and trash bagged but not covered in the transport gondolas. The immediate jeopardy finding was replaced with a Condition level finding upon a second survey a month later.

During the month between the two full CMS surveys, the infection prevention department conducted refresher training for the entire organization and increased audits for infection prevention practices. The second full CMS survey was immediately followed by a full TJC survey that identified additional deficiencies related to Standard # IC.02.02.01 EP 2 and EP 4 that addresses medical equipment, devices and supplies, specifically related to endoscopes, Ambu bags, and disinfection protocols.www.hospitalinspections.org/.

Following the results of these surveys, Parkland entered a "Systems Improvement Agreement" for an 18-month period from September 30, 2011, to April 30, 2013, with CMS, which required corrective actions under the oversight of a CMS-approved third party agency. The corrective action plan included 499 items, including more than 60 specific to infection control such as daily hand hygiene audits, monthly audit of the environment in all clinical areas, monitoring use of personal protective equipment, and revision of all infection

prevention policies. In addition, the infection prevention department used a surveyor decision tool in order to prepare for the re-survey in 2013. The tool included more than 200 items related to structures and processes, antimicrobial stewardship, occupational health, disinfection and sterilization, critical care, and procedures.

The full, unannounced CMS survey occurred in June 2013. During the survey, surveyors identified multiple opportunities for improvement in the hospital kitchen, such as ineffective labeling and disposal of expired foods, improper methods of cooling and maintaining temperatures, and deficiencies in maintenance of equipment. To restore compliance, infection preventionists did clinical rounds with dietary services management daily to help identify areas of improvement, and offered guidance in an effort to better protect patients, visitors, and staff from food borne illnesses. Infection preventionists also became certified food managers. CMS restored deemed status for Parkland on August 22, 2013 and transferred survey jurisdiction back to TJC.

Key lessons for hospital-based infection prevention leaders: 1. Visible infection control practices by healthcare personnel offer a "window" to everything else in the health system. 2. The experience afforded greater visibility to infection prevention within Parkland and its surrounding region and accelerated implementation of certain infection prevention measures such as documentation of sterilization and disinfection competencies and healthcare worker vaccinations. 3. The experience served as a strong reminder of the importance of being continually ready for a regulatory and accreditation survey and not allowing complacency after a successful survey.

Occupational Safety and Health Administration (OSHA) Survey

As OSHA oversees protection of healthcare personnel, the infection prevention program is expected to weigh in on infection-related occupational health issues such as respiratory protection, tuberculosis screening, prevention of bloodborne pathogen exposure and postexposure management. Preparation for an OSHA survey includes checking with the hospital regulatory and legal departments to understand the applicability of OSHA standards in the organization and its employees and licensed independent practitioners. A complete OSHA survey may include review of hazardous chemicals, radiation safety, and hazard notification in addition to infection-related occupational health items. An OSHA survey is conducted by its certified safety and health officials (CSHOs), and the key standards they assess for a hospital are the respiratory protection and bloodborne pathogen standards. OSHA holds the employer accountable for maintaining workplace safety. Ideally, a group that includes representatives from infection prevention, safety, occupational health, risk management, and administration ensures compliance with OSHA standards.

The specific OSHA standards are respiratory protection (29 CFR 1910.134; 29 CFR)10; hazard notification (29 CFR 1910.145); record keeping (29 CFR 1910.20), which requires that facilities allow CSHO access to employee exposure and medical records; and 29 CFR 1904, which requires a log of occupational injuries and illnesses, called the "OSHA 300 log." OSHA can issue citations under the General Duty clause if the CSHO can demonstrate that the employer failed to keep the workplace free of a recognized hazard that was causing, or was likely to cause, death or serious physical harm and that a feasible and useful method of abatement existed.

Twenty-four states have state-approved OSHA plans. These state-level plans must incorporate regulations that are "at least as effective" (at least as strict) as those set forth by OSHA at the federal level. It is critical to be knowledgeable of state and federal differences since many states enact regulations that go beyond federal rules.

If any deficiencies are found during the survey, the area director of OSHA will send citations and notices of proposed penalties to the hospital by certified mail. The hospital must post these citations on or near the areas where the alleged violations occurred. Penalties vary according to the seriousness of the violation. The area director may propose substantial fines for willful or repeated violations of a standard. Both the hospital and the employees have the right to appeal and should do so, since this is the expected process OSHA uses for resolution. Employees may request an informal review if OSHA decides not to issue a citation and also may contest the time frame allowed for the hospital to correct the hazardous conditions. If the facility decides to contest a citation, an abatement period, or a proposed penalty, it must submit a written "Notice of Contest" to the area director within 15 working days from the time of the citation. The area director will forward this notice to the Occupational Safety and Health Review Commission (which operates independently of OSHA); this commission will assign the case to an administrative law judge.

Healthcare epidemiologists should develop a cordial working relationship with their regional or state OSHA. By understanding the occupational health paradigm, finding common ground, and promoting dialogue, healthcare facilities can change a "regulatory burden" into a proactive safety program that affects the overall safety culture of an organization.

Regulations Governing Hospital Surveillance for Infections and MDRO

While expertise in surveillance methodology is a general expectation for healthcare epidemiologists, regulatory expectations and policy leave little room for creativity and innovation at the level of an individual hospital or health system. Public reporting and transparency with regulatory agencies compel individuals and organizations to adopt standardized metrics for quantifying HAI processes and outcomes. Following surveillance specifications such as case definitions and applicable populations is essential, and failure to meet these requirements can result in a notice of deficiency from the mandating agency. The CMS Hospital Compare website serves as a clearing house for many infection prevention measures, including central-line associated bloodstream infection (CLABSI), catheter-associated urinary tract infection (CAUTI) surgical site

infection (SSI), and MDRO including *Clostridium difficile* infection and MRSA.[10]

Regulatory agencies require that the NHSN definitions be used for surveillance of infections even though these criteria are acknowledged to be imperfect. Other measures often reported include hand hygiene compliance, healthcare worker influenza vaccination and care improvement processes such as timing of perioperative prophylactic antimicrobial agents and adherence to sepsis care bundle. Process measures like monitoring antimicrobial usage are not yet required at this time, although it would be worthwhile to become familiar with the antibiotic use module of the NHSN. Table 30.2 list key metrics covered by different programs.

Pay-for-Performance and Value-Based Care Programs

The main financial incentive leveraged by the US federal government through CMS for acute care hospitals is the IPPS. The overall goal of the IPPS is to improve health, improve care, and decrease costs. Currently, the components of the IPPS that include HAI-related quality outcomes and process measures include: (1) preventable healthcare-acquired conditions (HAC) not present on admission (POA); (2) excess readmissions; (3) HAC reduction program, excess readmissions; (3) value-based purchasing (VBP); and (4) inpatient quality reporting (IQR). Different components of IPPS rules modify payments to hospitals for providing patient care either upward (incentive) or downward (penalty). Generally speaking, when the metrics used for these programs are based on coded data, the opportunities for improvement are clinical, coding or documentation, whereas for surveillance-based metrics, the opportunities are mainly clinical. Several of these measures are described below.

Preventable HAC Not POA: Under this program, any ICU patient coded in administrative data as having CLABSI or CAUTI that was not present on admission will have reimbursement decreased if the code related to CLABSI or CAUTI was responsible for moving the patient's reimbursement category to a higher payment category.

Excess Readmissions: CMS calculates excess readmissions ratio for each hospital and adjusts payments negatively based on the amount of excess readmissions. Infections, including those acquired during prior hospitalization, have been shown to contribute significantly to the frequency of readmissions. It is important to understand what proportion of readmissions is caused by an HAI in one's hospital.

Healthcare-Associated Condition (HAC) Reduction Program: Under this program, CMS calculates a HAC score for each hospital, and any hospital in the worst quartile will have a reduction in payment. The penalty is 2 percent beginning in 2017. The HAI standardized infection ratio (SIR) per NHSN data (CLABSI, CAUTI, SSI after abdominal hysterectomy and colon surgery, MRSA lab-ID and *C. difficile* lab-ID) is weighted 75 percent, and the AHRQ PSI-90 (an aggregate measure of several "patient safety indicators" including PSI-13, which is based on coding data for postoperative sepsis) is weighted 25 percent. There is a 2-year time lag for this measure, and hospitals are penalized for performance two years prior to the payment year. The amount of reduction and the relative weight for individual measures is specified in the CMS IPPS rule.

Value-Based Purchasing Program: Under this program, CMS calculates a VBP performance score for each hospital, and the hospital gets an incentive commensurate with the performance score. The performance score is based on four domains – Safety, Clinical Processes and Care Coordination, Patient Experience, and Efficiency. The score includes points for good performance, faster rate of improvement, and consistency of performance across all measures. Hospitals are ranked by VBP performance score and will receive an incentive commensurate with performance score. The measures included in the safety domain are NHSN SIR for CLABSI, CAUTI, abdominal hysterectomy SSI, colon surgery SSI, MRSA lab-ID and *C. difficile* lab-ID, and AHRQ PSI-90. The weight for the safety domain is 25 percent in FY2018. Beginning in FY2019 for both HAC Reduction and VBP programs, the reference year for NHSN SIR will be 2015.

Inpatient Quality Reporting (IQR) Program: The IQR program is pay-for-reporting and not pay-for-performance. As such, hospitals are incentivized for reporting quality data. At the time of writing, infection metrics affected by this program are all the HAI reportable to NHSN, influenza vaccination among healthcare personnel, and severe sepsis and septic shock management bundle per chart abstraction.

It is important for the healthcare epidemiologist to understand the components of these programs related to HAI in order to maximize performance on these metrics. It is also useful to learn local exceptions (e.g., the state of Maryland is exempt from VBP) and presence of other programs in one's health system that are driven or affected financially by CMS (e.g., delivery system reform incentive payment program also known as the "1115 waiver program" for quality transformational initiatives in hospitals in certain states like California, Texas and New York). Knowledge of these details helps articulate the value of infection prevention and the value of the healthcare epidemiologist.

Policy and Regulatory Implications for the Environment of Care, Outbreak Control, and Occupational Health and Safety

Providing a safe environment of care is one of the cornerstone regulatory practices of infection control programs. This vast undertaking includes everything from routine heating, ventilation and air conditioning functions to the specialized environment in procedural areas, and also includes monitoring of construction sites including new hospital buildings. In many cases, the regulatory language around providing for a safe environment of care is somewhat unclear and subject to

Table 30.2 Key performance measures related to infection prevention and control examined by external agencies in the US
Of note, antimicrobial use reporting via NHSN is proposed for inclusion in CMS pay for reporting and TJC standards at the time of writing this chapter.

Selected metrics with regulatory and financial implications	Agency	Type of policy measure
(NHSN surveillance definitions used unless stated otherwise)		
CLABSI in ICUs and select wards	CMS	Mandatory Reporting, Public Reporting, HAC Reduction Program, Value-Based Purchasing
	TJC	National Patient Safety Goals
	State Health Department	Mandatory Reporting, Public Reporting
CAUTI in ICUs	CMS	Mandatory Reporting, Public Reporting, HAC Reduction Program, Value-Based Purchasing
	TJC	National Patient Safety Goals
	State Health Department	Mandatory Reporting, Public Reporting
VCAI (coding data)	CMS	Preventable HAC, not POA
CAUTI (coding data)	CMS	Preventable HAC, not POA
SSI-HYST, COLO	CMS	Mandatory Reporting, Public Reporting, HAC Reduction Program, Value-Based Purchasing
	TJC	National Patient Safety Goals
	State Health Department	Mandatory Reporting, Public Reporting
SSI-KPRO, HPRO	CMS	Mandatory Reporting, Public Reporting
	TJC	National Patient Safety Goals
	State Health Department	Mandatory Reporting, Public Reporting
SSI-PVBY, AAA, CABG, CEA	CMS	Mandatory Reporting, Public Reporting
MRSA lab-ID	CMS	Mandatory Reporting, Public Reporting, HAC Reduction Program, Value-Based Purchasing
	TJC	National Patient Safety Goals
CDI lab-ID	CMS	Mandatory Reporting, Public Reporting, HAC Reduction Program, Value-Based Purchasing
	TJC	National Patient Safety Goals
Severe sepsis and septic shock management bundle (coding and chart review data)	CMS	Pay for Reporting
Post-op sepsis PSI-13 (coding data)	CMS	Mandatory Reporting, Public Reporting
Peri-operative antibiotics, SCIP-urinary catheter (coding and chart review data)	CMS	Mandatory Reporting, Public Reporting
HCW influenza vaccination	CMS	Mandatory Reporting, Public Reporting
Patient influenza vaccination at discharge (chart review data)	CMS	Mandatory Reporting, Public Reporting
HCAHPS – environment and hand hygiene (Press Ganey survey)	CMS	Mandatory Reporting, Public Reporting

broad interpretation. One example is the need for air sampling in the absence of an outbreak or epidemic. In addition, regulations require that the infection control committee provide approval for hospital disinfectants. Monitoring thoroughness of room cleaning, although not directly mandated, is necessary to monitor the environment of care.

From a regulatory standpoint, for outbreak investigation and control, the hospital is required to have a policy stating the authority for infection control and a high-level overview of the approach that will be used. Quarantine laws apply for isolation for tuberculosis. For emerging pathogens, guidance is usually evolving. In these situations, consulting risk management and legal experts may be necessary.

Future Trends in the Regulatory Management of Infection Prevention

Regulating Mandatory Practices

When the earlier edition of this chapter was written, the issue of legislative mandates of specific infection prevention practices was timely, in light of a series of measures related to mandatory screening for MRSA. The ensuing years have provided an opportunity to reflect not only on the impact of such legislation but also to examine how this approach has been modified and applied since that time, with one example being influenza vaccination for healthcare workers. In doing so, one can still ask the question if regulating mandatory practices is generally acceptable, or whether the merit of such a mandate is largely determined by the specific nature of the practice itself.

In the large natural experiment regarding the application of mandatory MRSA screening laws, the outcome has not been conclusive and is subject to considerable interpretation. Publically reported infection rates remain high, and the burden of disease on individual patients is almost immeasurable. These results are confounded by insufficient information about the manner in which the "mandated" practices have actually been followed, the impact of widespread use of antimicrobial agents with activity against MRSA as empirical therapy, inadequate and unvalidated data about potential harms as a result of the new laws and disagreement about the optimal means by which to measure success.

Taken together, this experience fails to answer the question of the efficacy of mandatory MRSA screening. Skeptics argue that the expense of executing this mandate outweighs any measurable benefit and likely draws resources away from other interventions. Advocates counter by arguing that inefficiencies and a lack of rigor and commitment in application likely contributed to the unsatisfactory outcome. While this debate is not easily settled, it does point out the hazards of this approach in that without proper support and consensus, such questions will remain after the application of *any* mandatory practice.

Regulating Staffing, Structures, and Expertise

One approach to avoid some of the issues around mandating specific practices is to instead adopt expectations regarding staffing or structure. In general, this approach is thought to establish a minimal standard for organizational expertise in support of infection prevention while preserving the capacity for local risk assessment and targeted resource allocation. Originally, this approach was proposed to apply to establishing a minimum number of infection prevention providers per acute care hospital bed. This position, while endorsed by professional societies and some advocacy groups, has been largely rejected in practice owing to cost concerns, practicality, as well as a lack of clear evidence to justify these thresholds. Largely viewed as a compromise to this approach, but also reflecting the increasing awareness of the infection risk across the care continuum, accreditation standards have been established for multiple settings of care, compelling various committee structures and designations to ensure some degree of local authority over infection prevention. However, time spent at multiple healthcare facilities governed by these standards demonstrates the uneven nature with which these less rigorous standards are applied.

Over the past several years, antimicrobial stewardship has been highlighted as a crucial element of a comprehensive infection prevention strategy.[11] As a result, the establishment of stewardship programs in acute care hospitals, long-term care facilities, and even in the ambulatory setting has been strongly and persuasively championed by multiple stakeholders and experts.

But even when mandating promising and widely touted practices such as antimicrobial stewardship, the devil, as in all regulatory matters, is in the details. Fundamental questions about the nature and activities of an effective stewardship program have not been rigorously tested and defined. What activities constitute an active program: surveillance, reporting, interventions? Of available interventions (such as preapproval, pharmacy substitution, consultation), which work best in which settings? How will the effectiveness of such programs, once mandated, be assessed? Even the question of who is qualified to lead an antimicrobial stewardship program is not resolved.

The uncertainty around defining qualified leadership of antimicrobial stewardship programs simultaneously highlights another potential policy lever for strengthening the infrastructure of infection prevention and healthcare epidemiology in the US and other jurisdictions. At present, with the exception of a modest number of states and local jurisdiction (most notably California), there are almost no established standards or qualifications of training or experience to establish an individual's expertise in infection prevention and healthcare epidemiology. In the case of physician leaders, this heterogeneity is in part a result of supply. There are simply not a sufficient number of individuals who have completed dedicated training in these disciplines.

Pay-for-Performance and Reimbursement Pressures

While strictly speaking not the product of specific regulatory activity targeting HAI, the proliferation of incentives for value-based reimbursement can have an impact oninfection

prevention practice. When considering the future of infection prevention policy making, it is important to acknowledge the extent to which such measures and initiatives are apt to proliferate in the future. In principle, the premise of aligning reimbursement with outcomes should be attractive to clinicians and healthcare organizations. That said, the more widespread adoption of these measures as a primary tool for protecting patients and reducing infections has been limited by the validity of available measures, challenges in risk adjustment, and other technical challenges.

As reporting standards became more evidence based (most notably through the proliferation of the CDC's NHSN), related metrics have become more standardized. This in turn has allowed for a more rigorous and broad application of expectations for providers. Payers and providers alike will be aligned to promote the development of even more sophisticated measures that best reflect variations in care across an increasingly integrated delivery system. Infection prevention professionals and healthcare epidemiologists should be at the vanguard of this movement and progress.

Advocacy for Rational Public Policy in Infection Prevention

Much of this chapter has focused on how the healthcare epidemiologist and infection prevention professional can best respond to the policy and regulatory pressures. However, the relationship between policy and practice need not be one-directional, and experts in the field need not passively accept and acquiesce to the expectations of other powerful stakeholders.

In this final section, we introduce strategies and activities through which the infection prevention provider can take a more active role in influencing both existing and proposed public policy and regulation. While some may protest that their day jobs are busy enough, the question is whether practicing providers can afford to play such a minor role in shaping the policies and expectations that have a tremendous impact.

Organizational Policies and Practices as a Model

US Supreme Court Justice Louis Brandeis highlighted that all US states can serve as "laboratories of democracy," providing valuable experience and evidence that should influence the application of specific strategies and tactics at a broader level. In much the same way, innovation and dissemination of the work of institutional-level infection prevention and control are absolutely essential to driving future policy and practice. Virtually every impactful piece of infection prevention policy and regulation had its roots in the experience and practice of individual providers, programs, and organizations.

The work of infection prevention providers at the level of individual healthcare facilities can be amplified beyond just the protection of patients under their direct care. Rather, where innovation is applied to develop an effective new practice, technique, or approach, it is incumbent on local experts to assess performance rigorously and to disseminate the results and findings more broadly. Even outside the context of a controlled investigation, methods should be described and applied in a standardized fashion, meaningful metrics should be employed, and conclusions should be drawn from the experience should be appropriate.

No matter the results of the intervention (effective or not), the experience should be shared with other providers. Such knowledge transfer need not be restricted to national scientific meetings, but can occur in local roundtables, professional gatherings, and even informal discussions with peers. When executed in this manner, innovation follows a natural path from the provider at the bedside to sophisticated scrutiny in a controlled research environment. For those practices with broad application and implications, then and only then could consideration be given to embedding innovations into broader practice through policies and regulations.

Leveraging Organization Resources

In addition to leading by example through the development and deployment of innovative new methods and approaches, the practicing healthcare epidemiologist and infection prevention professional has other means at their disposal to influence policy in the context of their existing organizational responsibilities.

As discussed, effective performance in preventing HAI and stopping the spread of MDRO is increasingly aligned with the financial incentives of healthcare organizations, and especially acute care hospitals. Governmental pay-for-performance measures, public reporting requirements, and performance incentives or penalties built into commercial payer contracts all compel hospitals and other providers to ensure that performance in HAI prevention is optimized.

While this linkage might be most important for "making the business case" for infection prevention and ensuring that appropriate internal resources are marshaled in support of this work, there is a reciprocal arrangement that should be activated and developed. Specifically, hospitals and health systems, through their investments in government affairs, managed care relationships and public relations programs, have an opportunity to influence and shape the local and national discourse on HAI control policy and regulations. Infection prevention professionals should encourage this type of organizational engagement.

Engaging through Professional Societies

Professional societies play an important role in the practice of infection prevention and healthcare epidemiology. Through development and publication of practice guidelines, organization of national meetings at which ideas and innovation are spread and support for the professional development of individuals in our fields, organizations such as the Society for Healthcare Epidemiology of America (SHEA), the Association for Professionals in Infection Control (APIC), and others have proven vital to the advancement of knowledge and practice in infection prevention and healthcare epidemiology.

Individual Activism

Having discussed the influence that healthcare epidemiologists and infection prevention professionals have through their work, their institution and professional societies, this section and chapter ends with the individual actions available to all readers to shape future US infection prevention policy. These individual actions, absent the need for specific affiliations or positions, are ultimately at the root of effective legislation and regulation in a democratic society.

Political activism offers a range of opportunities to shape policy. The ultimate incentive for political figures and the individuals that they employ is the opportunity for election and re-election. Individually, each action may seem quite small and potentially not very influential; however when matched with similar activities across the entire constituency, the effect can be substantial and may significantly influence policy.

At all levels, politicians and policymakers aim to be accessible to the concerns and issues of those that they represent. Staffers and indeed entire offices are established in order to manage "constituent relations." It is difficult, if not impossible, to quantify the specific influence and weight that comes from outreach through communication with the office of congressman, state legislators, and even municipal council measures. Those who have experience in organizing successful communication campaigns offer the following points of advice when reaching out to political figures and policy makers:

1. Reach out in as personal a style and method manner as possible. Most legislators make themselves available through public forums and more intimate settings for conversations with the individuals they represent. Where that is not possible, written outreach can also have an impact.
2. Requests should be personalized and tell a story. In this space, personal and patient stories and experience can be powerful motivators of action.
3. Target outreach to the individuals who represent you where you vote. While it is tempting to reach out to committee chairs and other legislative leaders, the relationship between elected official and voter is a direct one that should be developed and fostered as a means of influencing policy.
4. It is also a good idea to reach out to hospital government affairs professionals and/or professional society public policy officers before preparing to meet elected officials or their staff, as they may have helpful additional helpful advice and perspective, including knowledge of the personal preferences and outlook of key elected officials.

The chapter closes with perhaps the most idealistic option available to those who wish to shape policy. Engage in the election process. Understand the issues and select candidates on the basis of the themes already discussed, even if you do not plan to provide any support other than your vote. In doing so, don't be reluctant to share your opinion with other voters. Infection prevention professionals and healthcare epidemiologists are often opinion leaders in their social circle and peer groups. Given the importance of these issues not just to our profession but also to our patients, we should not be reluctant to take a public stand on matters.

References

1. U.S. Department of Health and Human Services. HHS Organizational Chart. HHS.gov. Available at: www.hhs.gov/about/agencies/orgchart/index.html. Updated May 2016. Accessed July 2016.
2. Office of the Law Revision Counsel of the United States House of Representatives. United States Code. Available at: http://uscode.house.gov. Accessed July 2016.
3. U.S. Government Publishing Office. Electronic Code of Federal Regulations. Available at: www.ECFR.gov. Updated June 2016. Accessed July 2016.
4. Centers for Disease Control and Prevention. CDC Organizational Chart. Available at: www.cdc.gov/about/organization/orgChart.htm. Accessed July 2016
5. Centers for Medicare and Medicaid Services. Policy & Memos to States and Regions. Available at: www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertificationGenInfo/Policy-and-Memos-to-States-and-Regions.html. Updated July 2015. Accessed July 2016.
6. The Joint Commission. The Joint Commission's Electronic Accreditation & Certification Manuals. Available at: www.jointcommission.org/standards_information/edition.aspx. Accessed July 2016.
7. United States Department of Labor. Occupational Safety & Health Administration. Available at: www.osha.gov. Accessed July 2016.
8. Consumers Union. Safe Patient Project. Available at: http://safepatientproject.org. Accessed July 2016.
9. The Leapfrog Group. The Leapfrog Group. Available at: www.leapfroggroup.org. Accessed July 2016.
10. Centers for Medicare and Medicaid Services. Hospital Compare. Available at: www.medicare.gov/hospitalcompare/search.html. Accessed July 2016.
11. Centers for Disease Control and Prevention. Core Elements of Hospital Antibiotic Stewardship Programs. Available at: www.cdc.gov/getsmart/healthcare/implementation/core-elements.html. Accessed July 2016.

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