Healthcare-Associated Infections

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- Read the enclosed course.
- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a physician or Florida nurse, please return the included Answer Sheet/Evaluation.) Your postmark or facsimile date will be used as your completion date.
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Faculty Disclosure
Contributing faculty, Lori L. Alexander, MTPW, ELS, MWC, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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Division Planners Disclosure
The division planners have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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Audience
This course is designed for healthcare professionals who would benefit from enhanced knowledge of healthcare-associated infections, including physicians, physician assistants, nurses, surgical technologists/assistants, and others involved with the care of patients in hospitals, long-term care facilities, or other healthcare institutions.

Accreditations & Approvals
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A complete Works Cited list begins on page 67.

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NetCE designates this continuing education activity for 18 hours for Alabama nurses.

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About the Sponsor

The purpose of NetCE is to provide challenging curricula to assist healthcare professionals to raise their levels of expertise while fulfilling their continuing education requirements, thereby improving the quality of healthcare.

Our contributing faculty members have taken care to ensure that the information and recommendations are accurate and compatible with the standards generally accepted at the time of publication. The publisher disclaims any liability, loss or damage incurred as a consequence, directly or indirectly, of the use and application of any of the contents. Participants are cautioned about the potential risk of using limited knowledge when integrating new techniques into practice.

Disclosure Statement

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Course Objective

The purpose of this course is to provide physicians, nurses, pharmacists, microbiologists, and other healthcare professionals with an updated review of healthcare-associated infections, including evidence-based guidelines, strategies for prevention, and selection of appropriate treatment options.

Learning Objectives

Upon completion of this course, you should be able to:

1. Describe the effect of healthcare-associated infections on morbidity, mortality, and cost of health care, including the importance of surveillance and prevention.
2. Discuss the pathogenesis of infection and modes of antimicrobial resistance.
3. Identify the environmental, patient-related, and iatrogenic risk factors for healthcare-associated infection.
4. Anticipate the impact of nonimplanted and implanted devices and procedures on healthcare-associated infection.
5. List the most common types of healthcare-associated infections.
6. Identify the most common pathogens and risk factors associated with catheter-related urinary tract infections, and outline the appropriate prevention measures, means of diagnosis, and treatment.
7. List the most common pathogens and causes of surgical site infections, and develop a strategy for prevention, diagnosis, and treatment.
8. Define the most common pathogens and risk factors associated with healthcare-associated pneumonia, and devise appropriate measures for prevention, diagnosis, and treatment.
9. Outline the most common pathogens and risk factors associated with intravascular device-related bloodstream infections, and discuss the appropriate prevention measures, diagnosis, and treatment.
10. Discuss the risk factors and prevention strategies for nosocomial *Clostridium difficile* infection.
11. Implement an effective hand hygiene program and strategies to increase compliance.
12. Outline interventions to control influenza transmission in the healthcare setting.
13. Describe the appropriate use of precautions and isolation techniques.
14. Define additional elements of an institution's infection control program, including the education of healthcare workers and patients with respect to healthcare-associated infections and the need to address challenges in educating non-English-proficient individuals.
15. Discuss the need for hospital preparedness for potential outbreaks.

EVIDENCE-BASED PRACTICE RECOMMENDATION

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

OVERVIEW

This course is structured to provide essential education regarding the epidemiology, prevention, diagnosis, and treatment of healthcare-associated infections (HAIs). The course begins with background information on the pathogenesis of bacterial infections, transmission of infection in the healthcare setting, and the development of drug resistance. The primary sources of HAIs related to the environment, patient factors, and iatrogenic factors are also discussed. The core of the course is a comprehensive description of the most common and costly HAIs: catheter-related urinary tract infections, surgical site infections, hospital-acquired pneumonia, intravascular device-related bloodstream infections, and *Clostridium difficile* infections. The overall incidences, related costs, risk factors, common pathogens, prevention, diagnosis, and treatment are presented for each of these infections, with the implications of drug-resistant infections also noted. An overview of the responsibilities of an infection control program in the healthcare setting is provided, with a discussion of surveillance, adherence to infection control guidelines, management of drug-resistant micro-organisms, precautions and isolation techniques, preparedness for outbreaks and epidemics, and education targeted to both healthcare workers and patients and families. The course content is limited to infections in adults in acute care hospitals, although many measures for prevention are applicable in all settings for all patient populations.

EPIDEMIOLOGY AND BACKGROUND

HAI is one of the leading causes of death and increased morbidity for hospitalized patients. About 1 in 31 patients hospitalized has at least one healthcare-associated infection, a complication estimated to affect more than 1 million patients each year who reside in hospitals or other inpatient care facilities [1; 2]. Historically, these infections have been known as nosocomial infections or hospital-acquired infections because they develop during hospitalization. As health care has increasingly expanded beyond hospitals into outpatient settings, nursing homes, long-term care facilities, and even home care settings, the more appropriate term has become healthcare-acquired or healthcare-associated infection. Many factors have contributed to an increase in HAIs. Advances in medical treatments have led to more patients with decreased immune function or chronic disease. The increase in the number of these patients, coupled with a shift in health care to the outpatient setting, yields a hospital population that is both more susceptible to infection and more vulnerable once infected. In addition, the increased use of invasive devices and procedures has contributed to higher rates of infection; more than 80% of HAIs are caused by four types of infection: catheter-related urinary tract infection, intravascular device-related bloodstream infection, surgical site infection, and ventilator-associated pneumonia [1]. These HAIs, along with infections caused by *C. difficile* and drug-resistant micro-organisms (especially methicillin-resistant *Staphylococcus aureus* [MRSA]), have garnered the most attention and research because of their impact in terms of morbidity, mortality, economic costs, and potential for prevention.

EXAMPLES OF NATIONAL INITIATIVES TO REDUCE FREQUENCY OF HEALTHCARE-ASSOCIATED INFECTIONS	
Organization	**Initiative(s)**
Agency for Healthcare Research and Quality: *Making Health Care Safer: A Critical Analysis of Patient Safety, 2001* (25 safety practices)	Prevent central line-related infections with use of maximum sterile barriers during insertion Use antibiotic prophylaxis appropriately to prevent surgical site infections Prevent ventilator-associated pneumonia with use of semirecumbent positioning
Institute of Medicine: *Priority Areas for National Action: Transforming Health Care Quality*, 2003 (20 priority areas)	Prevent nosocomial infections and implement surveillance programs
Institute for Healthcare Improvement: 5 Million Lives Campaign, 2006 (12 safety interventions)	Prevent central line-related infections Prevent surgical site infections Prevent ventilator-associated pneumonia Reduce methicillin-resistant *Staphylococcus aureus* (MRSA) infection
Surgical Care Improvement Project (partnership of several organizations), 2006	Reduce postoperative complications, including surgical site infections
Centers for Medicaid and Medicare Services (effective October 1, 2008)	No reimbursement for hospital costs related to catheter-associated urinary tract infections, vascular catheter-associated infections, and mediastinitis after coronary artery bypass graft surgery
U.S. Department of Health and Human Services, 2009	National Action Plan to Prevent Healthcare-associated Infections (9 targets for elimination of HAIs)
U.S. Department of Health and Human Services, 2011	Partnership for Patients: Better Care, Lower Costs
National Quality Forum: Patient Safety, 2012 (3 broad goals)	Goal 2: Reduce the incidence of adverse healthcare-associated conditions
The Joint Commission, National Patient Safety Goals, 2013 (6 broad goals)	Prevent Infection: Follow the CDC guidelines for hand hygiene, and use proven guidelines to prevent bloodstream infections from central lines, to prevent infection after surgery, and to prevent catheter-related urinary tract infections
Source: [5; 6; 7; 8; 9; 10; 11; 12; 13]	*Table 1*

The prevalence of HAIs has come down somewhat in recent years, the result of an ongoing national collaborative effort, though much remains to be accomplished. Based on CDC-sponsored hospital surveillance data from 2018, about 3% to 4% of inpatients are infected and an estimated 633,000 hospitalized patients develop an HAI each year [3]. These infections lead to excess mortality and add billions of dollars in total direct medical costs annually [1; 4]. The increased focus on healthcare quality over the past decade has highlighted the need to prevent HAIs as part of overall efforts to enhance patient safety as well as reduce costs, and national initiatives have been developed by healthcare quality agencies, advocacy organizations, healthcare regulating bodies, and policymakers (***Table 1***) [5; 6; 7; 8; 9; 10; 11; 12; 13].

In 2009, the U.S. Department of Health and Human Services developed the national Action Plan to Prevent Healthcare-Associated Infections, an initiative with a steering committee that represents a host of government health-related agencies. The plan includes 5-year goals for nine specific measures of improvement in HAI prevention [14]. Phase I of the plan called for reducing the rate of HAIs in acute care hospitals by the implementation of a collaborative 10-point strategy aimed at prevention [14]:

Frontline Clinicians

- Reduce inappropriate/unnecessary use of devices
- Improve adherence to hand hygiene and barrier precautions
- Implement and improve antimicrobial stewardship

Clinical Leaders, Executives, and Administrators

- Demonstrate leadership support at the highest levels of the facility
- Implement a culture of safety

Government, Advocates, Clinical Leaders, and Administrators

- Enhance financial incentives and regulatory oversight
- Implement system-based approaches/ protocols/checklists
- Achieve better use of technology
- Improve public reporting of credible data
- Enhance traditional and nontraditional partnerships

Phase two of the HAI Action Plan focused on ambulatory surgical centers, renal dialysis facilities, and influenza vaccination of healthcare personnel. Phase three is focused on long-term care facilities, and phase four focused on antibiotic stewardship and prevention of antibiotic resistance [14].

Evidence-based guidelines are at the heart of strategies to prevent and control HAIs and drug-resistant infections and address a wide range of issues from architectural design of hospitals to hand hygiene (***Table 2***) [15; 16; 17; 18; 19; 20; 21; 22; 23; 24; 25; 26; 27; 28; 29; 30; 31; 32; 33; 34; 35; 36; 37; 38]. Adherence to individual guidelines varies but, in general, is low. For example, hand hygiene is the most basic and single most important preventive measure, yet compliance rates among healthcare workers have averaged 30% to 50% [26; 39; 40; 41; 42]. Decreasing the number of HAIs will require research to better understand the reasons behind lack of compliance with guidelines and to develop education and interventions that target those reasons.

"Zero tolerance" of HAIs became a common catchphrase as a call to improve prevention strategies and eliminate HAIs. Zero tolerance for HAIs is a worthy goal, but the complete elimination of all HAIs is not feasible, primarily because interventions address only exogenous sources of infection and do not address many other important factors, such as host response, patient case mixes, pathogen virulence, and lack of specificity in definitions and diagnostic criteria [43; 44]. Furthermore, the literature has not supported the complete elimination of HAIs with enhanced compliance to prevention protocols. The results of the CDC's Study of Efficacy of Nosocomial Infection Control (SENIC) suggested that 6% of all HAIs could be prevented by minimal infection control efforts and 32% by "well organized and highly effective infection control programs" [45; 46]. A later review of 30 studies suggested that an estimated 20% of HAIs are preventable [47]. A 2011 study estimated that approximately 65% to 75% of central line-associated bloodstream infections and catheter-associated urinary tract infections were preventable using current evidence-based strategies; 55% of ventilator-associated pneumonia and surgical site infections were estimated to be preventable [48]. Furthermore, complete elimination is not needed to reap substantial benefit. The U.S. Department of Health and Human Services estimates that a 40% decrease in preventable HAIs (compared with the 2010 rate) would result in 1.8 million fewer injuries and more than 60,000 lives saved over 3 years [8]. A 70% decrease in the rate of HAIs would save an estimated $25 to $31.5 billion [1].

SAMPLE OF GUIDELINES RELATED TO PREVENTING AND MANAGING HEALTHCARE-ASSOCIATED INFECTIONS	
Organization	**Guideline(s)**
American College of Chest Physicians/American Association for Bronchology	Consensus statement: prevention of flexible bronchoscopy-associated infection (2005)
American Institute of Architects	*Guidelines for Design and Construction of Health Care Facilities* (2014)
American Thoracic Society/ Infectious Diseases Society of America	Management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia (2005, updated 2016)
Canadian Critical Care Trials Group/Canadian Critical Care Society	Prevention of ventilator-associated pneumonia (2004)
Centers for Disease Control and Prevention (CDC)	Prevention of catheter-associated urinary tract infections (2009) Disinfection and sterilization in healthcare facilities (2008) Isolation precautions (2007) Management of multidrug-resistant organisms in healthcare settings (2006) Prevention of healthcare-associated pneumonia (2003) Environmental infection control in healthcare facilities (2003) Hand hygiene in healthcare settings (2002) Prevention of intravascular device-related infections (2011) Prevention of surgical site infections (1999, updated 2017)
Infectious Diseases Society of America	Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults (2010) Strategies to prevent catheter-associated urinary tract infection in acute care hospitals (2014)
Society for Healthcare Epidemiology of America	Prevention of nosocomial transmission of multidrug-resistant strains of *Staphylococcus aureus* and enterococcus (2003, 2014) Multi-society guideline for reprocessing flexible gastrointestinal endoscopes (2003)
Society for Healthcare Epidemiology of America/ Infectious Diseases Society of America	*Clostridium difficile* infection in adults (2010, updated 2017)
Society for Healthcare Epidemiology of America/ Infectious Diseases Society of America/Joint Committee on the Prevention of Antimicrobial Resistance	Prevention of antimicrobial resistance in hospitals (1997)
Society for Healthcare Epidemiology of America/ Infectious Diseases Society of America (published as supplement to *Infection Control and Hospital Epidemiology*, 2008)	Strategies to prevent central line-associated bloodstream infections, ventilator-associated pneumonia, catheter-associated urinary tract infections, surgical site infections in acute care hospitals, and transmission of methicillin-resistant *S. aureus* and *C. difficile* infections
World Health Organization (WHO)	*Prevention of Hospital-Acquired Infections: A Practical Guide*, 2nd ed. (2002)
Source: [15; 16; 17; 18; 19; 20; 21; 22; 23; 24; 25; 26; 27; 28; 29; 30; 31; 32; 33; 34; 35; 36; 37; 38]	*Table 2*

The results of studies evaluating strategies to prevent HAIs have shown a wide range in efficacy, particularly with respect to specific HAIs. For example, the effectiveness of strategies to prevent surgical site infections has not been consistent, with some studies showing significant improvement and other studies showing no substantial improvement [49; 50; 51]. Still, research has shown that strict adherence to prevention interventions has an effect; one study demonstrated a decrease of as much as 66% in the prevalence of intravascular device-related bloodstream infections with adherence to a combination of interventions [52; 53; 54; 55; 56]. Combinations of interventions, or "bundles," have been found to be the most effective for preventing HAIs, and the Institute of Healthcare Improvement (IHI) has developed how-to guides on implementing these bundles, which are available for download from the IHI website [57; 58; 59]. More research is needed to determine the direct impact of many guideline recommendations and the combinations of "best practices" that yield the lowest rates of individual HAIs.

Among the national initiatives to reduce the number of HAIs was a move by the Centers for Medicare and Medicaid Services (CMS) to suspend reimbursement of hospital costs related to HAIs it considers "reasonably preventable:" catheter-related urinary tract infection, central line-associated bloodstream infection, and some surgical site infections [9; 10]. However, studies have shown that this policy has not been a contributor to any decrease in the rate of HAIs, and a survey indicated that adherence to only some prevention strategies has increased as a result of the policy [60; 61]. The policy also has the potential to lead to increased unnecessary use of antimicrobials in an effort to prevent infections [62].

In contrast, educating healthcare personnel helps to reduce HAIs, with a systematic review showing a statistically significant decrease in infection rates after an educational intervention in 21 of 26 studies [63]. Education is one of the key elements found to be necessary for a successful HAI prevention program. When such programs at 33 diverse hospitals were evaluated, the following were found to be essential for success [64]:

- Educate and re-educate
- Foster change by first understanding resistance
- Engage frontline staff by involving them in the program and enlisting champions
- Commit to regular strategic communication and join a collaborative
- Start small and tailor implementation to local needs and cultures
- Convince administration to provide leadership, funds, and dedicated staff and assign accountability
- Provide timely, relevant feedback and celebrate successes

Accurate data collection is crucial for understanding trends and the burden of HAIs and for identifying emerging infectious threats. The Association for Professionals in Infection Control and Epidemiology (APIC), the Infectious Diseases Society of America (IDSA), and the Society for Healthcare Epidemiology of America (SHEA) have led efforts to establish uniform standards for surveillance of HAIs and standardized systems for collecting and reporting. The CDC's National Healthcare Safety Network (NHSN), the nation's most widely used HAI surveillance system, is a shared resource for HAI prevention. More than 23,000 hospitals and other healthcare facilities provide data to NHSN, which in turn is used for national- and state-level analyses, including for periodic HAI reports and for targeted prevention initiatives by healthcare facilities, states, regions, quality groups, and national public health agencies, including the CDC [65; 66].

In response to a call for mandatory reporting of HAIs, several states passed legislation requiring the mandatory reporting of specific HAIs, and reporting requirements vary by state. The number of states with mandates for public reporting grew from 3 in 2004 to 31 (and the District of Columbia) in 2015 [67; 68].

MICROBIAL PATHOGENESIS AND DEVELOPMENT OF DRUG RESISTANCE

A comprehensive description of the pathogenesis of infection is beyond the scope of this course. However, a broad overview of pathogen-host interaction will aid in the understanding of how infection develops in the healthcare setting. In addition, a discussion of the development of antibiotic resistance is warranted because of the substantial impact of resistant pathogens on the management of HAIs.

A healthy human body has several defenses against infection: the skin and mucous membranes form natural barriers to infection, and immune responses (nonspecific and specific) are activated to resist micro-organisms that are able to invade. The skin can effectively protect the body from most micro-organisms unless there is physical disruption. For example, the human papillomavirus can invade the skin, and some parasites can penetrate intact skin, but bacteria and fungi cannot [69]. Other disruptors of the natural barrier are lesions, injury, or, in the healthcare setting, invasive procedures or devices.

In addition to breaks in the skin, other primary entry points for micro-organisms are mucosal surfaces, such as the respiratory, gastrointestinal, and genitourinary tracts. The membranes lining these tracts comprise a major internal barrier to micro-organisms due to the antimicrobial properties of their secretions. The respiratory tract filters inhaled micro-organisms, and mucociliary epithelium in the tracheobronchial tree moves them out of the lung. In the gastrointestinal tract, gastric acid, pancreatic enzymes, bile, and intestinal secretions destroy harmful micro-organisms. Nonpathogenic bacteria (commensal bacteria) make up the normal flora in the gastrointestinal tract and act as protectants against invading pathogenic bacteria. Commensal bacteria are a source of infection only if they are transmitted to another part of the body or if they are altered by the use of antibiotics [15].

The transmission of infection follows the cycle that has been described for all diseases, and humans are at the center of this cycle [15]. In brief, a micro-organism requires a reservoir (a human, soil, air, or water), or a host, in which to live. The micro-organism also needs an environment that supports its survival once it exits the host and a method of transmission. Inherent properties allow micro-organisms to remain viable during transmission from a reservoir to a susceptible host, another essential factor for transmission of infection. The primary routes of transmission for infections are through the air, blood (or body fluid), contact (direct or indirect), fecal-oral route, food, animals, or insects. Once inside a host, micro-organisms thrive because of adherent properties that allow them to survive against mechanisms in the body that act to flush them out. Bacteria adhere to cell surfaces through hair-like projections, such as fibrillae, fimbriae, or pili, as well as by proteins that serve as adhesions [70]. Fimbriae and pili are found on gram-negative bacteria, whereas other types of adhesions are found with both gram-negative and gram-positive bacteria. Receptor molecules in the body act as ligands to bind the adhesions, enabling bacteria to colonize within the body. The virulence of the micro-organism will determine whether only colonization occurs or if infection will develop. With colonization, there is no damage to local or distant tissues and no immune reaction; with infection, bacterial toxins that break down cells and intracellular matrices are released, causing damage to local and distant tissues and prompting an immune response in the host. Bacteria continue to thrive within a host through strategies that enable them to acquire iron for nutrition and to defend against the immune response. These virulence factors enhance a micro-organism's potential for infection by interrupting or avoiding phagocytosis or living inside phagocytes [70].

A healthcare environment increases the risk of infection for two primary reasons. First, it is likely that normally sterile body sites will become exposed, allowing pathogens to cause infection through contact with mucous membranes, non-intact skin, and internal body areas. Second, the likelihood of a susceptible host is high due to the vulnerable health status of patients. Especially in an era of decreased hospital stays and increased outpatient treatments, it is the sickest patients who are hospitalized, increasing the risk not only for infection to develop in these patients but also for their infection to be more severe and to be transmitted to others.

Infection is transmitted in a healthcare environment primarily through exogenous and endogenous modes. Exogenous transmission is through patient-to-patient or staff-to-patient contact. Patients who do not have infection but have bacterial colonization can act as vectors of transmission. Staff members can also act as vectors because of colonization or contamination. Endogenous infection occurs within an individual patient through displacement of commensal micro-organisms.

In general, the spread of infectious disease is prevented by eliminating the conditions necessary for the micro-organism to be transmitted from a reservoir to a susceptible host. This can be accomplished by:

- Destroying the micro-organism
- Blocking the transmission
- Protecting individuals from becoming vectors of transmission
- Decreasing the susceptibility of potential hosts

Antiseptic techniques and antibiotics will kill micro-organisms, and proper hand hygiene will block their transmission. Gloves, gowns, and masks remove healthcare workers from the transmission cycle by protecting them from contact with micro-organisms. Contact precautions and isolation techniques help patients avoid being vectors of transmission. Lastly, ensuring that patients and healthcare workers are immune or vaccinated can help decrease the availability of potential hosts.

DEVELOPMENT OF DRUG-RESISTANT MICRO-ORGANISMS

The prevalence of drug-resistant micro-organisms has reached a critical level, and the inappropriate use of antibiotics is often cited as a primary cause of drug-resistant infections. As much as 50% of antimicrobial use is inappropriate [71]. The prophylactic use of antibiotics preoperatively and the empiric use of antibiotics have helped bacteria to develop resistance in the healthcare setting. To meet the challenge of drug resistance, the management of antibiotic use has been a priority recommendation in guidelines developed for infection control programs in healthcare institutions, and review of the antibiotic formulary is required by institutions as part of compliance with Joint Commission standards [15; 23; 72; 73]. (Guidelines for preventing drug-resistant infections in the healthcare setting are discussed in the Infection Control section.)

Although the inappropriate use of antibiotics is a major contributor to the development of drug resistance, other factors play an important role. These other factors include the natural ability of micro-organisms to adapt through genetic plasticity and rapid replication and the lack of antibiotic discovery and development over the past decades [74]. For example, when the efficacy of antibiotics was first demonstrated in the late 1920s, their development and manufacture increased rapidly, and they began to be widely used (too widely, perhaps). However, over the next 40 years, no new class of antibiotics was developed, and the number of new antibiotics decreased substantially between 1983 and 2014 [74]. In 2009, 16 antimicrobial compounds were in late-stage clinical development (phase II or later); however, these compounds represent only incremental advances compared with currently available options, and few address the most commonly resistant pathogens [75]. A 2013 IDSA report identified seven drugs in clinical development that were not included in the 2009 list, but indicated that these agents fell short of addressing the clinically relevant spectrum of resistance [76]. Only two new antibiotics were approved between 2009 and 2013, but five new antibiotics were approved in 2014–2015. Drug

resistance typically emerges first in the healthcare setting, varies according to healthcare setting and geography, and subsequently extends to the community setting [23]. The transmission and persistence of resistant strains of pathogens in a healthcare setting depends on several factors: availability of vulnerable patients, selective pressure from use of antimicrobial agents, number of patients with colonization of infection, and presence and adherence to prevention efforts [23].

Several risk factors for HAI caused by multidrug-resistant organisms have been identified [77; 78]:

- Older age
- Underlying disease and severity of illness
- Transfer of patients from another institution, especially from a nursing home
- Exposure to antimicrobial drugs, especially cephalosporins
- Prolonged hospitalization
- Gastrointestinal surgery or transplantation
- Exposure to invasive devices (urinary catheter, central venous catheter)

Antimicrobial-resistant pathogens have been reported to be the source of approximately 14% to 20% of HAIs, and these HAIs are associated with higher rates of morbidity and mortality and greater economic costs than antimicrobial-susceptible infections [39; 79; 80; 81].

The most common drug-resistant HAI is MRSA, which emerged as a significant problem in the 1980s and increased steadily in prevalence, with a rate of approximately 59% of *S. aureus* infections in U.S. intensive care units (ICUs) in 2004 [78]. Since that time, however, the rate of MRSA associated with HAIs has decreased, most likely because of increased preventive strategies [78; 81]. Overall, the rate of HAIs attributable to antimicrobial-resistant pathogens has not changed substantially since 2010 [81]. According to data on HAIs reported to the NHSN in 2009–2010, 20% of the infections were with antimicrobial-resistant phenotypes: MRSA (8.5%); vancomycin-resistant *Enterococcus* (3%); extended-spectrum cephalosporin-resistant *Klebsiella pneumoniae* and *K. oxytoca* (2%); *Escherichia coli* (2%); *Enterobacter* spp. (2%); and carbapenem-resistant *Pseudomonas aeruginosa* (2%) [81]. The discovery of carbapenem-resistant *Enterobacteriaceae* as a new threat led the CDC to issue a guidance for control of infections with carbapenem-resistant or carbapenemase-producing *Enterobacteriaceae* in the healthcare setting [82; 83]. Data from the 2015 HNSN network survey report showed that 45% of *S. aureus* isolates were methicillin-resistant, and among *E. coli*, *Enterobacter*, and *Klebsiella* isolates, 5% were carbapenem-resistant [3].

Antimicrobial-resistant HAIs are associated with substantial morbidity and mortality compared with antimicrobial-susceptible HAIs, with longer hospital stays (excess of approximately 7 to 13 days), greater attributable mortality (up to 15%), and higher costs (additional $7,000 to $15,000) [78]. Guidelines for the prevention and management of multidrug-resistant pathogens in the hospital setting have been developed by the CDC, SHEA, and IDSA, with the most recent guidelines focusing specifically on the treatment of MRSA [23; 30; 33; 84]. More information on antimicrobial-resistant pathogens is given in the discussions of each type of HAI. In addition, prevention of MRSA infection is addressed in the Infection Control section, as prevention is an important aspect of a healthcare facility's infection control program.

ENVIRONMENTAL SOURCES OF PATHOGENS IN THE HEALTHCARE SETTING			
Source	**Bacteria**	**Viruses**	**Fungi**
Air	Gram-positive cocci (originating from skin) Tuberculosis	Varicella zoster (chickenpox) Influenza	*Aspergillus*
Water (tap and bath)	Gram-negative bacteria (*Pseudomonas aeruginosa*, *Aeromonas hydrophilia*, *Burkholderia cepacia*, *Stenotrophomonas maltophilia*, *Serratia marcescens*, *Flavobacterium meningosepticum*, *Acinetobacter calcoaceticus*, and *Legionella pneumophila*) Mycobacteria (*Mycobacterium xenopi*, *Mycobacterium chelonae*, or *Mycobacterium avium-intracellularae*)	Molluscum contagiosum Human papillomavirus (bath water) Noroviruses	*Aspergillus* *Exophiala jeanselmei*
Source: [15; 85; 86]			*Table 3*

SOURCES OF HAIs

In general, the sources of HAIs can be categorized as being related to environmental factors (air, water, architectural design), patient-related factors (age, degree of illness/immune status, length of hospital stay), and iatrogenic factors (invasive procedures, devices, and equipment).

ENVIRONMENTAL FACTORS

Factors specifically related to the healthcare environment are not common causes of HAIs [15; 85; 86]. However, consideration should be given to the prevention of infection with environmental pathogens, such as fungi (e.g., *Aspergillus*), bacteria (e.g., *Legionella* species), or viruses (e.g., varicella) (***Table 3***). CDC guidelines provide clear recommendations for infection control measures according to several environment-related categories, including air (normal ventilation and filtration, as well as handling during construction or repair), water (water supply systems, ice machines, hydrotherapy tanks and pools), and environmental services (laundry, housekeeping). The infection control program of a facility has oversight of these measures.

Air

Droplets containing micro-organisms can be transmitted in the air, causing infection in patients either directly or indirectly (through contamination of devices or equipment). Cleaning activities, such as sweeping, dry mopping, dusting, or shaking linen, can contribute to the transmission of airborne micro-organisms. Bacteria in the air primarily consist of gram-positive cocci from the skin, and they can be eliminated with appropriate ventilation and circulation of air [87]. Many airborne viruses, such as influenza and other respiratory viruses and measles, do not carry far from the source; others, such as tuberculosis and varicella zoster, may be spread over long distances [15]. The most common fungal spore to be transmitted through air is *Aspergillus*, which is carried through dust particles, can survive for long periods, and is easily inhaled [88]. Under normal circumstances, the level of contamination with this airborne fungus' spores is not high enough to cause disease in otherwise healthy individuals. However, in the healthcare setting, the fungus causes respiratory infection, primarily pneumonia, in susceptible hosts.

The prevalence of infection with *Aspergillus* within a healthcare setting has been strongly associated with *Aspergillus* spore counts. Consequently, air conditioning systems with high-efficiency particulate air (HEPA) filters are needed to minimize contamination [89]. HEPA filters are especially needed to prevent infection with *Aspergillus* in patients at high risk for infection due to a suppressed immune system. In one study, the risk of transplant-related mortality and overall mortality in the first 100 days after transplantation were significantly lower among patients treated in rooms with HEPA and/or laminar flow units than among patients treated in conventional isolation units [90]. In these units, the air exchange rate should be high (more than 15 exchanges per hour), rooms should be tightly sealed, and the air pressure in the rooms should be positive in relation to the hallway [89; 91; 92]. HEPA filters are also used in the hoods in microbiology laboratories and pharmacies, laminar flow units in ICUs, and unidirectional flow units in operating room suites [15].

Air in the Operating Room

Maintaining a high quality of air in operating rooms is an essential factor in preventing postoperative infection. The number and movement of staff within the operating room create the primary sources of airborne bacteria. Other factors influencing airborne contamination include the type of surgery, the rate of air exchange, the initial quality of the air, the quality of the staff clothing and cleaning processes, and the level of compliance with infection control practices [15].

The CDC makes several suggestions about ventilation in the operating room in its guidelines for prevention of surgical site infections [28]. The Level I recommendations include:

- Maintain positive-pressure ventilation in the operating room with respect to the corridors and adjacent areas.
- Maintain a minimum of 15 air changes per hour, of which at least three should be fresh air.
- Filter all air, recirculated and fresh, through the appropriate filters per recommendations of the American Institute of Architects.
- Introduce all air at the ceiling and exhaust near the floor.
- Do not use ultraviolet radiation in the operating room to prevent surgical site infection.
- Keep operating room doors closed except as needed for passage of equipment, personnel, and the patient.

Air During Construction

Special care must be taken to protect patients during repair or renovation of a healthcare facility, as construction work can facilitate the spread of airborne organisms such as *Aspergillus* species [15]. Some construction issues that contribute to the spread of infection include water-damaged building materials, disruption of duct work, open windows, and improper setting of fans or installation of filters [93].

The Joint Commission requires an inspection process for construction on a facility, and a risk assessment is part of that process [93]. Risk factors to consider include the patient population, the extent and duration of the project, the impact of the project on mechanical systems, and whether space with construction will be occupied [93]. A representative from a facility's infection control program should review any plans for construction to ensure that barriers are used as appropriate and patients, especially those with compromised immune systems, are moved to an area away from construction [87].

Water

Water is a reservoir for several types of micro-organisms, including bacteria, fungi, and viruses, with viruses accounting for only a small percentage [85; 94]. The quality of water within a healthcare setting must meet standards that vary according to use. Tap water must be safe to drink and use for baths (for hygiene and therapy) according to criteria dictated by local regulations and public health standards. The water supply to the healthcare facility can be disinfected by several methods, including chlorination, thermal eradication, ultraviolet light, and metal ionization [89].

The most common pathogen identified in tap water is *P. aeruginosa* [78]. In one study, researchers evaluated the association between tap water from faucets in a surgical ICU and patients with colonization or infection with *P. aeruginosa* [95]. The pathogen was found in 58% of water samples taken from individual faucets but was not identified in the main water supply. The genotypes of the micro-organism in 21 of the 45 patients were identical to those found in the tap water from the sink in the patient's room (15 patients) or in the adjacent room (6 patients). According to epidemiologic analysis, transmission of the pathogen had occurred from faucet to patient as well as from patient to faucet. *P. aeruginosa* is also the primary bacterial pathogen found in bath water [96]. The effect of infection with *P. aeruginosa* may be mild, as in folliculitis and external otitis, but wound infection may be more severe. Greater morbidity is associated with infection in individuals who have a compromised immune system or who have another health condition, such as diabetes [15].

Legionella, which causes infection of the respiratory tract, is another micro-organism commonly found in tap water and bath water. The highest concentrations of *Legionella* are found in areas of water distribution systems (hot water storage, cooling towers, condensers), where it colonizes [89]. Infection with *Legionella* is transmitted only through water, not through person-to-person contact. Inhalation of contaminated water droplets from shower heads or faucet aerators may cause disease [85]. In addition, high humidity levels in a room (through mists produced by respiratory equipment, for example) may promote the growth of *Legionella* and molds [90].

The WHO suggests that there is potential risk for HAIs if tap water is used for such purposes as ice machines or devices for washing eyes or ears, or for cleaning equipment [15]. Point-of-use filtration may help to reduce the risk of HAIs related to water [94]. Ducts, humidifiers, dehumidifiers, and other areas of a ventilation system should be kept clean and dry, as micro-organisms can colonize in water that accumulates in these areas [90]. Patients at high risk for infection should not be exposed to hospital water and sterile water should be used instead [86].

Architectural Design

Another factor in the transmission of infection in the healthcare setting is the architectural design of the facility, and the AHRQ lists "good hospital design principles" as one of its 10 patient safety tips for hospitals [97]. When the American Institute of Architects and the Facility Guidelines Institute updated its *Guidelines for Design and Construction of Hospital and Health Care Facilities* in 2006, they set single-bed private rooms as the minimum standard for new hospital construction [18]. This new standard was based on a literature review that showed, in part, that private rooms have been associated with lower rates of HAIs [98]. Among the benefits of single-patient rooms compared with multibed rooms are decreased risk of infection through contaminated surfaces (e.g., blood pressure cuffs, privacy curtains); availability of private bathrooms; greater ease of cleaning and decontamination; increased likelihood of appropriate hand hygiene between rooms (rather than between beds within a single room); and decreased risk of prolonged hospital stays and patient transfers, all of which are risk factors for HAIs [98].

The WHO guidelines on infection control refer to "architectural segregation" according to risk [15]. Four areas of a healthcare facility are defined, with administrative sections considered as low-risk areas; regular patient wards as moderate-risk areas; ICUs, burn units, or isolation units as high-risk

areas; and operating rooms as very high-risk areas. The WHO and others have recommended that traffic flow should be limited in higher risk areas [15].

The type of sink and the placement of sinks throughout a healthcare facility have been of critical concern because of the substantial role of handwashing in reducing the transmission of infection. As a result, sinks have been placed within easy access in each patient room. However, it is unclear that such placement promotes better hand hygiene, with no long-term clinically significant improvement in handwashing found when sinks are placed near points of clinical activity [99].

With the advent of alcohol-based handrub solutions as more effective hand hygiene, the placement of handrub dispensers has become more important than the placement of sinks [26]. The CDC guidelines on hand hygiene recommend placing dispensers in convenient locations, such as at the entrance of each patient room or at the bedside.

PATIENT-RELATED FACTORS

Patient-related risk factors for HAIs include age, general health status, and the type of procedure to be carried out, and risk can be classified as minimal, medium, or high [15]. Patients are at minimal risk if they have no significant underlying disease, have an intact immune system, and will not undergo an invasive procedure. Medium risk is assigned to older patients who are susceptible to disease for a variety of reasons, including decreased immune function, comorbid conditions, and low nutritional status. Medium risk also refers to patients who are to have a nonsurgical invasive procedure, such as a peripheral venous catheter or a urinary catheter.

Advances in medical treatments have led to longer lives for individuals of all ages who have had organ transplantation, cancer, or infection with human immunodeficiency virus (HIV), and their compromised immune system puts them at high risk for HAI. High risk is also assigned to patients with multiple trauma or severe burns, or those who have surgery or an invasive procedure that is considered to be high risk, such as endotracheal intubation or insertion of a central venous catheter.

IATROGENIC FACTORS

The primary iatrogenic factors contributing to the development of HAIs are devices (nonimplanted and implanted) and invasive procedures. As noted, the four most common HAIs—catheter-associated urinary tract infection, intravascular device-related bloodstream infection, surgical site infection, and pneumonia (ventilator-associated and hospital-acquired)—are related to the use of invasive devices or invasive procedures.

Nonimplanted Devices

HAIs have been associated with several types of devices and equipment unique to healthcare facilities. The Spaulding classification, developed in 1968, is widely used to categorize devices according to their associated risk of infection [100]. The system includes three categories:

- Critical: A device that enters normally sterile tissue or the vascular system
- Semicritical: A device that comes into contact with intact mucous membranes and does not ordinarily penetrate sterile tissue
- Noncritical: A device that does not ordinarily touch a patient or touches only intact skin

Most HAIs can be attributed to devices in the critical and semicritical categories, including intravascular catheters, surgical drains, urinary catheters, and endoscopic instruments [87]. Discussion here is limited to endoscopic instruments, as infections related to the other devices are addressed in detail later. In general, the transmission of pathogens on endoscopic devices has been attributed to noncompliance with appropriate reprocessing (cleaning, disinfection, sterilization, and drying) [16; 31; 101; 102]. In particular, appropriate drying has been overlooked as an integral component of reprocessing, and guidelines have been inconsistent in recommendations on drying [103].

Bronchoscopes and gastrointestinal endoscopes are the primary diagnostic scopes used in healthcare settings. Both types of devices are associated with a low risk of infection transmission. Approximately 500,000 flexible bronchoscopies are done in the

United States each year [16; 104]. Few studies, however, have been carried out to evaluate the risk of infection; nosocomial infection related to bronchoscopy is difficult to detect and is likely under-recognized and under-reported [105]. In 2003, there were two reports of multiple pseudoinfections and true infections, primarily with *P. aeruginosa*, associated with bronchoscopes that had been reprocessed according to current standards [106; 107]. However, in both reports, loose fittings over the valve stem for the working channel of the bronchoscope were thought to have prevented effective mechanical cleaning and disinfection [105]. Overall, the pathogens associated with bronchoscopy-related infection have been *P. aeruginosa*, *Serratia marcescens*, nontuberculous mycobacteria, and environmental fungi [105]. In 2014, the U.S. Food and Drug Administration (FDA) received 50 medical device reports that mentioned infection or device contamination associated with reprocessed flexible bronchoscopes [104]. During the course of investigating these reports, the FDA identified two recurrent themes that contributed to device contamination or device-associated infection: failure to meticulously follow the manufacturer's instructions for reprocessing (e.g., failure to perform thorough manual cleaning before high-level disinfection), and continued use of devices, despite integrity, maintenance, and mechanical issues (e.g., persistent channel kinks or bends).

More studies have evaluated the risk of infection associated with gastrointestinal endoscopy, which is performed on approximately 10 to 20 million people each year [108]. The American Society for Gastrointestinal Endoscopy (ASGE) estimates that infectious organisms are transmitted in 1 of 1.8 million gastrointestinal endoscopies [101]. Furthermore, all instances of infection during endoscopy have been the result of noncompliance with established guidelines for reprocessing of endoscopy equipment, highlighting the importance of adhering to these recommendations [31; 108; 109; 110].

As with bronchoscopy, the pathogen with the highest rate of transmission associated with gastrointestinal endoscopy is *P. aeruginosa* [108; 110]. As is true for other pathogens associated with endoscopy, infection with *P. aeruginosa* has resulted from nonadherence to reprocessing guidelines; however, this pathogen differs from the others because of its predilection for a moist environment. Many cases of infection with *P. aeruginosa* have been linked to the water supply to the endoscope and to failure to completely dry the endoscope channels with a 70% alcohol solution and forced air [103; 108; 110]. *Salmonella* species have also been associated with endoscopy, but no cases have been reported since the publication of the 1988 guidelines for standardized cleaning and disinfection of the devices [108; 110]. Infection with *Helicobacter pylori* has also been related to suboptimal cleaning and disinfection [108]. Low rates of hepatitis B and C virus transmission have been reported, and most cases of infection with hepatitis C were found to be related to the inappropriate use of multiple-dose vials and/or syringes rather than to the endoscope itself [31; 108].

Noncritical devices are often overlooked by healthcare workers as vectors for infection. These devices include diagnostic equipment, stethoscopes, and other commonplace items. A systematic review of 23 studies found bacterial contamination of 87% of sampled healthcare equipment, primarily stethoscope membranes, as well as diagnostic ultrasound equipment, otoscopes, and auriscopes [111]. The organisms found on healthcare equipment have primarily been *S. aureus*, including MRSA; *Pseudomonas* spp.; *Acinetobacter* spp.; and *Pasteurella* spp. [112]. Washing stethoscopes with either an ethanol-based cleanser or isopropyl alcohol pads significantly reduces bacterial growth, even that of MRSA [113; 114; 115].

Contamination of therapeutic ultrasound transducer heads and ultrasound gels were evaluated in another study, and the rate of contamination was 27% for the heads and 28% for the gels [116]. The transducer heads had low levels of contamination, and most of the micro-organisms were normal flora; however, high levels of contamination were found in the gels, and the micro-organisms included such pathogens as *Stenotrophomonas maltophilia*, *S. aureus*, *Acinetobacter baumannii*, and *Rhodotorula mucilaginosa*. In two other studies, contamination of dermatoscopes was evaluated. One study indicated colonization of only nonpathogenic bacteria and the other showed that use of an alcohol-based antibacterial gel as immersion fluid yielded no bacterial growth [117; 118].

Ward-based computer terminals have also been shown to have low levels of contamination. In a study of two hospitals, MRSA was found on one of 13 computer terminals in one hospital and on five of 12 in another hospital. The rate of MRSA transmission was significantly higher at the hospital with the greater number of contaminated computers [119].

In summary, a high rate of micro-organism colonization has been found on equipment within the hospital setting, but contamination is usually at low levels and the risk of direct infection is low. In general, the findings of studies have suggested that adequate cleaning of equipment can prevent as many as one-third of HAIs [111].

Implanted Devices

Surgically implanted devices are a major source of HAI, and the development and use of intracardiac devices, orthopedic implants (prostheses and fixation devices), neurosurgical devices, cochlear implants, and breast and penile implants have increased over the past several years. The most common complication with all of these devices is infection [120; 121; 122]. The prevalence of infection associated with these devices varies, with the prevalence highest for left ventricular assist devices (***Table 4***) [120]. Orthopedic implants, such as joint prostheses and fracture fixation devices, are associated with the lowest rate of infection, but reported mortality rates have been as high as 18% [120].

Many implanted device-related infections are caused by contamination during insertion, but these infections are not always the result of micro-organisms transmitted in the healthcare setting. Rather, bacteria (and sometimes fungi) colonize by adhering to the surface of the implant through the development of a biofilm [120]. Biofilms present another challenge in managing infection; biofilms provide bacteria with an extremely high level of resistance to antimicrobial agents. In fact, biofilms can tolerate antibiotic concentrations of 10 to 1,000 times of that needed to destroy free-floating (planktonic) bacteria [120]. Many bacteria, including *P. aeruginosa*, are capable of existing in a planktonic state [110].

The CDC defines implanted device-related HAIs as those occurring within one year after implantation of a device, and the typical interval between implantation and infection varies according to the type of implant [123]. For some implants, early and late infections differ with respect to etiology and the causative micro-organisms [120].

The treatment of infections related to these devices depends on the severity of the infection and the patient's underlying condition. A multidisciplinary approach involving antibiotic therapy and surgical intervention (either debridement or removal of the device) can have a substantial impact on morbidity and mortality. For example, prosthetic valve endocarditis is associated with mortality rates of 42% to 100%, but the rate can be decreased 20-fold through an approach that combines medical and surgical therapy rather than medical therapy alone [120]. Empiric antibiotic therapy is usually appropriate once specimens have been obtained for culture, with the antibiotic agent chosen on the basis of the most common micro-organisms.

DEVICE-RELATED INFECTIONS							
Type of Device	**Prevalence**	**Probable Cause**	**Typical Duration to Occurrence after Implantation**	**Most Common Micro-organisms**	**Signs and Symptoms**	**Diagnosis**	**Treatment**
Left ventricular assist devices	25% to 50%	Biofilm formation	Within 2 to 6 weeks	Methicillin-resistant staphylococcal spp., *Pseudo-monas* spp., *Klebsiella* spp., *E. coli*, *Enterobacter* spp., *Proteus* spp., *Serratia* spp., *Candida* spp., *Enterococ-cus* spp.	Signs of poor healing, localized inflammation, pocket abscess, frank sepsis, new and persistent drainage	Blood cultures	Empiric therapy with vancomycin and an anti-pseudomonal agent (ceftazidime or ciprofloxacin) or empiric antifungal therapy
Cerebrospinal fluid (CSF) shunts	10%	Bacteria originating from patient's skin introduced at time of operation	Within 30 days	*Staphylococcus epidermidis* (40% to 45%), *S. aureus* (25%), *Klebsiella* spp., *Enterobacter* spp., *Pseudomo-nas aeruginosa*, *Acinetobacter baumanii*, *Corynebacterium* spp., *Propioni-bacterium* spp., and streptococci/ enterococci	Fever, focal pain, ventriculitis with lethargy and malaise (proximal shunts), infected intraperitoneal fluid cysts, or frank peritonitis (distal shunts)	CSF analysis (cell count, glucose, protein), gram stain, culture; abdominal ultra-sonography (distal shunts)	Antimicrobial agent effective against noted micro-organisms, modified with results of culture; removal of shunt
Prosthetic cardiac valves	3% to 5.7%	Contamina-tion of the valve at time of implantation or transient bacteremia	Within 60 days (early)	Coagulase-negative staphylococci, specifically methicillin-resistant *S. epidermidis*, *S. aureus*	Fever, new or changing regurgitant murmurs, CHF, shock, cardiac conduction disturbances on EKG	Blood cultures, transesophageal echocardiog-raphy	Delayed anti-biotic therapy until results of culture available (if subacute course and hemodynami-cally stable); empiric anti-biotic therapy with vancomy-cin, gentami-cin, rifampin (evidence of significant valve dysfunction); valve replace-ment (new or increasing murmurs, severe CHF, persistent fever)

Table 4 continues on next page.

DEVICE-RELATED INFECTIONS *(Continued)*							
Type of Device	**Prevalence**	**Probable Cause**	**Typical Duration to Occurrence after Implantation**	**Most Common Micro-organisms**	**Signs and Symptoms**	**Diagnosis**	**Treatment**
Penile implants	2% to 8%	Contamination at time of implantation	Not available	*S. epidermidis*	Erythema, induration, tenderness, fever, discharge, device extrusion, prosthesis-associated pain	Culture of specimen from the operative site	Empiric antibiotic therapy with ciprofloxacin or a cephalosporin for 10 to 12 weeks; removal of implant if pain persists or recurs after antibiotic treatment or if purulent discharge
Cochlear implants	1.7% to 3.3%	Contamination at time of implantation	Within 30 to 90 days	*S. aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*	Skin flap necrosis, wound dehiscence, wound infection	Not available	Antibiotic therapy, incision and drainage, local wound care; removal of device if extrusion of device or implant-related sepsis
Transvenous permanent pacemakers/ automatic implantable cardioverter defibrillators	1% to 7%	Intraoperative contamination of the device or the pocket (early); contamination of pocket as a result of erosion of generator/ defibrillator through skin (late)	Within 30 days (early); within 60 days (late)	*S. aureus*, *Propionibacterium acnes*, *Micrococcus* spp., *E. coli*, *Klebsiella* spp., *Enterobacter* spp., *Serratia* spp. (early); coagulase-negative staphylococci (late)	Erythema, pain, warmth at site ("pocket cellulitis"), draining sinus tract or erosion of overlying skin, systemic symptoms (fever, chills, malaise, nausea)	Blood cultures, transesophageal echocardiography	Prolonged antibiotic therapy, removal of all hardware; empiric therapy with vancomycin, gentamicin, or rifampin
Breast implants	1.7% to 2.5%[a]	Not available	Within 2 to 4 weeks	*S. aureus*, peptostreptococci, *Clostridium perfringens*	Erythema, edema, poor healing, purulent discharge, inflammatory symptoms (breast or axillary pain, paresthesia of upper extremity)	Wound or fluid culture	Empiric antibiotic therapy, local debridement
Orthopedic implants	<1% to 2%	Intraoperative contamination (early and late)	<2 to 4 weeks (early); >30 days (late)	*S. aureus*, coagulase-negative staphylococci, *Propionibacterium* spp. (early and late)	Persistent pain, fever, evidence of wound infection (early); loosening of prosthesis, sinus tract formation with discharge	Joint aspiration, complete blood count, erythrocyte sedimentation rate, C-reactive protein, imaging	Surgical exploration and debridement followed by empiric antibiotic therapy
[a]After augmentation mammoplasty; rates may be higher after mastectomy.							
Source: [120]							*Table 4*

TYPES OF INFECTIONS

HAI is clearly defined by the CDC in the NHSN as a "localized or system condition (1) that results from adverse reaction to the presence of an infectious agent(s) or its toxin(s); and (2) that was not present or incubating at the time of admission to the hospital" [2; 123]. Thus, an infection is considered to be healthcare associated if it is unrelated to the admitting diagnosis and develops within 48 hours after admission. The CDC notes that an infection should be considered healthcare associated if it is thought that the infection was acquired in the hospital but did not become evident until after discharge [2; 123]. The diagnosis of infection is made on the basis of a combination of clinical findings and the results of laboratory studies or other diagnostic testing [123]. The NHSN provides comprehensive details about the criteria for infection at 13 major anatomic sites and has developed clinical and biologic criteria for 48 specific sites or types of infection [123]. The WHO has simplified the criteria to facilitate infection control in healthcare institutions with limited resources [15].

The rates of the five most common HAIs and the percentage each infection accounts for among all HAIs vary according to several factors, including time, geography, healthcare setting (including specific units within a hospital), and the data source. In general, catheter-related urinary tract infections are the most common, representing nearly one-third of all HAIs, and are the least costly; intravascular device-related bloodstream infections tend to be the most costly (in dollars); and ventilator-associated pneumonia is associated with the highest number of deaths (***Table 5***) [1; 2; 29; 78; 81; 124; 125; 126; 127; 128; 129; 130]. Other HAIs defined in the NHNS include infection of bones and joints; the central nervous system; the cardiovascular system; the eye, ear, nose, throat, or mouth; the lower respiratory tract (other than pneumonia); the reproductive tract; skin and soft tissue; and systemic infection. Many of these other HAIs develop as complications of surgically implanted devices [120].

The risk factors for each of these HAIs have been delineated in many studies (***Table 6***) [19; 78; 131; 132; 133; 134; 135; 136; 137; 138]. Yet, predicting which patients are at risk can be difficult. In one study, physicians in a surgical ICU were asked to assess at admission the individual risk of major HAI during the patient's stay in the unit. The investigators found that the physicians could not accurately predict risk, with positive predictive values that ranged from 8.4% to 14.5% and negative predictive values that ranged from 92.1% to 100% [139].

HAIs are predominantly caused by bacteria. Of the 81,139 pathogens (69,475 HAIs) reported to the NHSN between January 2009 and December 2010, 90% were bacteria and 10% were fungi [81]. Approximately 82% of the reported pathogens belonged to one of eight main pathogen groups [81]:

- *S. aureus* (16%)
- *Enterococcus* spp. (14%)
- *E. coli* (12%)
- Coagulase-negative staphylococci (11%)
- *Candida* spp. (10%)
- *Klebsiella* spp. (8%)
- *P. aeruginosa* (8%)
- *Enterobacter* spp. (5%)

The micro-organisms causing HAIs vary according to several factors, including the type of infection; in the overviews of the HAIs that follow, the most common micro-organisms specific to each infection are noted. Infectious agents also vary among healthcare facilities and even units within a single institution. Knowledge of trends in the pathogens responsible for HAIs is important in determining appropriate empiric therapy. This information changes frequently, and healthcare professionals should remain up-to-date with the pathogens identified in their own healthcare facilities and even on specific units within the facility. The IDSA/SHEA recommends computer-based surveillance (level II, B) as part of an overall antimicrobial stewardship program [71].

CHARACTERISTICS OF THE MOST COMMON HEALTHCARE-ASSOCIATED INFECTIONS					
Infection	**Proportion of All HAIs**	**Incidence**	**Costs**		
			Excess Stay	**Attributable Mortality**	**Mean Hospital Cost per Infection (U.S. Dollars)**
Catheter-associated urinary tract infection	32%	20% to 40% of patients with an indwelling catheter	10 days	1%	$1,006
Surgical site infection	22%	1% to 3% of surgical patients	7 to 10 days	3% to 5%	$25,546
Central line-associated bloodstream infection	14%	1% of patients with a central line	10 to 20 days	35%	$36,441
Ventilator-associated pneumonia	15%	10% to 65% of intubated patients	4 days	10% to 50%	$9,966
Healthcare-associated pneumonia (other than ventilator associated)	<1%	NA	NA	NA	NA
Clostridium difficile-associated diarrhea	Not available	30% of hospitalized adults with diarrhea	3 to 6 days	6% to 7%	$9,000–$11,000
NA = Not available.					
Source: [1; 2; 29; 37; 78; 81; 125; 126; 127; 128; 129; 130]					*Table 5*

CATHETER-ASSOCIATED URINARY TRACT INFECTIONS

The IDSA defines a catheter-associated urinary tract infection as an infection occurring in a patient with an indwelling urinary catheter either currently in place or in place within the previous 48 hours [29]. Approximately 15% to 25% of inpatients will have a urinary catheter inserted at some time during the hospital stay, and a urinary tract infection will develop in 20% to 40% of them [20; 29]. The risk of infection varies from 3% to 8% per day when an indwelling catheter is in place [29].

The NHSN survey in 2011 found the rate of catheter-associated urinary tract infections to be 4.7 to 5.3 infections per 1,000 catheter-days [140]. Of the estimated 722,000 HAIs in U.S. acute care hospitals in 2011, approximately 93,300 were catheter-associated urinary tract infections. The most recent NHSN survey observed a significant reduction in catheter-associated urinary infection in 2015, compared with 2011, and the national status report the following year showed a 7% reduction over that reported in 2015 [3; 66]. This improvement has been attributed in part to a reduction in urinary catheter use and to the implementation of a Comprehensive Unit Based Safety Program (focused on prevention of urinary infection) in 603 US hospitals between 2011 and 2013 [3].

Risk Factors

The duration of catheterization is the most important risk factor for infection [29]. Studies have shown that catheterization for more than 2 days is a significant risk factor for urinary tract infection as well as increased 30-day mortality [143]. Other risk factors for catheter-related urinary tract infection include no treatment with systemic antimicrobial agents, positive results on culture of the urethral meatus, microbial colonization of the urinary drainage bag, insertion of the catheter outside the operating room, and nonadherence to guidelines for appropriate catheter care. Patient-related risk factors include female gender, older age, diabetes, and an elevated level of serum creatinine at the time of catheterization [29].

RISK FACTORS FOR HEALTHCARE-ASSOCIATED INFECTIONS		
Infection	**Patient-Related Factors**	**Iatrogenic Factors**
Urinary tract infection	Older age Female gender Diabetes mellitus Renal insufficiency Other site of infection Urethral stent	Use of catheter to measure output Disconnection of catheter from drainage tube Duration of catheterization Retrograde flow of urine from drainage bag
Surgical site infection	Nutritional status History of smoking History of alcohol use disorder Obesity Diabetes Hypovolemia Poor tissue perfusion Compromised immune system Pre-existing infection (local or other site) Anesthesia score Nonviable tissue in wound Hematoma Dead space Wound classification	Foreign material (including drains and sutures) Skin antisepsis Duration of operation Length of time sterile tray left open Intraoperative contamination Duration of preoperative hospital stay Hypothermia during operation Duration of surgical scrub Antimicrobial prophylaxis Preoperative preparation (wash/shave) Surgical technique
Central line-associated bloodstream infection	Severity of illness Burns or surgical wounds Compromised immune system Nutritional status	Heavy colonization on skin at site of insertion Location in internal jugular or femoral vein Length of time in place Contamination of catheter hub Type of infusate Total parenteral nutrition Location of insertion
Ventilator-associated pneumonia	Older age Severity of illness Chronic pulmonary disease Head trauma Elevated gastric pH Upper abdominal or thoracic surgery	Reintubation Supine position Aspiration of gastric contents Nasogastric tube Sedation Duration of mechanical ventilation
Hospital-acquired pneumonia (not associated with a ventilator)	Older age Chronic pulmonary disease Surgery ASA class 2 or higher Functional dependence Congestive heart failure History of tobacco use	Duration of operation Emergency surgery Surgical site Sedation Enteral nutrition
Clostridium difficile-associated diarrhea	Age Severity of illness Compromised immune system Gastrointestinal surgery or manipulation Debilitation Length of stay	Antibiotic use Nasogastric intubation
ASA = American Society of Anesthesiologists.		
Source: [19; 78; 131; 132; 133; 134; 135; 136; 137; 138]		*Table 6*

Transmission and Common Pathogens

Urinary tract infections can be caused by both endogenous and exogenous transmission. Normal flora from the gastrointestinal tract can spread to the urinary tract, or pathogens can be transmitted by caregivers carrying out tasks related to the catheter or drainage bag. Occasionally, pathogens are transmitted through urologic equipment that has not been adequately disinfected. Extraluminal ascension of bacteria along the catheter-urethral mucosa interface is the most common pathway of infection, accounting for approximately two-thirds of infections [29].

According to NHSN data for 2015, the pathogens most commonly isolated from catheter-related urinary tract infections are *E. coli* (46%), followed by *K. pneumonia/oxytoca* (18%), *Enterococcus faecalis* (10%), *P. aeruginosa* (13%), and *Enterobacter* species (8%) [3]. Infections related to short-term catheterization is usually caused by a single agent, whereas infections related to long-term catheterization (30 days or more) is typically caused by multiple pathogens. *P. mirabilis*, *Morganella morganii*, and *P. stuartii* are additional common pathogens in infections related to long-term catheterization [29].

With regard to antimicrobial-resistant pathogens, the percentage of *S. aureus* infections resistant to oxacillins decreased in 2009–2010 (59% vs. 65% in 2007–2008) [81]. The percentage of *Enterococcus faecium* resistant to vancomycin increased, to 83% (from 80% in 2007–2008), as did the percentage of vancomycin-resistant *E. faecalis* (approximately 8% vs 6% in 2007–2008). The prevalence of multidrug-resistance among *E. coli*, *Klebsiella*, and *Enterobacter* spp., previously reported as having increased from 3% in 2007–2008 to nearly 5% in 2015 [3; 81].

Prevention

The principles of care required for prevention of catheter-associated urinary tract infection are well established: appropriate use, sterile catheter placement, maintenance of a closed drainage system, avoidance of back-flow, and minimal duration of catheter insertion. In addition to these technical aspects, a systems approach that standardizes care, educates, and fosters an interprofessional culture of attentiveness is also necessary for optimal preventive care [20; 150].

The evidence-based guidelines for prevention of catheter-associated urinary tract infections were published by the CDC in 2009 (***Table 7***). The IDSA has published evidence-based clinical practice guidelines on the prevention, diagnosis, and treatment of catheter-associated urinary tract infections in 2010 [20; 29]. According to both guidelines, the most important principles for prevention are:

- Limit the use of indwelling urinary catheters.
- Use aseptic technique and sterile equipment when inserting a catheter.
- Secure the catheter properly.
- Use a closed sterile drainage system.
- Maintain unobstructed urine flow.
- Remove the catheter as soon as feasible.

As with prevention of all HAIs, handwashing is an essential element of aseptic technique and care of patients with catheters. In addition, healthcare staff should be educated and trained in proper techniques of catheter insertion and care.

SUMMARY OF LEVEL I RECOMMENDATIONS FROM THE CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC) FOR THE PREVENTION OF CATHETER-ASSOCIATED URINARY TRACT INFECTION[a]

Appropriate Urinary Catheter Use

Insert catheters only for appropriate indications, and leave in place only as long as needed.
Minimize urinary catheter use and duration of use in all patients, particularly those at higher risk for infection or mortality from catheterization, such as women, individuals older than 65 years of age, and patients with impaired immunity.
Avoid use of urinary catheters in patients and nursing home residents for management of incontinence.
Use urinary catheters in operative patients only as necessary, rather than routinely.
For operative patients who have an indication for an indwelling catheter, remove the catheter as soon as possible postoperatively, preferably within 24 hours, unless there are appropriate indications for continued use.

Proper Techniques for Urinary Catheter Insertion

Perform hand hygiene immediately before and after insertion or any manipulation of the catheter device or site.
Ensure that only properly trained persons (e.g., hospital personnel, family members, or patients themselves) who know the correct technique of aseptic catheter insertion and maintenance are given this responsibility.
In the acute care hospital setting, insert urinary catheters using aseptic technique and sterile equipment.
Use sterile gloves, drape, sponges, an appropriate antiseptic or sterile solution for periurethral cleaning, and a single-use packet of lubricant jelly for insertion.
Properly secure indwelling catheters after insertion to prevent movement and urethral traction.
If intermittent catheterization is used, perform it at regular intervals to prevent bladder overdistension.

Proper Techniques for Urinary Catheter Maintenance

Following aseptic insertion of the urinary catheter, maintain a closed drainage system.
If breaks in aseptic technique, disconnection, or leakage occur, replace the catheter and collecting system using aseptic technique and sterile equipment.
Maintain unobstructed urine flow.
Keep the catheter and collecting tube free from kinking.
Keep the collecting bag below the level of the bladder at all times. Do not rest the bag on the floor.
Empty the collecting bag regularly using a separate, clean collecting container for each patient; avoid splashing, and prevent contact of the drainage spigot with the nonsterile collecting container.
Use Standard Precautions, including the use of gloves and gown as appropriate, during any manipulation of the catheter or collecting system.
Unless clinical indications exist (e.g., presence of bacteriuria when catheter is removed after urologic surgery), do not use systemic antimicrobial agents routinely to prevent catheter-associated urinary tract infection for patients requiring either short-term or long-term catheterization.
Do not clean the periurethral area with antiseptics to prevent infection while the catheter is in place. Routine hygiene (e.g., cleansing of the meatal surface during daily bathing or showering) is appropriate.

Quality Improvement Programs

Implement quality improvement programs or strategies to enhance appropriate use of indwelling catheters and to reduce the risk of catheter-associated urinary tract infections based on a facility risk assessment. The purposes of quality improvement programs should be to: ensure appropriate utilization of catheters; identify and remove catheters that are no longer needed (e.g., daily review of their continued need); and ensure adherence to hand hygiene and proper care of catheters.

Administrative Infrastructure

Provide and implement evidence-based guidelines that address catheter use, insertion, and maintenance.
Ensure that healthcare personnel and others who take care of catheters are given periodic in-service training regarding techniques and procedures for urinary catheter insertion, maintenance, and removal. Provide education about catheter-associated urinary tract infections, other complications of urinary catheterization, and alternatives to indwelling catheters.

[a]Level I recommendations are supported by high-to-moderate quality evidence suggesting net clinical benefits or harms, or by low-quality evidence suggesting net clinical benefits or harms, or an accepted practices supported by low-to-very low quality evidence.

Source: [20] *Table 7*

Alternatives to indwelling catheters have been evaluated as an approach to preventing catheter-related urinary tract infections. The IDSA guidelines note that a suprapubic catheter may be considered as an alternative to short-term catheterization (level III, C), but use of this type of catheter is limited because an invasive procedure is needed for insertion [29]. Intermittent catheterization may also be considered as an alternative to short-term (level I, C) or long-term (level III, A) catheterization, and, for men who have minimal postvoid residual urine, condom catheterization can be considered as an alternative to short-term (level II, A) or long-term (level II, B) catheterization in those who are not cognitively impaired [29].

The use of catheters coated with an antimicrobial surface has been evaluated, especially those coated with silver, a highly effective antibacterial substance. In one study, the addition of silver did not reduce the incidence of bacteriuria when compared with silicone-based, hydrogel-coated urinary catheters with and without silver impregnation [144]. One meta-analysis (12 trials; 13,392 patients or catheters) showed that antimicrobial-coated catheters prevented or delayed the onset of bacteriuria in select patients, but the magnitude of the effect varied substantially according to several variables, including catheter type and publication year [145]. A subsequent systematic review (eight studies) found a favorable trend toward a lower rate of infection with silver alloy (vs uncoated) catheters, but the quality of some studies was poor and there was significant heterogeneity among the studies [146]. The 2009 CDC guidelines state that antimicrobial/antiseptic-impregnated catheters can be considered if the rate of catheter-associated urinary tract infections does not decrease after a comprehensive prevention strategy has been implemented [20]. The guidelines add that further research is needed to determine the effect of these catheters in reducing the risk of symptomatic infection, their inclusion among the primary interventions, and the patient populations most likely to benefit from them [20].

Similarly, the IDSA states that catheters coated with an antimicrobial surface may be considered to reduce the risk of infection for patients who are to have short-term catheterization (level II, B), but notes that the data on the effectiveness of this strategy are insufficient [29].

The IDSA guidelines note several prevention strategies that should not be used routinely, primarily because of insufficient data [29]:

- Systemic antimicrobials in patients with short-term (level III, A) or long-term (level II, A) catheterization
- Antimicrobials or antiseptics added to the drainage bag (level I, A)
- Catheter irrigation with antimicrobials (level II, A) or normal saline (level II, B)
- Enhanced meatal care (level I, A)
- Cranberry products
- Methenamine salts (although prophylaxis with methenamine salts may be considered after gynecologic surgery for women who have a catheter for less than 1 week) (level 1, C)

Diagnosis

The CDC and the IDSA classify catheter-associated urinary tract infections as symptomatic urinary tract infection, asymptomatic bacteriuria, or other infection of the urinary tract. Urine samples for urinalysis and quantitative urine culture (using a clean catch technique or catheterization) are necessary for accurate diagnosis [29; 123].

The IDSA notes that catheter-associated urinary tract infection is defined by the presence of signs or symptoms compatible with a urinary tract infection with no other identified source, and at least one bacterial species at a count of $\geq 10^3$ cfu/mL in one urine specimen (level III, A) [29]. This threshold differs from that defined by the CDC ($\geq 10^5$ cfu/mL), which is intended for infection control surveillance rather than detection of infection in an individual patient [123]. In addition, the 2009 CDC guidelines define the criteria

for symptomatic catheter-associated urinary tract infection as symptoms plus a positive urine culture at the threshold of $\geq 10^5$ cfu/mL; if the urine culture result is between $\geq 10^3$ and $\leq 10^5$ cfu/mL, a positive urinalysis is needed to meet the diagnostic criteria [20].

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA), signs and symptoms compatible with catheter-associated urinary tract infection include new onset or worsening of fever, rigors, altered mental status, malaise, or lethargy with no other identified cause; flank pain; costovertebral angle tenderness; acute hematuria; pelvic discomfort; and in those whose catheters have been removed, dysuria, urgent or frequent urination, or suprapubic pain or tenderness.

(https://academic.oup.com/cid/article/50/5/625/324341. Last accessed January 28, 2019.)

Strength of Recommendation/Level of Evidence: AIII (Good evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees)

Urine specimens for culturehould not be obtained from the drainage bag; instead, a sample should be taken through the catheter port with use of aseptic technique [29]. If there is no port, a needle and syringe can be used to puncture the catheter tubing and collect the specimen [29]. For patients with a long-term indwelling catheter, the IDSA recommends replacing the catheter and collecting the specimen from the newly placed catheter [29].

Signs and symptoms suggestive of catheter-associated urinary tract infections include fever (new or worsening), flank pain, hematuria, pelvic discomfort, altered mental status, and malaise or lethargy not attributable to another cause; among patients without a current indwelling catheter, dysuria, urgency, and frequent urination are other symptoms [29]. However, studies have shown that the classic symptoms of urinary tract infection are uncommon among patients with a catheter-associated infection [29]. Pyuria is not diagnostic of catheter-associated urinary tract infection in patients with an indwelling catheter [29].

Asymptomatic bacteriuria is defined as the presence of significant bacteriuria with no signs or symptoms referable to the urinary tract [29].

Treatment

The presence of bacteriuria (as defined by a positive urine culture) in a patient with a chronic indwelling catheter should be interpreted with caution. Often, this represents poor culture technique or may reflect an asymptomatic infection that need not be treated until the catheter can be removed or unless there is fever, flank pain, or worsening renal function. The IDSA recommends that in the absence of such signs these infections not be treated, as treatment has not been found to be beneficial [29; 147; 148]. However, for symptomatic infection, the results of urine culture and antibiotic sensitivities are an essential guide to effective treatment [29]. For patients with a catheter in place, the catheter should be discontinued, if possible, and the urine specimen should be one that is voided midstream (level III, A) [29]. If the catheter has been in place for more than 2 weeks and continued catheterization is necessary, the catheter should be replaced (level I, A) and the urine specimen should be collected from the newly placed catheter (level II, A) [29].

The IDSA guidelines do not specify which antimicrobial to use for treatment but do recommend duration of treatment. Treatment for 7 days is recommended for patients in whom symptoms resolve promptly, and treatment for 10 to 14 days is recommended for patients in whom symptom response is delayed (level III, A) [29]. The guidelines note that a five-day regimen of levofloxacin may be considered for patients who are not severely ill (level III, B) [29].

Guideline Adherence and Quality Improvement

It has been suggested that catheter-associated urinary tract infection is the most preventable HAI [48]. Some studies have noted an increase in adherence to strategies to prevent catheter-associated urinary tract infection [52]. The greatest adherence has been to guidelines for wearing gloves (97%), using appropriate hand hygiene (89%), and maintaining a sterile barrier (81%) [149]. However, adherence to appropriate catheterization (in terms of both initial indication and duration) has been suboptimal, with studies demonstrating the following [29; 143; 150; 151; 152]:

- No justifiable indication or an inappropriate indication (such as incontinence) for more than 50% of catheterizations
- Lack of awareness of catheterization in 25% of physicians
- Catheterization for more than two days among 50% of postoperative patients
- No system for monitoring which patients had insertion of catheters in 56% of hospitals
- No system for monitoring duration of catheterization in 74%
- Policy for nurse-initiated discontinuation of catheterization in 10% of hospitals

Use of alternatives to catheterization is also low, ranging from 14% to 20% [151; 152].

The use of provider reminder systems—alone or in combination with base strategies—has a moderate strength of evidence [1]. In one study, the combination of prompts in a computerized order-entry system and handheld bladder scanners led to an 81% decrease in the use of catheters and a 73% reduction in HAIs [153]. For hospitals without order-entry systems, a handwritten reminder that the patient has a catheter has been effective in reducing the rate of infection [154]. However, the use of reminder systems has been reported to be 9% to 12% [151; 152].

Despite the lack of adherence to prevention guidelines, some progress has been made in reducing this HAI; the rate of symptomatic catheter-associated urinary tract infections decreased 19% to 67% between 2000 and 2007 in ICUs [155]. Compliance with a nurse-driven evidence-based checklist led to a decrease in infections from 2.88/1,000 catheter days to 1.46/1,000 catheter days [156].

The CDC guidelines note that the following are effective elements of a quality improvement program [20]:

- A system of alerts or reminders to identify all patients with urinary catheters and assess the need for continued catheterization
- Guidelines and protocols for nurse-directed removal of unnecessary urinary catheters
- Education and performance feedback regarding appropriate use, hand hygiene, and catheter care
- Guidelines and algorithms for appropriate perioperative catheter management (such as procedure-specific guidelines for catheter placement and postoperative catheter removal and protocols for management of postoperative urinary retention, such as nurse-directed use of intermittent catheterization and use of bladder ultrasound scanners)

SURGICAL SITE INFECTIONS

According to National Hospital Discharge Survey data, 51.4 million inpatient surgical procedures were performed in 2010, creating a large population at risk for surgical site infections [157]. The CDC healthcare-associated infection (HAI) prevalence survey found that there were an estimated 157,500 surgical site infections associated with inpatient surgeries in 2011 [142]. Infection will develop postoperatively in approximately 2.6% of all patients who have surgery [158]. The rate has decreased since the 1990s, but the lower rate is not thought to be an accurate representation because

DISTRIBUTION OF SURGICAL SITE INFECTION AND MOST COMMON PATHOGENS ACCORDING TO TYPE OF SURGERY: DATA REPORTED TO THE NATIONAL HEALTHCARE SAFETY NETWORK, 2009–2010		
Type of Surgery	**Percentage of Reported Surgical Site Infections**	**Most Common Pathogens**
Orthopedic	41%	*Staphylococcus aureus* (47%), coagulase-negative staphylococci (14%), *Streptococcus* spp. (6%)
Abdominal	23%	*Escherichia coli* (19%), *S. aureus* (12%), *Enterococcus faecalis* (9%)
Cardiac	22%	*S. aureus* (31%), coagulase-negative staphylococci (17%), *Pseudomonas aeruginosa* (8%)
Obstetric/ gynecologic	10%	*S. aureus* (20%), *E. coli* (13%), coagulase-negative staphylococci (9%)
Neurologic	2%	*S. aureus* (37%), coagulase-negative staphylococci (23%), *Enterobacter* spp. (7%)
Vascular	2%	*S. aureus* (33%), coagulase-negative staphylococci (8%), *P. aeruginosa* (8%), *E. coli* (8%)
Transplant	1%	Coagulase-negative staphylococci (16%), *Enterococcus faecium* (15%), *E. coli* (10%)
Source: [81]		*Table 8*

of the increased number of operations done on an outpatient basis; a decrease in the length of the postoperative hospital stay; and a wound infection incubation period of 5 to 7 days [39]. This potential for underestimation of the number of surgical site infections is reflected in the findings of a study in which one-third of healthcare-associated wound infections were detected after the patient had been discharged [159]. Surgical site infections are associated with extended lengths of stay, a high rate of readmissions, excess hospital costs, and a mortality rate of 3%, with a higher mortality rate reported for patients 70 years of age and older [2; 160; 161].

The NHSN program enables the CDC to monitor the distribution, etiology, and antimicrobial resistance pattern of infections in relation to the category of surgical procedure. The number of surgical site infections reported through NHSN increased from 10,778 in 2007–2008 to 16,019 in 2009–2010 [81]. However, this may in part be a measure of improved surveillance, as the CDC reported a 19% decrease in infection associated with 10 select procedures performed between 2008 and 2013 [162]. The 2016 NHSN progress report showed a further 6% decrease in surgical site infections for 10 procedures tracked during the previous year [66]. ***Table 8*** shows the distribution of procedure-associated infections and common pathogens, by type of surgery, as reported to NHSN for 2009–2010 [81]. Please note that the distribution percentage is primarily a reflection of the frequency (commonality) with which the given category of surgery is performed and not an indication of the actual rate, or risk, of infection from the specific procedure itself. It may be seen that, with the exception of abdominal procedures and transplant surgery, *S. aureus* (of which 44% of isolates were MRSA) accounted for the majority of these infections [81].

The category of surgery and the duration of the procedure are factors affecting the incidence of post-procedure surgical site infection. The rate of infection by type of surgery varies across facilities; for example, in a multicenter Veterans Administration study, the overall rate of surgical site infection was 6%, with the highest rate (11.3%) following colorectal procedures and the lowest (1.3%) following orthopedic procedures [163].

Risk Factors

Several patient-related and surgery-related factors increase the risk for surgical site infection. Patient-related factors include [28; 132; 136; 164]:

- Older age (≥65 years)
- Obesity
- Poor nutritional status
- Low serum albumin concentration
- History of smoking
- History of alcohol use disorders
- Existing infection
- Diabetes mellitus
- Trauma
- Blood transfusion
- Hypothermia, hypoxia, or hyperglycemia

Among the most common surgery-related factors are anesthesia score, duration of the operation, the use of drains, and inadequate aseptic technique [87]. In a study to determine the influence of risk factors on complications after colorectal surgery, body mass index, duration of the operation, and the surgeon who performed the operation were the three most important factors influencing surgical site infections [165].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Institute for Clinical Systems Improvement recommends that a basic nutritional assessment should be considered on all patients undergoing surgery, as malnutrition is a known risk factor for decreased wound healing and increased surgical site infections.

(http://www.guideline.gov/content.aspx?id=48408. Last accessed January 28, 2016.)

Level of Evidence: Consensus Statement/Expert Opinion

Transmission and Common Pathogens

Surgical site infections arise from both endogenous and exogenous transmission. The microbial sources of surgical site infections vary according to the type of surgery, and the micro-organism reported as being the most common in 2009–2010 was *S. aureus*, which accounted for nearly half of all reported orthopedic surgical site infections [81]. Other common causative pathogens were coagulase-negative staphylococci and *E. coli* [81].

Among the facilities reporting data on surgical site infections to the NHSN in 2009–2010, the percentage of resistant phenotypes was low for pathogens most often associated with surgical site infections [81]. The percentage resistance for most pathogens decreased compared with data for 2007–2008; for example, 44% of *S. aureus* infections were resistant to oxacillins, a significant decrease from 48% in 2007–2008. The percentage of vancomycin-resistant *E. faecium* remained relatively stable (62% in 2009–2010), but the percentage of vancomycin-resistant *E. faecalis* increased from 4.6% to 6.2% in 2009–2010 [81]. Also increasing were rates of resistance of *E. coli* to extended-spectrum cephalosporins (11%) and of *P. aeruginosa* to aminoglycosides (6%) [81].

Prevention

The CDC guideline for preventing surgical site infections, published in 1999, addresses a wide variety of issues, including preoperative preparation of the patient, antisepsis of the surgical team, management of surgical personnel with colonization or infection, antimicrobial prophylaxis, ventilation, cleaning and disinfection of environmental surfaces, microbiologic sampling, sterilization of surgical instruments, surgical attire and drapes, asepsis and surgical technique, postoperative incision care, and surveillance. The CDC's current guideline for prevention of surgical site infection was published in 2017 [28; 166]. The guidelines recommend a combination of key components as a strategy to prevent surgical site infection (***Table 9***).

LEVEL IA and IB RECOMMENDATIONS FOR THE PREVENTION OF SURGICAL SITE INFECTIONS[a]	
1999 Guideline	**2017 Additions**
Preoperative	
Whenever possible, identify and treat all infections remote to the surgical site before elective operation, and postpone elective operations on patients with remote site infections until the infection has resolved. Do not remove hair preoperatively unless the hair at or around the incision site will interfere with the operation. If hair is removed, remove immediately before the operation, preferably with electric clippers. Adequately control serum blood glucose levels in all diabetic patients and particularly avoid hyperglycemia perioperatively. Encourage tobacco cessation. At minimum, instruct patients to abstain for at least 30 days before elective operation from smoking cigarettes, cigars, pipes, or any other form of tobacco consumption (e.g., chewing/dipping). Do not withhold necessary blood products from surgical patients as a means to prevent surgical site infection. Thoroughly wash and clean at and around the incision site to remove gross contamination before performing antiseptic skin preparation. Use an appropriate antiseptic agent for skin preparation.	Implement perioperative glycemic control; use serum blood glucose target (upper) level <200 mg/dL in diabetic and nondiabetic patients. Maintain perioperative normothermia. Perform intraoperative skin preparation with an alcohol-based antiseptic agent, unless contraindicated.
Antimicrobial Prophylaxis	
Administer a prophylactic antimicrobial agent only when indicated, and select it based on its efficacy against the most common pathogens causing surgical site infection for a specific operation and published recommendations. Administer by the intravenous route the initial dose of prophylactic antimicrobial agent, timed such that a bactericidal concentration of the drug is established in serum and tissues when the incision is made. Maintain therapeutic levels of the agent in serum and tissues throughout the operation and until, at most, a few hours after the incision is closed in the operating room. Before elective colorectal operations, in addition to above recommendation, mechanically prepare the colon by use of enemas and cathartic agents. Administer nonabsorbable oral antimicrobial agents in divided doses	In all cesarean sections, administer the appropriate parenteral prophylactic antimicrobial agent prior to skin incision. In clean and clean-contaminated procedures, do not administer additional prophylactic antimicrobial agent doses after the surgical incision is closed in the operating room, even in the presence of a drain. Do not apply antimicrobial agents (i.e., ointments, solutions, powders) to the surgical incision for the prevention of surgical site infection.
Oxygenation	
—	For patients with normal pulmonary function undergoing general anesthesia with endotracheal intubation, administer increased FiO_2 both intraoperatively and postextubation in the immediate postoperative period. To optimize tissue oxygen delivery, maintain perioperative normothermia and adequate volume replacement.
Postoperative Incision Care	
Protect with a sterile dressing for 24 to 48 hours postoperatively an incision that has been closed primarily. Wash hands before and after dressing changes and any contact with the surgical site.	—
[a]Level I recommendations are supported by high-to-moderate quality evidence suggesting net clinical benefits or harms, or by low-quality evidence suggesting net clinical benefits or harms, or are accepted practices supported by low-to-very low quality evidence.	
Source: [28]	*Table 9*

Before surgery, patients should be advised to shower or bathe (full body) with soap (antibacterial or non-antibacterial) or an antiseptic agent on at least the night before the operative day [28]. Antimicrobial prophylaxis should be administered only when indicated based on published clinical practice guidelines and timed such that a bactericidal concentration of the agents is established in the serum and tissues when the incision is made [28]. Antibiotic prophylaxis need not be maintained longer than a few hours after the incision has been closed. Additional guidance is provided in reference to specific surgical procedures and specialty operations (e.g., prosthetic joint arthroplasty) [28].

The CDC guidelines reference appropriate antibiotics on the basis of the type of surgery [28; 166]. Meta-analyses have demonstrated lower rates of infection with a single-dose (long-acting) antibiotic and broader spectrum antibiotics, such as third-generation cephalosporins [168]. However, a complication of perioperative antibiotic prophylaxis is an increased frequency of adverse events, the most serious of which is infection with *C. difficile*, and this risk may be higher in association with a broad-spectrum antibiotic [168].

Systematic reviews reported in the mid-2000s showed that two previously recommended measures for preventing postoperative infection have no effect on the rate of surgical site infection. One review involved six trials in which preoperative washing was evaluated in a total of 10,007 patients. There was no significant difference in the rate of surgical site infections when 4% chlorhexidine gluconate was compared with placebo or no washing [169]. The other review involved 11 randomized controlled trials in which preoperative hair removal practices were evaluated. Comparison of razor, depilatory cream, or no hair removal showed no significant difference in the rate of surgical site infection [170; 171]. However, when shaving was compared with clipping, there were significantly more surgical site infections after shaving. No difference was found in the rate of surgical site infections between clipping 1 day preoperatively or on the day of surgery. On the basis of these findings, preoperative antiseptic washing and shaving are no longer recommended.

Attention should also be directed at strategies to prevent surgical site infections with MRSA. The use of an MRSA prevention bundle—adherence to the guidelines for hand hygiene, decontamination of environment and equipment, active surveillance cultures, and contact precautions for patients with MRSA infection or colonization—led to significant decreases in the overall rate of surgical site infections in one study, with a 1% decrease in surgical site infections after cardiac surgery and a 65% decrease after orthopedic surgeries [172].

Diagnosis

IDSA guidelines on the diagnosis and management of skin and soft tissue infections include a section on surgical site infections [158; 173]. The guidelines note that the most reliable diagnostic information is the physical appearance of the site; local signs of infection include pain, swelling, erythema, and purulent drainage [158; 173]. Clinical manifestations of a surgical site infection do not occur for at least 5 days postoperatively, with many infections not becoming apparent for as long as 2 weeks [158; 173]. The IDSA notes that most postoperative fevers are not associated with a surgical site infection [158; 173].

Surgical site infections are classified as superficial incisional, deep incisional, and organ/space infections. Strict criteria and standardized definitions are used in reporting infections and in surveillance programs [28; 168]. The CDC described the criteria for each type of infection in its guidelines for the prevention of surgical site infections and defined the infections in the NHSN system according to this classification [28; 123; 174].

Superficial Incisional Classification

Infection occurs within 30 days after the operative procedure and involves only skin and subcutaneous tissue of the incision *and at least one of the following*:

- Purulent draining 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 superficial incision is deliberately opened by surgeon, unless incision is culture-negative
- Diagnosis of superficial incisional surgical site infection by the surgeon or attending physician

Deep Incisional Classification

Infection occurs within 30 days after the operative procedure if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operative procedure and involves deep soft tissues (e.g., fascial and muscle layers) of the incision *and at least one of the following*:

- Purulent drainage from the deep incision but not from the organ/space component of the surgical site
- Deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38 degrees Centigrade) or localized pain or tenderness, *unless* incision is culture-negative
- Abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiographic examination
- Diagnosis of a deep incisional surgical site infection by a surgeon or attending physician

Organ/Space Classification

Infection occurs within 30 days after the operative procedure if no implant is left in place or within 1 year if the implant is in place and the infection appears to be related to the operative procedure and infection involves any part of the body, excluding the skin incision, fascia, or muscle layers, that is opened or manipulated during the operative procedure *and at least one of the following*:

- Purulent drainage from a drain that is placed through a stab wound into the organ/space
- Organisms isolated from an aseptically obtained culture or fluid or tissue in the organ/space
- Abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiographic examination
- Diagnosis of an organ/space surgical site infection by a surgeon or attending physician

Treatment

Based on expert opinion, the IDSA recommends opening an infected surgical site, removing the infected material, and continuing dressing changes until the wound heals by secondary intention [158]. Although treatment with antibiotics is commonly started when a surgical site infection is diagnosed, the IDSA notes that little evidence has supported this approach [158]. A short course (24 to 48 hours) of antibiotics may be indicated for patients with a temperature higher than 38.5 degrees Centigrade or a pulse rate of more than 100 beats/min [158]. The guidelines add that treatment is usually empirical but may be selected according to results of wound culture [158]. IDSA offers guidance on the selection of antibiotics according to the operative site [158].

Intestinal or Genital Tract

Single agents: ticarcillin/clavulanate, piperacillin/tazobactam, imipenem/cilastatin, meropenem, ertapenem

Combination agents: ceftriaxone/metronidazole, ciprofloxacin/metronidazole, levofloxacin/metronidazole, ampicillin-sulbactam/gentamicin ampicillin-sulbactam/ tobramycin

Trunk and Extremities (away from axilla or perineum)

Oxacillin, nafcillin, cefazolin, cephalexin, SMX-TMP, vancomycin

Axilla or Perineum

Metronidazole/ciprofloxacin, levofloxacin, ceftriaxone

For surgical site infections after implantation of a joint prosthesis, the approach depends on the duration of infection, stability of the implant, antimicrobial susceptibility of the pathogen, and condition of the surrounding soft tissue [175]. In this setting, rifampin has shown excellent activity against adherent staphylococci and may be useful in combination with beta-lactams, glycopeptides, fluoroquinolones, minocycline, trimethoprim, or fusidic acid [176].

Guideline Adherence and Quality Improvement

The effect of prevention strategies—primarily the appropriate use of prophylactic antibiotics—on the rate of surgical site infection has been evaluated in several studies, and the results have been conflicting. For example, 56% adherence to this measure significantly reduced the incidence of surgical site infections in one study of patients who had colorectal surgery, with the rate decreasing from 22% to 3.5% [177]. There was no significant difference in the rate of surgical site infection between compliant and noncompliant prophylactic antibiotics [177]. In a retrospective review of 605 patients who had colorectal surgery with intestinal anastomosis showed that early administration of antibiotic prophylaxis and a nonstandard antibiotic were significantly associated with a greater risk of surgical site infection [178]. However, the timely administration of prophylactic antibiotics did not improve the rate of surgical site infections among nearly 9,200 elective major surgeries (all types); the rate was 5% for patients who received timely antibiotics compared with 6% for patients who received antibiotic prophylaxis outside of the recommended time [50].

More recent studies have analyzed adherence to the Surgical Care Improvement Project (SCIP) quality measures, with analysis of individual measures as well as groups of measures. Some studies have indicated that an increase in compliance with SCIP measures leads to a decrease in the rate of surgical site infection; the rate decreased from nearly 26% to 16% in one study and in another study, increasing compliance with SCIP measures from 38% to 92% led to a decrease in the rate of superficial surgical site infections from 13% to 8% [49; 179]. Among patients who had laparotomy related to trauma (gunshot wound, stab wound, or blunt trauma), adherence to SCIP measures related to antibiotic prophylaxis resulted in a significantly lower rate of surgical site infection (17% vs 33%) as well as a shorter hospital stay (14 vs 19 days), even after controlling for several factors [180].

However, these data have not been consistent. In a study of nearly 500 patients who had colorectal surgery, compliance with all SCIP measures improved—from 40% to 68%—but the rate of surgical site infections remained essentially the same (approximately 19%) [51]. In addition, a retrospective review of 60,853 surgeries done over a five-year period at 112 Veterans Administration (VA) hospitals showed that improving adherence to five SCIP measures did not significantly lower the odds of surgical site infection [163].

Many have been critical of the SCIP strategy, noting that the evidence has not indicated that adherence to these quality measures alone has had an effect on reducing the overall risk of surgical site infection [181]. The quality measures do not factor in the skill of the surgeon, and other factors, such as state-of-the-art skin antisepsis and innovative antimicrobial technology, should be included in quality improvement programs [181; 182].

PRACTICAL STEPS IN FOLLOWING GUIDELINES TO PREVENT SURGICAL SITE INFECTIONS
Appropriate Use of Prophylactic Antibiotics
Use preprinted or computerized standing orders specifying antibiotic, timing, dose, and discontinuation. Develop pharmacist- and nurse-driven protocols that include preoperative antibiotic selection and dosing based on surgical type and patient-specific criteria (e.g., age, weight, allergies, renal clearance). Change operating room drug stocks to include only standard doses and standard drugs, reflecting national guidelines. Reassign dosing responsibilities to anesthesia or holding area nurses to improve timeliness. Involve pharmacy, infection control, and infectious disease staff to ensure appropriate timing, selection, and duration. Verify administration time during "time-out" or preprocedural briefing so action can be taken if not administered.
Appropriate Hair Removal
Ensure adequate supply of clippers and train staff in proper use. Remove all razors throughout the hospital. Work with the purchasing department to ensure that razors are no longer purchased by the hospital. Use signs or posters as reminders. Educate patients about not shaving preoperatively.
Maintaining Adequate Glycemic Control
Implement one standard glucose control protocol (sliding scale or insulin drip). Regularly check preoperative blood glucose levels on all patients. Assign responsibility and accountability for blood glucose monitoring and control.
Maintaining a Warm Body Temperature
Use hats and booties on patients preoperatively. Use warmed forced-air blankets preoperatively, during surgery, and in the recovery room. Use warmed intravenous fluids. Use warming blankets under patients on the operating table.
Maintaining a Warm Body Temperature
Prevent hypothermia at all phases of the surgical process. Use hats and booties on patients perioperatively. Use warmed forced-air blankets preoperatively, during surgery, and in the recovery room. Use warmed intravenous fluids. Use warming blankets under patients on the operating table. Adjust engineering controls so that operating rooms and patient areas are not permitted to become excessively cold overnight, when many rooms are closed. Measure temperature with a standard type of thermometer.
Source: [184] *Table 10*

Ways to help increase adherence to effective prevention strategies are the use of computerized standard orders for antibiotics, reminders and checklists, and auditing of the rates for individual physicians, with feedback [28]. A study demonstrated that point-of-care prompts increased compliance with timely antibiotic prophylaxis from 62% to 92%, with a corresponding decrease in the incidence of surgical site infections, from 1.1% to 0.7% [183]. In an extensive systematic review, there was moderate strength of evidence for the use of audit and feedback, with or without provider reminder systems, for improving adherence to appropriate timing of prophylactic antibiotics [1]. The IHI how-to guide for the prevention of surgical site infection outlines practical steps to help healthcare professionals ensure that prevention strategies are carried out (***Table 10***) [184].

PNEUMONIA

Pneumonia associated with healthcare facilities is classified in three categories: hospital-acquired, ventilator-associated, and healthcare-associated. Hospital-acquired pneumonia refers specifically to pneumonia that develops 48 hours after hospital admission (usually occurring postoperatively), and ventilator-associated pneumonia refers to pneumonia that develops 48 hours after tracheal intubation [185]. Healthcare-associated pneumonia develops in individuals in healthcare facilities outside hospitals, such as long-term care facilities and outpatient settings.

Hospital-acquired pneumonia, also referred to as post-procedure pneumonia, is not included in most discussions of HAIs because it represents less than 1% of all such infections; although this type of pneumonia is not reportable to NHSN, 23 cases were reported in 2009–2010 [81]. Still, hospital-acquired pneumonia can increase the length of stay by more than 1 week and is associated with increased mortality and financial cost [186].

The rate of ventilator-associated pneumonia is higher than that for hospital-acquired pneumonia, with a reported rate of 1 to 4 cases per 1,000 ventilator-days, and rates as high as 10 cases per 1,000 in some neonatal and surgical populations [17; 187]. An estimated 10% of patients requiring mechanical ventilation will develop pneumonia as a complication, and the mortality rate directly attributable to ventilator-associated pneumonia is estimated at 13% [17]. Excess cost of care resulting from prolongation of hospital stay is estimated to be range from $30,000 to $40,000 per patient [17].

Risk Factors

Hospital-Acquired Pneumonia

In a systematic review, the American College of Physicians found several patient-related and surgery-related factors that increased the risk of postoperative pulmonary complications. The most common patient-related factors were the presence of COPD and an age older than 60 years [137]. Other significant factors were an American Society of Anesthesiologists (ASA) class 2 (defined as a patient with mild systemic disease) or higher, functional dependence, and congestive heart failure. Cigarette use was associated with a modest increase in risk, and obesity and mild or moderate asthma were not found to increase risk [137]. Use of a PPI or histamine-2 receptor antagonist is also thought to be a risk factor [138]. Surgery-related factors included prolonged duration of surgery (more than three to four hours), emergency surgery, and surgical site, with abdominal surgery, thoracic surgery, neurosurgery, head and neck surgery, vascular surgery, and aortic aneurysm repair being associated with the greatest risks [137].

Ventilator-Associated Pneumonia

The risk of ventilator-associated pneumonia correlates with the duration of intubation; the risk has been estimated to be 3% per day during the five-day period after intubation, decreasing to 2% per day for days 5 through 10 and to 1% per day for longer durations [190].

Nearly half of all cases of ventilator-associated pneumonia develop within the first four days of mechanical ventilation [185]. In addition to duration of ventilation, several other risk factors among adults have been identified, including a supine head position; use of a nasogastric tube, paralytic agents, or PPI or histamine-2 receptor antagonists; patient age; chronic lung disease; and head trauma [19; 138]. In one study, ventilator-associated pneumonia was most frequently associated with ICU admission diagnoses of postoperative care, neurologic conditions, sepsis, and cardiac complications [191].

Transmission and Common Pathogens

Gram-negative enteric bacilli and *Pseudomonas* spp. rarely colonize the upper respiratory tract of healthy individuals, but often do so in persons with an underlying disease, such as alcohol use disorder, and in those who are hospitalized or reside in nursing homes. Most cases of pneumonia that develop in a healthcare facility are caused by aspiration of oropharyngeal or gastric secretions colonized with hospital bacterial flora. Consequently, the prevalent causation as well as the antibiotic sensitivity pattern of resident pathogens will vary from region to region in relation to the type of facility and burden of antimicrobial usage. The selection of initial antibiotic therapy in these cases is based on the patient's risk factors for infection with a multidrug-resistant organism, such as MRSA, *P. aeruginosa*, *K. pneumoniae*, or *Acinetobacter*. The infectious disease and pulmonary specialty societies (IDSA and American Thoracic Society [ATS]) list the following risk factors for multidrug-resistant pathogens in patients presenting with hospital-acquired or ventilator-associated pneumonia [17]:

- Prior intravenous antibiotic use within 90 days
- Septic shock at time of ventilator-associated pneumonia
- Acute respiratory distress syndrome prior to onset of ventilator-associated pneumonia
- High frequency of antibiotic resistance in the community of residence or the hospital unit of residence
- Five or more days of hospitalization prior to onset of pneumonia
- Home infusion therapy
- Chronic dialysis within 30 days
- Family member with multidrug-resistant infection
- Immunosuppression

Approximately 50% of all cases of healthcare-associated pneumonia develop following surgical procedures, of which cardiac, abdominal, and orthopedic surgery confer the greatest risk. Viral and fungal pathogens are rare causes of hospital-acquired and ventilator-associated pneumonia in immunocompetent adults. Outbreaks of viral pneumonia may occur during influenza season, and influenza, parainfluenza, adenovirus, and respiratory syncytial virus (RSV) are involved in about 70% of those cases [17]. *Candida* spp. and *Aspergillus fumigatus* may cause pneumonia in patients who have had organ transplantation or who have a compromised immune system and neutropenia.

Hospital-Acquired Pneumonia

Among adults with no previous antibiotic exposure, the most common bacterial causes of hospital-acquired pneumonia are *S. aureus*, *S. pneumoniae*, *H. influenzae*, *E. coli*, and *K. pneumoniae* [17; 185; 186; 193]. Gram-negative bacilli resistant to first-generation cephalosporins also frequently develop in late-onset hospital-acquired pneumonia. When patients who have previously received antibiotics develop late-onset hospital-acquired pneumonia, the likelihood of causation by a multidrug-resistant pathogen, such as *P. aeruginosa*, *A. baumannii*, or MRSA, approaches 40% [186]. In a study of more than 3,600 patients admitted to an ICU, *Pseudomonas* spp. was the cause of pneumonia in 25% of patients; MRSA in 18%; and *Acinetobacter* spp. in 6% [193]. Other studies have shown that *S. aureus* is common among patients who are in a coma or have diabetes or renal failure; *P. aeruginosa* is common among patients who have had a prolonged stay in the ICU, have received prior antibiotics or corticosteroids, or who have structural lung disease; and *Legionella* is usually found in patients who have compromised immune systems [193].

Ventilator-Associated Pneumonia

In 2009–2010, the most common pathogens reported with ventilator-associated pneumonia in adults were *S. aureus* (24%) and *P. aeruginosa* (17%), followed by *K. pneumonia/oxytoca* (10%), *Enterobacter* spp. (9%), and *A. baumannii* (7%) [81]. Almost half of all cases of ventilator-associated pneumonia are caused by infection with more than one pathogen [185]. As with other forms of HAI, the percentage of *S. aureus* resistant to methicillin has decreased in recent years [3; 142]. The percentage of vancomycin-resistant *E. faecium* has remained stable, but the percentage of vancomycin-resistant *E. faecalis* increased from 6% in 2007–2008 to nearly 10% in 2009–2010 [81]. In the past decade, rates of resistance among *Klebsiella* spp. have increased for extended-spectrum cephalosporins (24%), carbapenems (11%), and multidrug (13%), while the rate of multidrug-resistant *E. coli* is stable at about 3% [81].

Prevention

The CDC has published guidelines for the prevention of hospital-acquired and ventilator-associated pneumonia, with a focus on strategies to decrease or eliminate modifiable risk factors [24]. These strategies are related to preoperative and postoperative care and measures to reduce the risk of transmission of etiologic pathogens. In addition, steps to prevent the spread of influenza virus are essential, especially during influenza season.

Hospital-Acquired Pneumonia

For many years, preventing postoperative pneumonia has been a part of initiatives to decrease complications among patients who have surgery. The Respiratory Risk Index was developed to classify patients as being at low, medium, or high risk for postoperative respiratory failure [186]. The factors in the index include the complexity of the surgery, the ASA status, and comorbidities.

Smoking triples the risk for pulmonary complications after surgery, and smoking cessation for at least 8 weeks before surgery, when possible, is recommended for current smokers [186]. The risk for complications in patients with respiratory disease or congestive heart failure can be ameliorated by optimum treatment before surgery (e.g., treatment with steroids for patients with COPD or asthma) [186].

Effective pain management after surgery can also help decrease the risk of pulmonary complications. For postoperative patients who are not mechanically intubated, the ability to cough and clear secretions is important for preventing pulmonary complications [186]. The use of incentive spirometry and deep breathing exercises are recommended, especially for people at high risk for pulmonary complications, as are frequent coughing and early movement (in bed and/or walking) [24; 137; 186]. Fair evidence supports the selective (rather than routine) use of a nasogastric tube after abdominal surgery [137].

Ventilator-Associated Pneumonia

Two guidelines were developed to focus specifically on the prevention of ventilator-associated pneumonia; one was jointly developed by the SHEA and IDSA, and the other was jointly developed by the Canadian Critical Care Trials Group and the Canadian Critical Care Society [19; 35]. In addition, prevention of ventilator-associated pneumonia is addressed in the CDC's guidelines for preventing healthcare-associated pneumonia and in the IDSA/ATS guidelines on the management of healthcare-associated pneumonias [17; 24]. The following multicomponent prevention strategy is suggested by these guidelines:

- Assessment of readiness to extubate and daily interruptions of sedation
- Elevation of the head of the bed
- Daily oral care with chlorhexidine
- Prophylaxis of peptic ulcer disease
- Prophylaxis of deep vein thrombosis

Assessment of Readiness to Extubate

Because of the increasing risk of infection as the duration of ventilation increases, the primary goal is to extubate patients as early as possible. Thus, assessment of the readiness for extubation and weaning protocols are key aspects in the preventive approach [17; 193]. Daily interruption of sedation until the patient is awake has been shown to significantly decrease the number of days on mechanical ventilation, from 7.3 days to 4.9 days in one study [194]. There are risks to this approach, such as the potential for increased pain, anxiety, and desaturation. However, the use of sedation interruption has been further demonstrated to reduce the complications of prolonged mechanical ventilation [195]. The SHEA/IDSA guidelines recommend daily assessment of the readiness to wean and the use of weaning protocols [35].

Elevation of the Head of the Bed

Reducing the risk of aspiration and contamination with gastric secretions also helps to prevent the development of ventilator-associated pneumonia. The risk of aspiration has been significantly reduced by positioning the patient with the head of the bed at an angle of 30 to 45 degrees [19; 196; 197]. In one randomized controlled trial, there were 18% fewer cases of ventilator-associated pneumonia among intubated patients in the group assigned to the recumbent position (45 degrees) compared with the group assigned to the supine position [197]. In another study, elevation of the head of the bed at 30 degrees was the most effective measure among a group of preventive interventions, resulting in a 52% variance in the rate of ventilator-associated pneumonia [198]. Both the ATS/IDSA and SHEA/IDSA guidelines recommend maintaining the head of the bed at a 30- to 45-degree angle [17; 35].

Daily Oral Care with Chlorhexidine

Oral care interventions have been suggested by some, in part because of an association between a high level of dental plaque and a high rate of colonization with aerobic pathogens, including *S. aureus*, gram-negative bacilli, and *P. aeruginosa* [199]. Research has shown that oral decontamination with chlorhexidine leads to a significant reduction in the colonization of pathogens in the oropharynx; in most studies, the intervention has not had a significant effect on the rate of ventilator-associated pneumonia or associated mortality, but more recent studies showed significant decreases in the rate of ventilator-associated pneumonia [198; 200; 201; 202]. Including tooth brushing with chlorhexidine does not seem to add benefit [202]. Regular oral care with an antiseptic solution or chlorhexidine is recommended in the ATS/IDSA and SHEA/IDSA guidelines [17; 35].

Prophylaxis of Peptic Ulcer Disease

Prophylaxis of peptic ulcer disease has evolved with some conflicting views. Antacids, histamine-2 antagonists, and sucralfate have been traditionally given to patients receiving mechanical ventilation to prevent the formation of ulcers. However, reducing the amount of gastric acid can increase the risk of colonization of gram-negative bacilli in the stomach. As a result, WHO recommended avoiding the use of these agents [15]. The CDC noted that there was insufficient evidence on the use of peptic ulcer prophylaxis and included no recommendations in this regard in its guidelines [24]. The ATS/IDSA guidelines stated that the risks and benefits of prophylaxis should be weighed carefully [17]. The most recent guidelines, developed by SHEA/IDSA, notes that histamine-2 receptor antagonists and PPIs should be avoided in patients who are not at high risk for developing a stress ulcer or stress gastritis [35].

Prophylaxis of Deep-Vein Thrombosis

There is no clear relation between prophylaxis of deep-vein thrombosis and ventilator-associated pneumonia, but the American College of Chest Physicians reported a decrease in the rate of ventilator-associated pneumonia when such prophylaxis was implemented as part of a package of interventions and included this measure in its clinical practice guidelines [203].

Other Measures

In addition to these interventions, other measures have been recommended to help prevent ventilator-associated pneumonia. One such measure is selective decontamination of the digestive tract, which involves the use of either topical antiseptic, oral antibiotics, or a brief course of systemic antibiotics [186]. A meta-analysis (28 studies) showed that selective decontamination of the digestive or respiratory tract with use of topical antiseptic or antimicrobial agents helped reduce the frequency of ventilator-associated pneumonia in the ICU [204]. The estimate of efficacy in prevention was 27% for antiseptics and 36% for antibiotics. Neither had an effect on mortality. This intervention is recommended in the SHEA/IDSA guidelines [35].

Other preventive measures are targeted primarily to the care and use of ventilator equipment and practices in direct patient care. Meticulous attention to aseptic care of the equipment is necessary, and all reusable components, such as nebulizers, should be disinfected or sterilized. Tubing circuits should be replaced after more than 48 hours, or earlier if there are signs of malfunction or contamination [24]. Changes in the design of the endotracheal tube have also been evaluated; for example, a tube with a suction port above the cuff allows for continuous aspiration of subglottic secretions. Use of this specially designed endotracheal tube has led to significantly lower rates of ventilator-associated pneumonia, as well as shorter durations of ventilation and shorter stays in the ICU [205; 206].

Among patients who had major cardiac surgery, the greatest benefit was found for patients who received ventilation for more than 48 hours [206]. The cost of the tube is higher than traditional tubes but is offset by overall cost savings in preventing ventilator-associated pneumonia [205]. In one meta-analysis, subglottic secretion drainage was significantly associated with a decreased incidence of ventilator-associated pneumonia, shorter time on mechanical ventilation, and longer time to the development of ventilator-associated pneumonia [207]. The CDC, the ATS/IDSA, and the SHEA/IDSA guidelines recommend subglottic secretion drainage with this tube when possible [17; 24; 35].

The use of noninvasive ventilation is another measure that has reduced the incidence of ventilator-associated pneumonia [24; 208; 209]. In one study, the incidence decreased from 20% to 8% when noninvasive ventilation was used routinely for critically ill patients with acute exacerbation of chronic obstructive pulmonary disease or severe cardiogenic pulmonary edema [210]. Again, the CDC, the ATS/IDSA, and the SHEA/IDSA guidelines recommend the use of noninvasive ventilation when possible [17; 24; 35].

Diagnosis

The difficulty in diagnosing hospital-acquired or ventilator-associated pneumonia has been well established [17; 190; 211]. The clinical signs can resemble those of other, noninfectious conditions, and the specificity of clinical criteria is low [185]. According to the CDC definition, the diagnosis in adults is made on the basis of clinical signs and symptoms and results of laboratory testing or imaging and must meet one of two criteria [212].

Criterion 1

For any patient, *at least one of the following*:

- Fever (>38°C or >100.4°F)
- Leukopenia (<4,000 WBC/mm^3) or leukocytosis (≥12,000 WBC/mm^3)
- For adults ≥70 years of age, altered mental status with no other recognized cause

AND *at least two of the following*:

- New onset of purulent sputum, or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements
- New onset or worsening cough, or dyspnea, or tachypnea
- Rales or bronchial breath sounds
- Worsening gas exchange (e.g., oxygen desaturations [e.g., PaO_2/FiO_2 ≤240 mm Hg], increased oxygen requirements, or increased ventilator demand)

Criterion 2

Two or more serial chest radiographs showing *at least one of the following*:

- New or progressive and persistent infiltrate
- Consolidation
- Cavitation
- Pneumatoceles, in infants 1 year of age or younger

In patients without underlying pulmonary or cardiac disease (e.g., respiratory distress syndrome, pulmonary edema, chronic obstructive pulmonary disease), one definitive chest radiograph is acceptable.

There are no compelling data to recommend a specific approach to diagnosing hospital-acquired or ventilator-associated pneumonia. For patients who are not receiving mechanical ventilation, collection of a sputum specimen should be attempted before antibiotic therapy is begun [193; 213]. Specimens for culture can be obtained by bronchoscopy with a protected specimen brush to limit contamination or by bronchoalveolar lavage. The latter method has been found to lead to higher rates of treatment than that based on the CDC definition, and one study showed that preferential sampling of the right lung improved the diagnostic accuracy of bronchoalvolar lavage [193; 214; 215]. However, the invasive procedure has disadvantages, including high cost, need for technical expertise, and potential for false-negative results [193; 214].

The 2016 IDSA/ATS guidelines recommend collecting specimens from the lower respiratory tract for culture, preferably by noninvasive techniques and reliance on semiquantitative culture technique [17]. Noninvasive methods to obtain respiratory samples in patients with hospital-acquired (but not ventilator-associated) include spontaneous expectoration, sputum induction, nasotracheal suctioning (in a patient unable to produce a sample), and endotracheal aspiration in a patient who subsequently requires mechanical ventilation [17]. A 2012 meta-analysis found no evidence that the use of quantitative cultures of respiratory secretions resulted in decreased mortality, reduced time in ICU and on mechanical ventilation, or higher rates of antibiotic change compared with qualitative cultures in patients with ventilator-associated pneumonia [216]. In addition, there was no difference in mortality, whether invasive or noninvasive methods were used to obtain specimens.

Treatment

Treatment is complicated by two divergent needs: the need for empiric therapy with a broad-spectrum antibiotic, to aid in reducing mortality rates, and the need to avoid the indiscriminate use of antibiotics, to avoid the development of resistance. To address this complex issue, the strategy of de-escalation therapy was developed. With this treatment approach, a broad-spectrum antibiotic targeted to likely pathogens is administered, and the antibiotic regimen is altered, if necessary, after the results of cultures are known [218; 219]. This strategy has reduced the mortality rate while achieving an overall objective of a more judicious use of antibiotics [218; 220; 221]. In one study, de-escalation therapy led to a significantly lower mortality rate compared with either escalation therapy or therapy that was neither escalated nor de-escalated (17% compared with 43% and 24%, respectively) [191].

It has been emphasized that this approach, and empiric treatment of healthcare-acquired pneumonia in general, calls for knowledge of the infection history of the healthcare facility and of individual patient units [185; 193; 222]. Microbiology laboratory reports can provide such details, and physicians should prescribe initial antibiotics that are likely to be active against these pathogens.

The IDSA/ATS guidelines provide several recommendations for the management of both hospital-acquired and ventilator-associated pneumonia [17]:

- Obtain sputum samples from the lower respiratory tract for culture before beginning antibiotic therapy. Do not delay initiation of therapy for critically ill patients in order to obtain specimens.
- Begin treatment promptly, selecting an empiric antibiotic regimen that covers *S. aureus, Pseudomonas aeruginosa*, and other gram-negative bacilli.
- In selecting coverage for *S. aureus*, choose an agent active against MRSA (vancomycin or linezolid) for patients with any of the following:
  - Risk factor for antimicrobial resistance
  - Treatment in hospital or units where >10% of isolates are methicillin-resistant
  - Patients in settings where the prevalence of MRSA is unknown
- In selecting coverage for *P. aeruginosa*, one antibiotic active against this pathogen is satisfactory if the patient has no risk factors for antimicrobial resistance and <10% of gram-negative isolates from the patient's unit are resistant to the agent chosen; otherwise, prescribe two antipseudomonal antibiotics from different classes.
- Consider de-escalation of antibiotics after the results of cultures and sensitivities are known and the clinical response is satisfactory.

RECOMMENDED ANTIBIOTIC THERAPY FOR HEALTHCARE-ASSOCIATED PNEUMONIA ACCORDING TO SITE OF CARE	
Site of Care	**Recommended Regimen**
General ward	Antipseudomonal cephalosporin, antipseudomonal carbapenem, or extended-spectrum ß-lactam/ß-lactamase inhibitor and antipseudomonal fluoroquinolone or aminoglycoside and anti-MRSA agent (vancomycin or linezolid)
Intensive care unit	Empiric MRSA and double coverage of *Pseudomonas* pneumonia
Source: [17]	*Table 11*

- When an optimal antibiotic regimen is confirmed, a seven-day course of therapy is recommended, provided the rate of improvement of clinical, radiographic, and laboratory parameter is satisfactory.
- It is suggested to use serum procalcitonin levels plus clinical criteria to guide discontinuation of antibiotic therapy, rather than clinical criteria alone.

EVIDENCE-BASED PRACTICE RECOMMENDATION

In patients with suspected ventilator-associated pneumonia, the IDSA and the American Thoracic Society recommend including coverage for *S. aureus*, *Pseudomonas aeruginosa*, and other gram-negative bacilli in all empiric regimens.

(https://www.idsociety.org/practice-guideline/hap_vap. Last accessed January 28, 2019.)

Strength of Recommendation/Level of Evidence: Strong recommendation, low-quality evidence

Specific treatment depends on the timing of onset and the presence or absence of risk factors for infection with multidrug-resistant organisms. For early-onset pneumonia and/or patients with no such risk factors, limited-spectrum antibiotic therapy is recommended (***Table 11***) [17]. For late-onset pneumonia and/or patients at increased risk for multidrug-resistant bacteria, a broad-spectrum antibiotic therapy is recommended.

Vancomycin has been considered the first choice for treatment of MRSA infections [218]. However, the ATS/IDSA guidelines note that linezolid may have advantages over vancomycin for ventilator-associated pneumonia caused by MRSA [17]. Linezolid has been compared with vancomycin for the treatment of pneumonia caused by MRSA in many studies and has been found to improve survival and to be more cost-effective [223; 224; 225; 226]. In one study, the rate of early microbiologic cure was not significantly higher for linezolid than for vancomycin, although there were trends favoring linezolid in several secondary clinical outcomes, such as clinical cure; duration of ventilation, hospitalization, and stay in ICU; survival time not on a ventilator; and overall survival [227]. The findings led the authors to suggest that the benefit of linezolid may be related to factors other than bacterial clearance.

According to a meta-analysis, a short fixed-course (7 or 8 days) of antibiotic therapy may be more appropriate than a prolonged course (10 to 15 days) for patients with ventilator-associated pneumonia not caused by non-fermenting gram-negative bacilli [228]. The short course reduced the recurrence rate of ventilator-associated pneumonia caused by multiresistant organisms without adversely affecting other outcomes. Among patients with non-fermenting gram-negative bacilli, recurrence was greater after the short course. The authors confirmed these findings in a follow-up study published in 2015 [229].

PRACTICAL STEPS IN FOLLOWING GUIDELINES TO PREVENT VENTILATOR-ASSOCIATED PNEUMONIA
Elevation of the Head of the Bed
Include the intervention on nursing flow sheets and discuss at multidisciplinary rounds. Encourage respiratory therapy staff to notify nursing staff if the head of the bed is not elevated or empower respiratory therapy staff to place the bed in this position with help of nursing staff. Include the intervention on order sets for initiation and weaning of mechanical ventilation, delivery of tube feedings, and provision of oral care.
Sedative Interruptions and Assessment of Readiness to Extubate
Implement a protocol to lighten sedation daily at an appropriate time to assess for neurologic readiness to extubate. Include precautions to prevent self-extubation, such as monitoring and vigilance, during the trial. Include a sedative interruption strategy in the overall plan to wean the patient from the ventilator; add the strategy to the weaning protocol, if available. Assess compliance each day on multidisciplinary rounds. Consider implementation of a sedation scale, such as the Richmond Agitation Sedation Scale (RASS) scale, to avoid oversedation.
Prophylaxis of Peptic Ulcer Disease
Include intervention as part of the intensive care unit admission order set and ventilation order set. Make application of prophylaxis the default value on the form. Include intervention as an item for discussion on daily multidisciplinary rounds. Empower pharmacy staff to review orders for patients in the intensive care unit to ensure that some form of prophylaxis is in place at all times for patients.
Prophylaxis of Deep Venous Thrombosis
Include intervention as part of the intensive care unit admission order set and ventilation order set. Make application of prophylaxis the default value on the form. Include intervention as an item for discussion on daily multidisciplinary rounds. Empower pharmacy staff to review orders for patients in the intensive care unit to ensure that some form of prophylaxis is in place at all times for patients.
Source: [231] *Table 12*

EVIDENCE-BASED PRACTICE RECOMMENDATION

For patients with ventilator-associated pneumonia, the IDSA and the American Thoracic Society recommend a seven-day course of antimicrobial therapy rather than a longer duration. There exist situations in which a shorter or longer duration of antibiotics may be indicated, depending upon the rate of improvement of clinical, radiologic, and laboratory parameters.

(https://www.idsociety.org/practice-guideline/hap_vap. Last accessed January 28, 2019.)

Strength of Recommendation/Level of Evidence: Strong recommendation, moderate-quality evidence

Role of Inhaled Antibiotic Therapy

For cases of ventilator-associated pneumonia caused by gram-negative bacilli that are susceptible only to aminoglycosides or polymyxins the suggestion is to use both inhaled and systemic antibiotics, rather than systemic antibiotics alone [17]. It is also reasonable to consider adjunctive inhaled antibiotic treatment as a last resort for patients who are not responding to intravenous antibiotics alone, whether the infecting organism is or is not multidrug resistant.

Guideline Adherence and Quality Improvement

Adherence to guidelines for the prevention of ventilator-associated pneumonia is low, with surveys of nurses demonstrating rates of adherence to specific preventive measures ranging from 15% to 50% [187; 230]. Adherence to a bundle of prevention strategies (head-of-bed elevation, oral chlorhexidine gel, sedation holds, and a weaning protocol), with 70% compliance, led to a significant reduction in ventilator-associated pneumonia, from 32 cases per 1,000 ventilator-days to 12 cases per 1,000 ventilator-days [53]. The IHI how-to guide on preventing ventilator-associated pneumonia provides several practical recommendations, and posting compliance with the ventilator bundle in a prominent place in the ICU can encourage and motivate staff (***Table 12***) [231].

The use of physician-led multidisciplinary rounds with team decision making, checklists, and a focus on the ventilator bundle has led to significant reductions in ventilator-associated pneumonia [232; 233; 234]. Moderate strength evidence has shown that the use of audit and feedback and reminder systems improve adherence to an overall ventilator-associated pneumonia bundle as well as reduce infection rates [1]. Education sessions have also led to enhanced knowledge and practice among healthcare professionals caring for intubated patients [235].

The lack of adherence to guideline-directed treatment of pneumonia cases associated with healthcare facilities is evidenced by wide variations in practice. For example, one study showed that more than 100 different antibiotic regimens had been prescribed as initial treatment and that de-escalation therapy was used for only 22% of patients [191]. Adherence rates for treatment of pneumonia associated with healthcare facilities have been reported to be lower than rates of adherence to guidelines for treatment of community-acquired pneumonia. In one survey, guideline-recommended antibiotics were used 9% of the time for healthcare-associated pneumonia compared with 78% of the time for community-associated pneumonia [236]. This lack of adherence was not due to unfamiliarity or disagreement with the guidelines; 71% of the survey respondents said they were aware of the guidelines, and 79% said they agreed with and practiced according to them. It is reasonable to expect that strategies used to enhance adherence to guidelines in the community-acquired pneumonia setting would also be effective in the setting of hospital-acquired and ventilator-associated pneumonia. Such strategies include feedback on performance, reminder systems, standardized order sets, and education emphasizing outcomes and cost-effectiveness.

INTRAVASCULAR DEVICE-RELATED BLOODSTREAM INFECTIONS

Bloodstream infections, such as septicemia and bacteremia, can develop from other types of HAIs or infections at other sites in the body, but about half are caused by intravascular devices, primarily central venous catheters [87]. It has been estimated that 5.3 infections occur per 1,000 catheter-days in the ICU [27; 39; 237]. The number of infections reported to NHSN has increased substantially, with 27,766 reported in 2009–2010, compared with 18,651 reported in 2007–2008, perhaps in part a consequence of improved surveillance [81]. These infections are also the most costly, with a mean cost of more than $50,000 per infection [238]. In recent years, following implementation of the CDC/NHSN national action plan, the incidence of hospital-acquired intravascular bloodstream infection has declined somewhat. The 2016 progress report showed an 11% decrease in central line-associated bloodstream infections between 2015 and 2016 [66].

Risk Factors

There are several types of intravascular catheters, and the risk of intravascular device-related bloodstream infections varies according to type. These catheters include:

- Peripheral venous catheters
- Peripheral arterial catheters
- Midline catheters
- Nontunneled central venous catheters
- Pulmonary artery catheters
- Pressure monitoring system catheters
- Peripherally inserted central venous catheters
- Tunneled central venous catheters
- Totally implantable devices

The nontunneled central venous catheter accounts for the majority of all intravascular device-related bloodstream infections [27]. Peripheral catheters (arterial and venous) are rarely associated with bloodstream infections, and totally implantable catheters are associated with the lowest risk [27].

A systematic review of 200 prospective studies of intravascular device-related bloodstream infections indicated that the level of risk associated with various types of devices can vary substantially depending on whether risk is expressed as the number of infections per 100 intravascular device-days or 1,000 intravascular device-days [239]. The risks associated with peripheral intravenous catheters were much higher when expressed over 1,000 intravascular device-days, pointing to the need for prevention strategies targeted to all types of devices [239].

Other risk factors are the length of time the catheter is in place and factors related to the patient's health status (severity of illness, presence of burns or surgical wounds, compromised immune system, nutritional status) [34].

Transmission and Common Pathogens

Intravascular device-related bloodstream infections are transmitted by both endogenous and exogenous routes. The most common cause of infection related to short-term catheters is migration of skin organisms at the site of insertion, with the organisms traveling along the surface of the catheter and colonization at the catheter tip [27]. Direct contamination of the catheter or catheter hub by contact with hands or contaminated fluids or devices is another cause [27]. Hematogenous seeding from another focus of infection is a less common cause, and contamination of infusion fluid is rare [27].

The most commonly reported pathogens for intravascular device-related bloodstream infections in 2015 were *S. aureus* (23%), *Streptococcus* spp. (12%), coagulase-negative staphylococci (12%), *Enterococcus* spp. (12%), *Candida* spp. (12%), *E. coli* (8%), and *K. pneumonia/oxytoca* (6%) [3].

The percentage of resistant *S. aureus* was stable compared with previous data, with a rate of 55% in 2009–2010 [81]. Among the drug-resistant pathogens with the greatest increases compared with data for 2007–2008 were multidrug-resistant *E. coli* (4% vs. 2%), extended spectrum cephalosporin-resistant *E. coli* (19% vs. 12%), aminoglycoside-resistant *P. aeruginosa* (10% vs 7%), and carbapenems-resistant *A. baumannii* (62% vs. 50%) [81].

Prevention

The CDC guidelines on the prevention of intravascular device-related bloodstream infections were published in 2002 and updated in 2011 [27]. The most recent guidelines emphasize the following points [27]:

- Using maximal sterile barrier precautions during central venous catheter insertion
- Using a >0.5% chlorhexidine skin preparation with alcohol for antisepsis
- Avoiding routine replacement of central venous catheters as a strategy to prevent infection
- Using antiseptic/antibiotic impregnated short-term central venous catheters and chlorhexidine-impregnated sponge dressings if the rate of infection is not decreasing despite adherence to other strategies
- Educating and training healthcare providers who insert and maintain catheters

The CDC guidelines define maximal sterile barrier precautions as the use of a cap, mask, sterile gloves, sterile gown, and a sterile full-body drape during insertion of an intravascular device (level IB) [27]. A sterile sleeve should also be used to protect pulmonary artery catheters during insertion (level IB) [27].

The CDC guidelines recommend use of an antiseptic of 70% alcohol, tincture of iodine, or chlorhexidine gluconate solution with alcohol before insertion of peripheral venous catheters (level IB) and a >0.5% chlorhexidine preparation with alcohol before insertion of central venous catheters or peripheral artery catheters and during dressing changes (category IA) [27]. The guidelines note that chlorhexidine preparations with alcohol have not been compared with povidone iodine in alcohol and thus no recommendation can be made in this regard [27]. In a meta-analysis of eight studies (4,143 catheters, primarily central line catheters),

the chlorhexidine solution was found to reduce the risk for bloodstream infection by 49% [240]. In a subsequent study, use of this solution led to a 1.6% decrease in the rate of bloodstream infection, a 0.23% decrease in the incidence of death, and a cost savings of $113 per catheter used compared with povidone-iodine solutions [241].

Most intravascular device-related bloodstream infections develop at the site of insertion, due to the density of skin flora [27]. Rates of infection vary according to insertion site, with catheters in the internal jugular vein being associated with a greater risk of infection than catheters in the subclavian vein [27; 242; 243]. A 2005 study indicated that the site of insertion was not a risk factor for infection when experienced or trained healthcare workers inserted the catheters [244]. However, such experience will not always be the norm, and the subclavian vein has been recommended by the CDC as the preferred site when possible [27].

Another strategy to prevent infection has been the development of central venous catheters with antimicrobial coatings. These coatings have included a combination of chlorhexidine and silver sulfadiazine and a combination of minocycline and rifampin [245]. Both types of catheters are associated with a significantly lower rate of infection than that associated with standard catheters. When compared with each other, catheters impregnated with minocycline and rifampin were 12 times less likely to cause bloodstream infections than those coated with chlorhexidine and silver sulfadiazine [246]. The chlorhexidine-silver sulfadiazine coating has since been enhanced, and these second-generation catheters have significantly reduced bacterial colonization, with a trend toward fewer bloodstream infections [247]. Each coating adds to the cost of the catheter, and cost-effective analyses are necessary.

On the basis of studies of intravascular device-related bloodstream infections, a bundle consisting of five preventive measures has been recommended:

- Compliance with appropriate hand hygiene
- Use of maximal barrier precautions
- Use of 2% chlorhexidine solution for skin antisepsis
- Selection of optimal site for the catheter, with the subclavian vein as the preferred site for nontunneled catheters
- Daily review of the need for the line, with prompt removal if line is deemed unnecessary

Diagnosis

As defined by the CDC, bloodstream infections fall into two categories: laboratory-confirmed infection and clinical sepsis. Clinical sepsis is no longer used in reporting on adults and children and is restricted to use for neonates and infants [123]. For a diagnosis of laboratory-confirmed bloodstream infection, one of the two following criteria must be met [212].

Criterion 1

Recognized pathogen found on one or more blood cultures *and* organism cultured from blood is not related to an infection at another site

Criterion 2

At least one of the following signs or symptoms:

- Fever (>38 degrees Centigrade)
- Chills (with no other recognized cause)
- Hypotension (with no other recognized cause)

and signs and symptoms and positive laboratory results are not related to an infection at another site *and* common skin contaminant (e.g., diphtheroids, *Bacillus* spp., *Propionibacterium* spp., coagulase-negative staphylococci, viridans group streptococcus, *Aerococcus* spp., or *Micrococcus* spp.) is cultured from two or more blood cultures drawn on separate occasions. Criterion elements must occur within a timeframe that does not exceed a gap of one calendar day [212].

There are several approaches to diagnosing an intravascular device-related bloodstream infection. A meta-analysis of 51 studies published between 1966 and 2004 was designed to identify which method was the most accurate [248]. The studies had involved the eight most commonly

used diagnostic methods: culture (qualitative, semiquantitative, or quantitative) of a catheter segment; culture (qualitative or quantitative) of blood obtained through the catheter; paired quantitative cultures (blood obtained through the catheter as well as from a peripheral site); differential time to positivity (monitoring of cultures of blood obtained through the catheter and from a peripheral site); and acridine orange leukocyte cytospin. The paired cultures method was the most accurate, with a pooled specificity of 99%, followed by qualitative culture of blood drawn through the catheter and acridine orange leukocyte cytospin [248].

Treatment

The management of an intravascular device-related bloodstream infection does not always include removal of the device. Authors of consensus-based treatment guidelines advise that the decision to remove a tunneled catheter or implanted device suspected to be the source of bacteremia or fungemia should be based on the following factors [249]:

- Underlying health status of the patient
- Type of catheter
- Strength of the evidence that the catheter is the source of the infection
- Responsible pathogens
- Presence of local or systemic complications

Nontunneled central venous catheters should be removed in most cases of bacteremia or fungemia [249]. Antibiotic therapy alone has resolved 80% of infections caused by coagulase-negative staphylococcal bacteria, but in cases of infection with *S. aureus* or *Candida*, infection has persisted when the catheter has been maintained [249; 250].

One strategy was developed in an attempt to retain the catheter. With so-called antibiotic lock therapy, antibiotics are instilled through the catheter after injection of an anticoagulant, locking a high concentration of the antibiotic in the lumen [250]. This approach is used in combination with systemic antibiotic therapy, and the antibiotics used have included vancomycin, cefazolin, and clindamycin. Fluconazole and amphotericin B have been used occasionally for infection with *Candida* spp., and another flush solution (low concentrations of minocycline and EDTA) has demonstrated activity against staphylococci, gram-negative bacilli, and *Candida* spp. [250]. Early empiric antifungal therapy is important if infection with *Candida* is suspected, as delayed treatment has been associated with higher mortality [251].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Centers for Disease Control and Prevention recommends using a chlorhexidine/silver sulfadiazine- or minocycline/rifampin-impregnated central venous catheter in patients whose catheter is expected to remain in place longer than five days if, after successful implementation of a comprehensive strategy to reduce rates, the central line-associated bloodstream infection rate is not decreasing.

(https://www.cdc.gov/hai/pdfs/bsi-guidelines-2011.pdf. Last accessed January 28, 2019.)

Strength of Recommendation/Level of Evidence: IA (Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies)

The guidelines for treatment of intravascular device-related bloodstream infection suggest antimicrobial selection according to the known or suspected pathogen (***Table 13***) [249]. Empiric antibiotic therapy should be selected according to clinical features and context, with due consideration for the local prevalence of resistant pathogens. Vancomycin is recommended as initial treatment for coagulase-negative staphylococci and for *S. aureus* until the sensitivity to methicillin is determined, at which point treatment should be changed to semisynthetic penicillin if the identified pathogen is sensitive [249]. Vancomycin should not be used as a front-line treatment for infections with methicillin-sensitive *S. aureus*.

If fever or other signs of infection persist after removal of the catheter, the patient should be evaluated for complications such as septic phlebitis, distant abscess, and endocarditis. Bacterial endocarditis has been found in 25% of patients with intravascular device-related bloodstream infection caused by *S. aureus* [250]. The findings

TREATMENT OF INTRAVASCULAR DEVICE-RELATED BLOODSTREAM INFECTIONS IN ADULTS	
Pathogen	**Preferred Antimicrobial Agent**
Staphylococcus aureus	
Sensitive to methicillin	Penicillinase-resistant penicillin
Resistant to methicillin	Vancomycin
Resistant to vancomycin	Daptomycin or linezolid
Coagulase-negative staphylococci	
Sensitive to methicillin	Penicillinase-resistant penicillin
Resistant to methicillin	Vancomycin
Enterococcus spp.	
Sensitive to ampicillin	Ampicillin or (ampicillin or penicillin) + aminoglycoside
Resistant to ampicillin/sensitive to vancomycin	Vancomycin + aminoglycoside
Resistant to ampicillin/resistant to vancomycin	Linezolid or daptomycin
Escherichia coli and *Klebsiella* spp.	
ESBL negative	Third-generation cephalosporin
ESBL positive	Carbapenem
Enterobacter spp. and *Serratia marcescens*	Carbapenem
Acinetobacter baumannii	Ampicillin/sulbactam or carbapenem
Pseudomonas aeruginosa	Fourth-generation cephalosporin or carbapenem or antipseudomonal beta-lactam plus aminoglycoside
Burkholderia cepacia	SMZ-TMP or carbapenem
Candida albicans or *Candida* spp.	Echinocandin or fluconazole
Corynebacterium spp.	Vancomycin
Mycobacterium spp.	Susceptibility varies by species
SMZ-TMP: sulfamethoxazole/trimethoprim.	
Source: [249]	*Table 13*

of one study suggested that patients with MRSA bacteremia and underlying chronic liver disease were at higher risk for endocarditis [252].

Guideline Adherence and Quality Improvement

As is the case with guidelines for other HAIs, adherence to prevention guidelines is suboptimal. A survey of more than 500 hospitals showed that, while adherence to the two most strongly recommended prevention strategies—maximal sterile barrier precautions and antisepsis with chlorhexidine gluconate—was good at VA hospitals (84% and 91%, respectively), the rates were lower at non-VA hospitals (71% and 69%) [253]. Adherence to a combination of maximal sterile barrier precautions, chlorhexidine gluconate, and avoidance of central line changes was even lower: 62% and 44%, respectively [253]. In another study, central venous catheters were routinely changed to prevent infection in about 15% of hospitals [254].

Implementing a prevention bundle has significantly reduced intravascular device-related bloodstream infections: the decrease was from 5.9 per 1,000 catheter-days to 3.1 per 1,000 in one study and from 7.7 per 1,000 catheter-days to 1.4 per 1,000 in another [56; 232]. A how-to guide developed by the IHI provides practical suggestions for implementing the bundle (***Table 14***) [255]. A checklist should be developed for use when inserting a catheter to ensure adherence to all prevention strategies [34].

PRACTICAL STEPS IN FOLLOWING GUIDELINES TO PREVENT INTRAVASCULAR DEVICE-RELATED BLOODSTREAM INFECTIONS
Hand Hygiene
Include hand hygiene as part of the checklist for placement of central lines. Keep soap/alcohol-based hand hygiene dispensers prominently placed, and make universal precautions equipment, such as gloves, available only near hand sanitation equipment. Post reminder signs at the entry and exits to patient rooms. Initiate a campaign using posters including photos of celebrated hospital physicians/employees recommending hand hygiene. Create an environment in which reminding each other about hand hygiene is encouraged.
Maximal Barrier Precautions
Include maximal barrier precautions as part of the checklist for placement of central lines. Keep equipment stocked in a cart for central line placement to avoid the difficulty of finding necessary equipment to institute maximal barrier precautions. If a full-size drape is not available, apply two drapes to cover the patient or consult with the operating room staff to determine how to obtain full-size sterile drapes, as they are used routinely in surgical settings.
Chlorhexidine Skin Antisepsis
Include chlorhexidine antisepsis as part of the checklist for placement of central lines. Include chlorhexidine antisepsis kits in carts or grab bags storing central line equipment. (Many prepared central line kits include povidone-iodine kits, and these must be avoided.) Ensure that the solution dries completely before attempting to insert the central line.
Selection of Optimal Insertion Site
Include optimal site selection as part of the checklist for placement of central lines, with room to note appropriate contraindications (e.g., bleeding risks).
Daily Review of Need for Central Line
Include daily review of the need for the central line as part of multidisciplinary rounds. Include assessment for removal of central lines as part of daily goal sheets. Record time and date of line placement for record-keeping purposes and evaluation by staff to aid in decision making.
Source: [255] *Table 14*

Adherence to appropriate postinsertion care has been the focus of some studies. In one study, there were breaches in postinsertion care in 45% of cases [256]. The primary breaches were non-intact dressing (158 breaches per 1,000 catheter-days) and incorrectly placed caps and taps (156 breaches per 1,000 catheter-days) [256]. The rate of intravascular device-related bloodstream infection during the study period was 5.5 per 1,000 catheter-days [256]. In another study, nursing staff used a postinsertion care bundle that consisted of the following: daily inspection of the insertion site; site care if the dressing was wet, soiled, or had not been changed for 7 days; documentation of ongoing need for the catheter; proper application of a chlorhexidine gluconate-impregnated sponge at the insertion site; appropriate hand hygiene before handling the intravenous system; and application of an alcohol scrub to the infusion hub for 15 seconds before each entry [257]. Adherence to this bundle led to a significant decrease in intravascular device-related bloodstream infections, from 5.7 per 1,000 catheter-days to 1.1 per 1,000 catheter-days [257].

The availability of policies regarding prevention strategies is also lacking. Although 80% of 25 ICUs (10 hospitals) had written policies for insertion of central venous catheters, only 28% had a policy requiring maximal sterile barrier precautions, and 36% and 60% of the units required hand hygiene before accessing a central venous catheter or treating the exit site, respectively [254]. A formal educational program on catheter insertion was in place at 52% of the units [254]. Education, in the form of self-study modules with pretest and post-test, along with didactic lectures and integration of evidence-based guidelines have been associated with increases in adherence to recommended practices and decreases in bloodstream infections [258].

A systematic review demonstrated moderate strength of evidence for audit and feedback and provider reminder systems, along with base strategies [1].

CLOSTRIDIUM DIFFICILE INFECTIONS

C. difficile is the most common cause of infectious diarrhea among adults in healthcare settings [32]. Colonization with the inactive spore is much more prevalent in the healthcare setting than in the community. Studies show that the rate of asymptomatic colonization is approximately 2% to 3% in the community, 3% to 26% among adult inpatients in acute care hospitals, and 5% to 7% among elderly patients in long-term care facilities [32]. In contrast, the prevalence of *C. difficile* in the stool of asymptomatic adults without recent healthcare facility exposure is <2% [32]. Although colonization with *C. difficile* is relatively common among patients in healthcare facilities, clinical illness emerges only when there is production of toxins (A and B) that cause inflammation, secretion of mucous and fluid, and damage to the mucosa, resulting in diarrhea or colitis [259]. Disease can further progress to toxic megacolon, sepsis with or without intestinal perforation, and death [260; 261].

The incidence of *C. difficile*-associated diarrhea has increased dramatically in recent decades. The incidence more than tripled between the 1990s and 2005 (from 30 to 40 cases per 100,000 individuals to 131 per 100,000) [262]. During this same time, some bacterial strains have become more virulent and perhaps more resistant [263]. As with other HAIs, *C. difficile* infection in the healthcare setting has been associated with increased length of stays, increased mortality, and higher costs [129; 264; 265; 266; 267].

Beginning in 2009, the CDC has conducted ongoing surveillance of *C. difficile* infection in the community and healthcare environment through the Emerging Infections Program, a sentinel network of 10 reporting sites in 35 counties of 10 states. Data from 2015 showed a total of 17,340 *C. difficile* infections reported within this population group of 11,682,000 persons, for a total annual rate of 149 incident infections per 100,000 population [192]. The rate of *C. difficile* HAI was 83 cases per 100,000, compared with the community-based incidence of 66 per 100,000. The risk increases with age, and the elderly are especially vulnerable. Among persons older than 65 years of age the rate of HAI caused by this pathogen was 378 cases per 100,000 patients [192]. Serial surveys show that *C. difficile* accounts for 15% of all HAIs, and the incidence has remained stable during the period 2011 to 2015. When extrapolated to the nation at large, CDC data analysis shows that *C. difficile* causes more than 450,000 incident infections in the United States each year and is associated with approximately 29,000 deaths [192]. The 2016 HAI progress report showed a more positive trend, with about a 8% decrease in *C. difficile* infections reported from acute care hospitals between 2015 and 2016 [66].

Risk Factors

The primary risk factors for infection with *C. difficile* are antibiotic use, older age, and hospitalization [32]. Exposure to antibiotic agents is the most modifiable risk factor, an association reported in more than 96% of hospitalized patients in one study [268]. Antibiotics increase the risk by suppressing or altering normal bowel microflora, thereby facilitating overgrowth of relatively dormant *C. difficile* organisms. Many antibiotics have been implicated, but fluoroquinolones, cephalosporins, carbapenems, and clindamycin have been found to confer high risk [32]. The likelihood of infection increases with longer hospitalizations, with a 15% to 45% risk of colonization among patients hospitalized for one to three weeks [268].

Transmission

C. difficile is an exogenous infection that is transmitted person-to-person through the fecal-oral route and possibly via contact with contaminated environmental surfaces (e.g., bedding, commodes, bath tubs).

Prevention and Control

Guidelines developed by SHEA/IDSA in 2010, and updated in 2018, offer recommendations for prevention, diagnosis, and management of *C. difficile* [32]. Control measures include restriction of antibiotic use; isolation precautions for healthcare workers, patients, and visitors; and environmental cleaning and disinfection (***Table 15***) [32]. The guidelines note that the use of antibiotics should

SHEA/IDSA GUIDELINES FOR INFECTION CONTROL MEASURES FOR *CLOSTRIDIUM DIFFICILE*

Restriction of Antibiotic Use

- Minimize the frequency and duration of antimicrobial therapy and the number of antimicrobial agents prescribed (level II, A).
- Implement an antimicrobial stewardship program (level II, A). Antimicrobials to be targeted should be based on the local epidemiology and the C. *difficile* strains present, but restricting the use of fluoroquinolones, cephalosporin and clindamycin (except for surgical antibiotic prophylaxis) may be particularly useful (level III, C).

Measures for Healthcare Workers, Patients, and Visitors

- Healthcare workers and visitors must use gloves (level I, A) and gowns (level III, B) on entering the room of a patient with C. *difficile* infection.
- Emphasize compliance with appropriate hand hygiene (level II, A).
- Instruct visitors and healthcare workers to wash hands with soap (or antimicrobial soap) and water after caring for or contacting patients with C. *difficile* infection (level III, B).
- Use a private room with contact precautions for patients with C. *difficile* infection (level III, B); cohort patients if single rooms are not available, and provide a dedicated commode for each patient (level III, C).
- Maintain contact precautions until 48 hours after diarrhea has resolved (level III, C).

Environmental Cleaning and Disinfection

- Identify and remove environmental sources of C. *difficile*, to reduce the incidence of infection (level II, B).
- Use chlorine-containing cleaning agents or other sporicidal agents to address environmental contamination in areas associated with increased rates of C. *difficile* infection (level II, B).

Source: [32] *Table 15*

be minimized and that an antibiotic stewardship program should be developed and implemented by all hospitals [32]. Appropriate hand hygiene is essential, and soap and water should be used rather than alcohol-based handrubs, as alcohol is not effective at killing C. *difficile* spores [32]. Gowns, gloves, and contact precautions for the duration of diarrhea are also recommended. The guidelines suggest that removing environmental sources of C. *difficile*, such as replacing rectal thermometers with disposable ones, can help reduce the incidence of C. *difficile* infection. The guidelines also note that the following are not recommended: routine environmental screening for C. *difficile* (level III, C); routine identification of asymptomatic carriers for infection control purposes (level III, A); and use of probiotics to prevent infection (level I, B) [32].

Diagnosis

Infection with C. *difficile* is diagnosed on the basis of clinical findings and the results of laboratory testing [32]. C. *difficile* infection is defined as (1) the presence of diarrhea (passage of three or more unformed stools in up to 24 consecutive hours) and (2) positive results on stool testing for the presence of toxigenic C. *difficile* or its toxins or findings of pseudomembranous colitis on colonoscopy or histopathologic evaluation [32]. Diarrhea may be absent in up to 20% of patients with fulminant colitis or postoperative ileus [268]. Other symptoms include fever, nausea, vomiting, abdominal pain or tenderness, and loss of appetite, but these symptoms are found in about half of patients with the infection [32; 259].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The IDSA and the SHEA assert that patients with unexplained and new-onset of three or more unformed stools in 24 hours are the preferred target population for testing for C. *difficile* infection.

(https://academic.oup.com/cid/article/66/7/e1/4855916. Last accessed January 28, 2019.)

Strength of Recommendation/Level of Evidence: Weak recommendation, very low quality of evidence

Diagnostic stool testing should be done only on unformed stool (level II, B), and testing for asymptomatic patients is not useful (level III, B) [32]. Repeat testing during the same episode of diarrhea is discouraged, as it does not provide clinically useful information (level II, B) [32].

SHEA/IDSA GUIDELINES FOR THE TREATMENT OF *CLOSTRIDIUM DIFFICILE* INFECTION ACCORDING TO SEVERITY OF DISEASE	
Severity of Disease	**Preferred Treatment**
Mild to severe (WBC ≤15,000)	Vancomycin 125 mg orally four times daily for 10 days OR fidaxomicin 200 mg twice daily for 10 days (Strong/High) Alternative: Metronidazole 500 mg three times daily orally
Severe (WBC >15,000, serum creatinine >1.5 mg/dL)	Vancomycin PO 125 mg, four times per day for 10 days OR fidaxomicin 200 mg twice daily for 10 days (Strong/High)
Fulminant (hypotension, ileus, or megacolon)	Vancomycin 500 mg, four times per day by mouth or nasogastric tube If ileus, add rectal administration of vancomycin and intravenous metronidazole 500 mg every 8 hours[a] (Strong/Moderate)
Recurrent	
First recurrence	Vancomycin PO 125 mg four times daily for 10 days if metronidazole was used for initial treatment; fidaxomicin 200 mg twice daily for 10 days if vancomycin was used initially
Second recurrence or more	Vancomycin in a prolonged tapered and pulsed regimen OR vancomycin standard 10-day regimen followed by rifaximin 400 mg three times daily for 20 days
[a]If ileus is present, vancomycin may be given per rectum as a retention enema, at a dose of 500 mg/100 mL normal saline, every 6 hours.	
Source: [32]	*Table 16*

Several diagnostic tests are available to detect *C. difficile*, and they vary in terms of sensitivity, specificity, and turnaround times. Stool culture is the most sensitive test, but it is not clinically practical because of the slow turnaround time [32]. The sensitivity of cell cytotoxicity assay has been reported to range from 67% to 100%, whereas enzyme immunoassay testing for toxins A and B has a sensitivity ranging from 63% to 94% and a specificity of 75% to 100% [32]. Enzyme immunoassay testing is rapid and less expensive than other tests but it is a suboptimal choice compared with cell cytotoxicity assay (level II, B) [32]. The SHEA/IDSA guidelines note that polymerase chain reaction testing appears to be rapid, sensitive, and specific, but more data on its usefulness are needed before it can be recommended for routine use (level II, B) [32].

Treatment

The most important step in treating *C. difficile*-associated diarrhea is to discontinue the inciting antibiotic as soon as possible [32]. This approach alone will lead to resolution of diarrhea in approximately 15% to 25% of patients with mild infection [259; 268]. Antibiotic treatment of the diarrhea should not begin until the culture or toxin assay results are known, as approximately 30% of hospitalized patients with antibiotic-associated diarrhea will have *C. difficile* infection [32]. However, if severe or complicated *C. difficile* infection is suspected, empirical treatment should be started as soon as the diagnosis is suspected (level III, C) [32]. The SHEA/IDSA guidelines recommend either vancomycin or fidaxomicin over metronidazole for an initial episode of *C. difficile* gastrointestinal infection, whether mild or moderately severe. The dosage is vancomycin 125 mg orally four times per day or fidaxomicin 200 mg twice daily for 10 days [32]. ***Table 16*** outlines the guideline recommendations for treatment according to severity of illness [32].

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the IDSA and the SHEA, either vancomycin or fidaxomicin is recommended over metronidazole for an initial episode of C. *difficile* infection. The dosage is vancomycin 125 mg orally four times per day or fidaxomicin 200 mg twice daily for 10 days.

(https://academic.oup.com/cid/article/66/7/e1/4855916. Last accessed January 28, 2019.)

Strength of Recommendation/Level of Evidence: Strong recommendation, high quality of evidence

Surgical management may be necessary for severe, fulminant cases of C. *difficile* colitis. In such cases, subtotal colectomy with preservation of the rectum is advisable; alternatively, a diverting loop ileostomy with colonic lavage followed by antegrade vancomycin flushes may lead to improved outcomes [32].

In addition to infection-directed antibiotics, treatment of C. *difficile* infection also includes fluid replacement, and electrolyte normalization [269]. The use of antiperistaltic agents should be avoided, as they may obscure symptoms, lead to retained toxin, and precipitate toxic megacolon (level III, C) [32]. The use of probiotics has been suggested as an adjunct to antibiotic treatment, but a systematic review found insufficient data to support probiotics as adjunct therapy and no evidence to support its use alone [270].

INFECTION CONTROL

The development of formal infection control programs in hospitals and other healthcare facilities was spurred by the Joint Commission accreditation standards for infection control, published in 1976. According to the standards, accredited facilities must have a program for the surveillance, prevention, and control of HAIs [87]. In 1974, the CDC designed the Study on the Efficacy of Nosocomial Infection Control project to determine if infection surveillance and infection control programs could reduce the number of HAIs [271]. The nationwide study evaluated rates of HAIs in hospitals before and after the implementation of infection control programs; the researchers noted that programs with four components were associated with a one-third reduction in the rate of HAIs: an effective hospital epidemiologist, one infection control practitioner for every 250 beds, active surveillance mechanisms, and ongoing control efforts [272]. With the increased focus on prevention of HAIs, infection control professionals have come to be known as infection preventionists [273].

An infection control program is usually overseen by a committee chaired by an infectious disease physician and consisting of staff representing departments throughout the facility, such as nursing, pharmacy, surgery, clinical microbiology, central sterilization services, housekeeping, maintenance, food services, and laundry services. Among the responsibilities of an infection control program are to:

- Conduct surveillance of HAIs
- Develop policies regarding prevention and control, such as hand hygiene and precautions
- Ensure adherence to standards for environmental services
- Establish a program to monitor and evaluate antimicrobial therapy
- Provide education to healthcare workers about adherence to infection control policies
- Develop guidelines for outbreak preparedness

The policies and procedures in each of these areas, as well as guidelines for adherence, should be documented in an infection control manual.

All physicians and staff within a healthcare facility have responsibility for helping to advance infection control goals. Physicians should assume the following responsibilities [15]:

- Protect their patients from other infected patients or staff
- Comply with the practices approved by the infection control committee

- Obtain appropriate microbiologic specimens when infection is suspected or present
- Notify the infection control committee about confirmed cases of HAIs
- Comply with the institution's recommendations regarding the use of antibiotics
- Educate patients, visitors, and staff about techniques to prevent the transmission of infection.

As direct providers of care in a healthcare facility, the nursing staff plays a substantial role in carrying out infection control practices. Nursing administrators should promote the development and enhancement of nursing techniques, review nursing policies regarding aseptic techniques, and offer educational training programs on best practices [15]. Nurses on patient care units have the following responsibilities [15]:

- Comply with established infection control practices
- Monitor aseptic techniques, including handwashing and use of isolation precautions
- Report evidence of infection immediately to the attending physician
- Initiate patient isolation and order culture specimens when infection is suspected and a physician is not immediately available
- Limit patient exposure to infections from others (visitors, hospital staff, other patients, or equipment used for diagnosis or treatment)

Community hospitals have had success with participating in an infection control network. In 12 community hospitals in North Carolina and Virginia that joined such a network (the Duke Infection Control Outreach Network), there were significant decreases in the annual rates of healthcare-associated bloodstream infections, infection and colonization with MRSA, ventilator-associated pneumonia, and exposure of staff to bloodborne pathogens [274]. After network participation for five years, the average decrease in the number of device-related infections and HAIs due to MRSA decreased by an average of 50% [275]. The cost savings was approximately $100,000 per hospital, and in total, an estimated 52 to 105 deaths related to ventilator-associated pneumonia or intravascular device-related infection were prevented [275].

Most prevention and control policies focus on general measures, such as surveillance; adherence to guidelines for hand hygiene, influenza vaccination, precautions and isolation techniques, management of drug-resistant micro-organisms, and standards for environmental services; and education of healthcare workers as well as patients and families.

SURVEILLANCE

Surveillance is an essential component of an infection control program. The infection control team has traditionally conducted surveillance through open communication with the nursing staff and physicians and meticulous review of patient records and microbiology results. The infections most commonly targeted for surveillance are those associated with substantial costs in terms of morbidity, mortality, or economics, and those difficult to treat. In addition, infections with a predilection for epidemics are a focus. The data gathered should be evaluated in relation to regional and national norms, and temporal trends should also be noted. Continuing analysis of the data allows the infection control team to evaluate the efficacy of programs designed to enhance compliance with hospital-wide strategies to prevent HAIs.

HAND HYGIENE

Hand hygiene is the most important preventive measure in hospitals, and the Joint Commission mandates that hospitals and other healthcare facilities comply with the Level I recommendations in the CDC guidelines for hand hygiene [26]. The CDC guidelines state the specific indications for washing hands, the recommended hand hygiene techniques, and recommendations about fingernails and the use of gloves (***Table 17***) [26].

SUMMARY OF CDC RECOMMENDATIONS FOR HAND HYGIENE
Indications for Hand Hygiene
Wash hands with nonantimicrobial or antimicrobial soap and water when they are visibly dirty, contaminated, or soiled. If hands are not visibly soiled, use an alcohol-based handrub for routinely decontaminating hands.
Specific Indications
Wash hands before patient contact and before putting on gloves for insertion of invasive devices that do not require surgery (e.g., urinary catheters or intravascular devices). Wash hands after: • Contact with a patient's skin • Contact with body fluids or excretions, nonintact skin, or wound dressings • Removing gloves
Recommended Handrub Technique
Apply to palm of one hand, rub hands together, covering all surfaces until dry.
Recommended Handwashing Techniques
• Wet hands with water, apply soap, and rub hands together for at least 15 seconds. • Rinse and dry with disposable towel. • Use towel to turn off faucet.
Fingernails and Artificial Nails
Keep tips of natural nails to a length of ¼ inch. Do not wear artificial nails during direct contact with high-risk patients (e.g., patients in intensive care unit or operating room).
Use of Gloves
Use gloves when there is potential for contact with blood or other potentially infectious materials, mucous membranes, or nonintact skin. Change gloves after use for each patient.
Source: [26] *Table 17*

The guidelines also provide recommendations for surgical hand antisepsis, selection of hand-hygiene agents, skin care, educational and motivational programs for healthcare workers, and administrative measures.

Despite the simplicity of the intervention, its substantial impact, and wide dissemination of the guidelines, compliance with recommended hand hygiene has ranged from 16% to 81%, with an average of 30% to 50% [26; 39; 40; 41; 42] A 2010 systematic review of studies on compliance with hand-hygiene guidelines in hospital care found an overall median compliance rate of 40%, with lower rates in intensive care units (30% to 40%) than in other settings (50% to 60%), lower rates among physicians than among nurses (32% and 49%, respectively), and lower rates before (21%) rather than after (47%) patient contact [276]. Among the reasons given for the lack of compliance are inconvenience, understaffing, and damage to skin [26; 40; 87]. The development of effective alcohol-based handrub solutions addresses these concerns, and studies have demonstrated that these solutions, as well as performance feedback and accessibility of materials, have increased compliance [41; 276; 277; 278]. The CDC guidelines recommend the use of handrub solutions on the basis of several advantages, including [26]:

- Better efficacy against both gram-negative and gram-positive bacteria, mycobacteria, fungi, and viruses than either soap and water or antimicrobial soaps (such as chlorhexidine)
- More rapid disinfection than other hand-hygiene techniques
- Less damaging to skin
- Time savings (18 minutes compared with 56 minutes per 8-hour shift)

The guidelines suggest that healthcare facilities promote compliance by making the handrub solution available in dispensers in convenient locations (such as the entrance to patients' room or at the bedside) and provide individual pocket-sized containers [26]. The handrub solution may be used in all clinical situations except for when hands are visibly dirty or are contaminated with blood or body fluids. In such instances, soap (either antimicrobial or nonantimicrobial) and water must be used.

However, there are many other reasons for lack of adherence to appropriate hand hygiene, including denial about risks, forgetfulness, and belief that gloves provide sufficient protection [26; 40]. These reasons demand education for healthcare professionals to emphasize the importance of hand hygiene. Also necessary is research to determine which interventions are most likely to improve hand-hygiene practices, as no studies have demonstrated the superiority of any intervention [279]. Single interventions are unlikely to be effective [279].

Several single-institution studies have demonstrated that appropriate hand hygiene reduces overall rates of HAIs, including those caused by MRSA and VRE [42; 277; 278]. However, rigorous evidence linking hand hygiene alone with the prevention of HAIs is lacking, making it difficult to evaluate the true impact of hand hygiene alone in reducing HAIs [56]. One challenge in evaluating the impact of hand hygiene is that a variety of methodologies have been used to assess compliance (surveys, direct observation, measurement of product use), each with its own advantages and disadvantages [280]. Measuring the effect of appropriate hand hygiene alone is also difficult because the intervention is often one aspect of a multicomponent strategy to reduce infection [42]. Lastly, as noted previously, the development of HAIs is complex, with many contributing factors. Although more research is needed to assess the individual impact of appropriate hand hygiene, this basic prevention measure is the essential foundation of an effective infection control strategy and an element of every infection control guideline.

INFLUENZA VACCINATION

The vaccination status of healthcare workers has been found to have a direct effect on transmission of the influenza virus to patients. Outbreaks of influenza in healthcare settings have been associated with low rates of vaccination among healthcare workers, and lower rates of nosocomial influenza have been related to higher vaccination rates among healthcare workers [281; 282]. Because of these findings, several organizations have addressed the need for vaccination. The CDC and the Advisory Committee on Immunization Practices recommends annual influenza vaccination for all healthcare workers [283]. CDC guidelines include four Level I recommendations to help increase rates of vaccination [284]:

- Offer influenza vaccine annually to all eligible healthcare workers.
- Provide influenza vaccination to healthcare workers at the work site and at no cost as one component of employee health programs. Use strategies that have been demonstrated to increase influenza vaccine acceptance, including vaccination clinics, mobile carts, vaccination access during all work shifts, and modeling and support by institutional leaders.
- Monitor influenza vaccination coverage and declination of healthcare workers at regular intervals during influenza season and provide feedback of ward-, unit-, and specialty-specific rates to staff and administration.
- Educate healthcare workers about the benefits of influenza vaccination and the potential health consequences of influenza illness for themselves and their patients, the epidemiology and modes of transmission, diagnosis, treatment, and nonvaccine infection control strategies, in accordance with their level of responsibility in preventing healthcare-associated influenza.

In addition, the Joint Commission began including vaccination programs in its accreditation standards in 2007 [285].

Despite these guidelines, not all healthcare personnel are being vaccinated for influenza. During the 2017–2018 influenza season, vaccination coverage among healthcare personnel was 78.4%, similar to the 78.6% coverage observed during the 2016–2017 season [283]. By occupation, vaccination rates were highest among physicians (96.1%), pharmacists (92.2%), and nurse practitioners (87.8%). Vaccination coverage was higher among personnel working in hospitals (91.9%) than for those working in long-term care facilities (67.4%) [283].

Healthcare workers have given many reasons for not being vaccinated, and the reasons vary among categories of healthcare professionals [287]. Across all categories, shortage of the vaccine is the primary reason for not being vaccinated; other reasons include concern about side effects, inconvenience, and forgetfulness [287]. Many reasons for receiving the vaccine have also been identified, including [283; 287]:

- Fear of getting influenza
- Fear of transmitting influenza to patients
- Belief that the vaccine is safe
- Belief that the vaccine is effective
- Convenience

The CDC reports that vaccination rates are highest among healthcare personnel whose employers require (85.8%) or recommend (68.4%) that they be vaccinated, compared with personnel whose employers who do not recommend or have a policy recommending vaccination (43.4%) [283]. Efforts to increase the vaccination rate among healthcare workers are ongoing. The APIC issued a position paper acknowledging the problem and highlighting suggestions to improve vaccination rates [288].

PRECAUTIONS AND ISOLATION TECHNIQUES

The CDC guidelines for isolation precautions in hospitals, updated in 2007, synthesize a variety of recommendations for precautions based on the type of infection and the route of transmission [22]. As defined by the CDC, Standard Precautions represent measures that should be followed for all patients in a healthcare facility, regardless of diagnosis or infection status. Standard Precautions apply to blood; all body fluids, secretions, and excretions except sweat, regardless of whether or not they contain visible blood; nonintact skin; and mucous membranes [22]. For patients who are known to have or are highly suspected to have colonization or infection, Contact Precautions should be followed. This type of precaution is designed to reduce exogenous transmission of micro-organisms through direct or indirect contact from healthcare workers or other patients. Airborne Precautions are used for patients who have or are highly suspected of having infection that is spread by airborne droplet nuclei, such as tuberculosis, measles, or varicella. Droplet Precautions target infections that are transmitted through larger droplets generated through talking, sneezing, or coughing, such as invasive *Haemophilus influenzae* type b disease, diphtheria (pharyngeal), pertussis, group A streptococcal pharyngitis, influenza, mumps, and rubella [22].

The CDC guidelines include descriptions of all the elements involved in the four types of precautions, including hand hygiene; the use of personal protection equipment (gloves, gown, and face protection); handling of patient-care equipment; environmental services and occupational health; and placement of the patient. A new element of Standard Precautions added to the 2007 guidelines is respiratory hygiene/cough etiquette [22]. Recommendations in this area address the importance of educating healthcare workers about adherence to measures to control the transmission of respiratory pathogens, especially during seasonal outbreaks of viral respiratory tract infections. In addition, the guidelines state that efforts should be made

SUMMARY OF STRATEGIES FOR PREVENTION OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* AND OTHER DRUG-RESISTANT MICRO-ORGANISMS
Conduct MRSA risk assessment and implement an MRSA monitoring program[a]
System to identify patients with MRSA colonization or infection
Feedback of information to clinicians[a]
Education
Hand hygiene
Environmental decontamination
Dedicated equipment
Contact precautions
Masks[b]
Cohorting[c]
Antimicrobial stewardship
Active surveillance testing[c]
Decolonization therapy[d]
Compliance with hand hygiene
Compliance with cleaning protocols[e]
Compliance with Contact Precautions[a]
[a]Not discussed in the guidelines by the Society for Healthcare Epidemiology of America (SHEA). [b]Recommended in SHEA guidelines but not in guidelines by the Centers for Disease Control and Prevention (CDC). [c]Recommended by the CDC only for specific subpopulations or circumstances. [d]Recommended by both CDC and SHEA only for specific subpopulations or circumstances. [e]Not discussed in the SHEA guidelines and recommended by the CDC only for specific subpopulations or circumstances.
Source: [22; 30; 38; 72] *Table 18*

to contain respiratory secretions in patients and other individuals who have signs and symptoms of a respiratory infection, beginning at the point of initial encounter in a healthcare setting. Signs should be posted to instruct patients and visitors with symptoms of respiratory infection to cover their mouths/noses when coughing or sneezing, to use and dispose of tissues, and to perform hand hygiene after contact with respiratory secretions. Masks should be offered to coughing patients and other individuals with symptoms, and such persons should be encouraged to maintain an ideal distance of at least 3 feet from others in common waiting areas.

PREVENTION OF ANTIBIOTIC-RESISTANT INFECTION

Managing the problem of emerging drug-resistant microbial infection is a crucial aspect of an institution's infection control program. Any use of an antibiotic exerts selective pressure that can lead to the development of drug-resistance. The growing prevalence of antibiotic resistance is a serious problem for hospitals and for public health. Studies show that treatment indication, choice of antibiotic, or duration of therapy can be incorrect in up to 30% of instances in which antibiotics are prescribed. The national effort to promote antibiotic stewardship is intended to slow the development of resistance, help prevent untreatable infection, and extend the useful lifetime of the most urgently needed antibiotics [14].

Updated guidelines for the management of MRSA and other drug-resistant micro-organisms were published by the CDC in 2006 and the SHEA in 2014; the guidelines focus on the prevention of drug-resistant infections and the judicious use of antibiotics (antimicrobial stewardship) (***Table 18***) [22; 30; 38; 72].

The CDC's Be Antibiotics Aware program provides fact sheets, pocket cards, posters, and slide sets for a variety of patient populations, including hospitalized adults, individuals to have surgery, patients receiving dialysis, long-term care patients, and hospitalized children [319]. All of the resources are available on the CDC website at https://www.cdc.gov/antibiotic-use/week/toolkit.html.

The IHI defines five components of a program to reduce the risk of infection with drug-resistant micro-organisms [289]:

- Hand hygiene
- Decontamination of the environment and equipment
- Active surveillance
- Contact precautions for infected and colonized patients
- Bundled interventions to prevent intravascular device-related bloodstream infections and ventilator-associated pneumonia

Universal surveillance of MRSA at hospital admission has been suggested as a measure to help prevent the transmission of this infection in the healthcare setting; however, the CDC guidelines state that the evidence on universal surveillance is limited and recommends surveillance only in specific subpopulations, defined in the context of the infection characteristics of the facility [22].

Since the publication of the guideline, conflicting data have been reported. In a prospective study of surgical patients at a Swiss teaching hospital, a rapid MRSA screening test at the time of hospital admission did not reduce the rate of MRSA infections [290]. In contrast, a universal MRSA screening program at a three-hospital organization in the United States led to a large reduction in MRSA infection during hospitalization and at 30 days after discharge [291]. Rates of MRSA infection have been reduced when universal MRSA surveillance was incorporated into a bundle of interventions that included adherence to Standard Precautions and recommendations for hand hygiene, adherence to Contact Precautions for patients who have MRSA-positive cultures, and efforts to change the environmental culture through briefings on patient care units, leadership involvement, and other similar strategies [289]. In one study, implementation of such a bundle resulted in significant decreases in transmission of MRSA (from 5.8 per 1,000 bed-days to 3.0 per 1,000) and overall MRSA HAIs (from 2.0 per 1,000 bed-days to 1.0 per 1,000), as well as a 65% decrease in MRSA surgical site infections after orthopedic operations [172]. Three independent factors have been found to correlate with previously unknown MRSA carriage: recent treatment with antibiotics, history of hospitalization, and age older than 75 years. Predictive models with these factors may enhance MRSA screening by better targeting patients at risk for MRSA carriage [292].

Antimicrobial Stewardship

The principles underlying the judicious use of antibiotics are the limitation of unnecessary antibiotics, obtaining timely culture and sensitivity data, selecting the most appropriate treatment, and prescribing the appropriate dose [293]. In addition, studies have shown that antimicrobial use can be decreased by using explicit criteria to identify patients with HAIs as well as those at highest risk for infection [294]. Antibiotic stewardship programs provide guidance to clinicians and have been shown to improve patient outcomes, reduce the burden of antibiotic resistance, and save healthcare dollars [14; 286].

In their "Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship," SHEA and IDSA recommend that two core strategies of such a program are a prospective audit with intervention and feedback and formulary restriction and preauthorization [71]. Other elements of an effective antimicrobial stewardship program include [71]:

- Education to supplement interventions
- Guidelines and clinical pathways that incorporate local microbiology and resistance patterns
- Antimicrobial order forms
- Policy to avoid routine antimicrobial cycling
- Selective use of combination therapy
- Streamlining or de-escalation of therapy
- Dose optimization
- Systematic plan for parental-to-oral conversion

CDC'S CORE ELEMENTS FOR ANTIBIOTIC STEWARDSHIP PROGRAMS IN HOSPITALS, NURSING HOMES AND OUTPATIENT FACILITIES	
Core Element	**Definition**
Leadership commitment	Dedicating necessary human, financial and information technology resources
Accountability	Appointing a single leader responsible for program outcomes. Experience with successful programs show that a physician leader is effective.
Drug expertise	Appointing a single pharmacist leader responsible for working to improve antibiotic use
Action	Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e., "antibiotic time out" after 48 hours)
Tracking	Monitoring antibiotic prescribing and resistance patterns
Reporting	Regular reporting of information on antibiotic use and resistance to doctors, nurses and other relevant staff
Education	Educating clinicians about resistance and optimal prescribing
Source: [14]	*Table 19*

The goal of phase four of the CDC national HAI Action Plan is to "slow the emergence of resistant bacteria and prevent the spread of resistant infection" (***Table 19***) [14]. The CDC is coordinating stewardship activities among federal agencies, public health, and healthcare systems in order to achieve the following goals by 2020 [14]:

- Establishment of antibiotic stewardship programs in all acute care hospitals and improved stewardship across all healthcare settings
- Reduction of inappropriate antibiotic use by 50% in outpatient settings and by 20% in inpatient settings
- Establishment of Antibiotic Resistance Prevention Programs in all 50 states

EDUCATION FOR HEALTHCARE PROFESSIONALS

Education on best practices is a crucial aspect of preventing HAIs and is a recommendation in all infection control guidelines. Education should highlight the effect of prevention measures on the rates of HAIs, enhance knowledge about currently available guidelines, and provide instruction on carrying out guideline recommendations. Research has also suggested that education about prevention strategies may be more effective if patterns of care and levels of risk are incorporated into recommendations [295]. Numerous studies have shown that knowledge and practices related to HAIs and guidelines are improved after educational programs. The combination of a self-study module (with pretest and post-test), inservice lectures, posters, and fact sheets on the prevention of intravascular device-related bloodstream infections and appropriate practices led to substantial reductions in the prevalence of such infections [258; 296; 297]. A small study showed that ICU nurses' knowledge and practices were enhanced by education on the prevention of ventilator-associated pneumonia [235]. A Canadian study demonstrated that rates of nosocomial MRSA infection significantly decreased after a mandatory infection control education program on MRSA that included discussion of hospital-specific MRSA data and case-based practice [298].

Because increasing knowledge is not sufficient for effecting behavior change, theoretical models for behavior change should be considered when designing improvement initiatives [280; 299]. Among effective model-related strategies are the following [280; 299]:

- Education and discussion of barriers to adherence (cognitive model)
- External reinforcements, incentives, and reminders (behavioral model)
- Consensus, leadership, and role models (social influence model)
- Quality improvement teams, process redesign, and fostering of a safety-oriented culture (organizational model)

Healthcare facilities should explore innovative ways to develop quality improvement initiatives. In an effort to enhance adherence to the CDC guidelines on hand hygiene, a group of three hospitals used the Six Sigma approach with success. Six Sigma is a process established in the business world to achieve and sustain excellence in general operations and service [300]. The healthcare facility used the process to organize the knowledge, opinions, and actions of physicians, nurses, and other staff in four ICUs at the facilities, resulting in an increase in compliance from 47% to 80% [301].

Given the low rates of influenza vaccination among healthcare workers, education on the importance of this measure is also needed. Two literature reviews have shown high rates of misconceptions or lack of knowledge about influenza, the role of healthcare professionals in transmitting influenza to patients, and the importance and risks of vaccination [302; 303]. Education on vaccination should be targeted to address these attitudes and beliefs. In addition, some studies have indicated that self-protection is a primary reason healthcare professionals decide to be vaccinated, and education that focuses on this aspect may help improve vaccination rates [303].

EDUCATION FOR PATIENTS AND FAMILIES

Education for patients and families is an important component of an overall prevention strategy, and the U.S. Department of Health and Human Services notes that such education is a critical part of the national effort on preventing HAIs [14]. Many national-level initiatives have been launched to encourage individuals to become more active in their health care and to be their own advocates, and patients, family members, and hospital visitors should be encouraged to become partners in preventing the transmission of infection in the healthcare setting [22].

Hospitals should engage patients in their own care by discussing infection control measures for hand hygiene practices, respiratory hygiene practices, and contact precautions (according to the patient's condition) with the patient and his or her family members on the day the patient enters the hospital or as soon as possible thereafter. For patients who are to have surgery, healthcare professionals should describe the measures that will be taken to prevent adverse events. This information may be provided in any form of media, and the patient's understanding of the information should be evaluated and documented.

Physicians and other healthcare professionals should educate patients and families about ways to prevent infection, especially with regard to their specific factors (e.g., surgery, insertion of a urinary catheter). Clinicians should also explain the importance of the appropriate use of antibiotics, including the need to complete the recommended antibiotic treatment course; the relationship between the inappropriate use of antibiotics and the increasing prevalence of drug-resistant bacteria; and the implications of drug-resistant bacteria. Patients should be encouraged to help promote adequate hand hygiene by asking their healthcare providers if they have washed their hands. The IHI has addressed this topic with the "It's OK to Ask" campaign, and patient educational pamphlets can be downloaded from the IHI website (http://www.ihi.org). The CDC has developed a video for newly admitted patients on the topic of hand hygiene, which is available on its website (https://www.cdc.gov/handhygiene/campaign/index.html). The SHEA and the CDC collaborated to develop a series of patient guides on the top five HAIs, as well as on MRSA and VRE, and the guides are available on the SHEA website (http://www.shea-online.org/index.php/practice-resources/patients).

The ability to understand health information and make informed health decisions, known as health literacy, is integral to good health outcomes [304]. Yet, the National Assessment of Adult Literacy estimated that only 12% of adults have "proficient" health literacy and 14% have "below basic" health literacy [305]. Rates of health literacy are especially low among ethnic minority populations and individuals older than 60 years of age [304]. Compounding the issue of health literacy is the high rate of individuals with limited English proficiency. According to the U.S. Census Bureau data from 2017, more than 64.2 million Americans speak a language other than English in the home, with more than 25.6 million of them (8.5% of the population) speaking English less than "very well" [306].

Clinicians should assess their patients' literacy level and understanding and implement interventions as appropriate. Healthcare professionals should use plain language in their discussions with patients who have low literacy or limited English proficiency. They should ask them to repeat pertinent information in their own words to confirm understanding. Reinforcement with the use of low-literacy or translated educational materials may be helpful.

Translation services should be provided for patients who do not understand the clinician's language. "Ad hoc" interpreters (family members, friends, bilingual staff members) are often used instead of professional interpreters for a variety of reasons, including convenience and cost. However, clinicians should check with their state's health officials about the use of ad hoc interpreters, as several states have laws about who can interpret medical information for a patient [307]. Children should especially be avoided as interpreters, as their understanding of medical language is limited and they may filter information to protect their parents or other adult family members [307]. Individuals with limited English language skills have actually indicated a preference for professional interpreters rather than family members [308]. Most important, perhaps, is the fact that clinical consequences are more likely with ad hoc interpreters than with professional interpreters [309; 310; 311].

The American Medical Association offers several health literacy resources for healthcare professionals on its website (https://www.ama-assn.org), and the U.S. Department of Health and Human Services offers valuable information on cultural competency from the Health Resources and Services Administration (HRSA) (https://www.hrsa.gov/culturalcompetence) and the Office of Minority Health (http://www.thinkculturalhealth.org).

PREPAREDNESS AND CONTROL OF OUTBREAKS

Another responsibility of an infection control team is establishing response plans for outbreaks and epidemics and controlling them should they occur. An outbreak is defined by the WHO as "an unusual or unexpected increase of cases of a known nosocomial infection or the emergence of cases of a new infection" [15]. The number of individuals affected can vary from a few to 100 or more. Outbreaks and epidemics account for approximately 5% to 10% of HAIs, and most hospitals lack adequate equipment, isolation space, and staff to treat a large increase in the number of patients with an infectious disease [39; 87]. The two primary concerns are to confirm the existence of the outbreak and to establish control measures to confine the spread.

An outbreak should be identified and investigated as early as possible to prevent morbidity and mortality. Any healthcare professional who suspects an outbreak should notify infection control staff, and an outbreak team should be established. Investigating an outbreak involves [15; 312]:

- Establishing the existence of an outbreak
- Verifying the diagnosis
- Defining and identifying cases
- Describing and orienting the data in terms of time, place, and person
- Developing and evaluating hypotheses

- Refining hypotheses and carrying out additional studies
- Implementing control and prevention measures
- Communicating findings

The outbreak team should collaborate with all appropriate healthcare workers to identify either the carriers or the common sources of the infection and to review aseptic practices and disinfectant use for a breach in compliance. Data on potential cases should be reviewed and a case definition should be developed. The case definition should include [15; 312]:

- Unit of time and place
- Specific biologic and/or clinical criteria
- Inclusion/exclusion criteria
- Gradient of definition (definite, probable, or possible)
- Differentiation between colonization and infection
- Specific criteria to identify the index case, if relevant information is available

Data should be collected from all available sources, such as patient charts, microbiology reports, pharmacy reports, and log books from patient units. Describing the outbreak in terms of individuals, place, and time helps to create an epidemic curve, which shows the distribution of cases by time of onset [15]. An attack rate can then be defined as the number of people at risk who are infected compared with the total number of people at risk.

Developing and evaluating hypotheses will yield the source of the outbreak and/or the index case. The data should be reviewed carefully to evaluate the characteristics and similarities among affected individuals. The team must then determine the extent of the outbreak. Cohort isolation is implemented as needed (***Table 20***) [22; 313]. Throughout the investigation, the team should communicate routinely with hospital administration. At completion, data on the outbreak should be documented and published, as the information can provide valuable education to the healthcare community at large and can help staff prepare for future outbreak investigations [314].

Case Example

The following case outlines an investigative process and illustrates that the source of an outbreak may be unusual [315].

A cardiac surgeon noticed a cluster of cases of sternal wound dehiscence among his patients who had had surgery. Specimens from the wounds were obtained for culture. Microbiologic evaluation indicated that the infections were predominantly caused by Enterobacter cloacae, and molecular typing and serotyping demonstrated that the isolates were similar. No infections had developed after operations the surgeon had performed at other hospitals. No breach in aseptic technique was identified. All of the infected patients had been operated on in the same operating room, and the environment was screened. No source was found. Further questioning of the surgeon's operative practice revealed one difference from other cardiac surgeons: he used semi-frozen sodium lactate solution to achieve cardioplegia. Swabbing of the freezer used for the solution identified E. cloacae of the same typing as that found in the wound infections. The hypothesis was that contamination of the freezer led to contamination of the ice/slush solution, and the micro-organism was transmitted to the patients. The freezer was replaced, a rigorous cleaning schedule was instituted, and no further cases have occurred.

Potential Outbreaks

The following are overviews of selected potential outbreaks. Identification and early action in the case of any of these outbreaks will limit the adverse effects.

TYPE AND DURATION OF PRECAUTIONS REQUIRED FOR INFECTIONS WITH POTENTIAL FOR OUTBREAKS			
Infection/Condition	**Precaution Type**	**Precaution Duration**	**Notes**
Anthrax (cutaneous or pulmonary)	Standard	Ongoing	Use Contact Precautions if there is large amount of uncontained drainage from lesions.
Aspergillosis	Standard	Ongoing	Use Contact Precautions and Airborne Precautions if there is massive soft-tissue infection with copious drainage.
Botulism	Standard	Ongoing	Not transmitted person-to-person.
Diphtheria (cutaneous or pharyngeal)	Contact, Droplet	Until antibiotic therapy is completed and two cultures taken at least 24 hours apart are negative	—
Ebola (viral hemorrhagic fever)	Standard, Contact, Droplet	Duration to be determined on case-by-case basis, in conjunction with local, state, and federal health authorities	Single patient room with the door closed preferred. Maintain log of all people entering the patient's room. Use barrier protection against blood and body fluids upon entry into room (single gloves and fluid-resistant or impermeable gown, face/eye protection with masks, goggles or face shields). Use additional protective wear (double gloves, leg and shoe coverings) during final stages of illness when hemorrhage may occur. Use dedicated disposable (preferred) medical equipment for patient care. Clean/disinfect all nondedicated, nondisposable equipment. Limit use of needles, sharps as much as possible. Limit procedures, tests. Avoid aerosol-generating procedures. Notify public health officials immediately if Ebola is suspected.
Clostridium difficile gastroenteritis	Contact	Duration of illness	Discontinue antibiotics if appropriate. Use soap and water for hand-washing, as antiseptic handrubs lack sporicidal activity. Do not share equipment (e.g., electronic thermometers). Ensure consistent environmental cleaning and disinfection.
Influenza, seasonal	Droplet	5 days after onset of symptoms	Single patient room preferred or cohort. Use mask on patient when he or she is transported out of room. Use gown and gloves according to Standard Precautions. The duration of precautions for immunocompromised patients cannot be defined. Refer to CDC guidance (https://www.cdc.gov/flu/professionals/infectioncontrol/healthcaresettings.htm).
Influenza, pandemic	Droplet	5 days after onset of symptoms	Refer to CDC guidance (http://www.cdc.gov/flu/pandemic-resources).
Influenza, avian	Droplet	Duration of illness	Refer to CDC guidance (http://www.cdc.gov/flu/avianflu).
Malaria	Standard	Ongoing	Install screens in windows and doors in endemic areas.
Measles (rubeola), all presentations	Airborne	4 days after onset of rash (duration of illness for immunocompromised patients)	Use Airborne Precautions for exposed susceptible patients. Susceptible healthcare staff should not enter the room if immune caregivers are available. Exclude susceptible healthcare staff from duty from day 5 after first exposure to day 21 after last exposure, regardless of post-exposure vaccine.
Meningitis (*Haemophilus influenzae* or *Neisseria meningitidis* [meningococcal] known or suspected)	Droplet	Until 24 hours after initiation of effective therapy	—
Meningococcal pneumonia	Droplet	Until 24 hours after initiation of effective therapy	—

Table 20 continues on next page.

TYPE AND DURATION OF PRECAUTIONS REQUIRED FOR INFECTIONS WITH POTENTIAL FOR OUTBREAKS *(Continued)*			
Infection/Condition	**Precaution Type**	**Precaution Duration**	**Notes**
Norovirus	Standard	Duration of illness	Cohorting of affected patients to separate airspaces and toilet facilities may help interrupt transmission during outbreaks. Use Contact Precautions for diapered or incontinent persons for the duration of illness or to control outbreaks. Ensure consistent environmental cleaning and disinfection, with focus on restrooms even when apparently unsoiled. Persons who clean heavily contaminated areas may benefit from wearing masks as virus can be aerosolized.
Plague, bubonic	Standard	Ongoing	—
Plague, pneumonic	Droplet	Until 48 hours after initiation of effective therapy	Antimicrobial prophylaxis should be given to exposed healthcare staff.
Pneumonia caused by: Adenovirus *Legionella* Meningococcal *Mycoplasma* (primary atypical pneumonia)	 Droplet, Contact Standard Droplet Droplet	 Duration of illness Ongoing until 24 hours after initiation of effective therapy Duration of illness	—
Scabies	Contact	Until 24 hours after initiation of effective therapy	—
Staphylococcus aureus, skin, wound, or burn Major: no dressing or dressing does not contain drainage adequately Minor or limited: dressing covers and contains drainage adequately	 Contact Standard	Duration of illness Ongoing	—
Group A streptococci, skin, wound, or burn (major: no dressing or dressing does not contain drainage adequately)	Contact, Droplet	Until 24 hours after initiation of effective therapy	—
Toxoplasmosis	Standard	Ongoing	—
Toxic shock syndrome (staphylococcal or streptococcal disease)	Standard	Ongoing	—
Tuberculosis, extrapulmonary (draining lesion)	Airborne, Contact	Only when therapy is effective, patient is clinically improving, and the cultures of 3 consecutive sputum smears, collected on different days, are negative	Examine for evidence of active pulmonary tuberculosis. (If evidence exists, additional precautions are necessary.)
Tuberculosis, extrapulmonary, (no draining lesion, meningitis)	Standard	Ongoing	Examine for evidence of pulmonary tuberculosis. (If evidence exists, additional precautions are necessary.)

Table 20 continues on next page.

TYPE AND DURATION OF PRECAUTIONS REQUIRED FOR INFECTIONS WITH POTENTIAL FOR OUTBREAKS *(Continued)*			
Infection/Condition	**Precaution Type**	**Precaution Duration**	**Notes**
Tuberculosis, pulmonary or laryngeal disease (confirmed)	Airborne	Only when therapy is effective, patient is clinically improving, and the cultures of 3 consecutive sputum smears, collected on different days, are negative	—
Tuberculosis, pulmonary or laryngeal disease (suspected)	Airborne	Only when the likelihood of infectious disease is negligible and the cultures of 3 consecutive sputum smears, collected on different days, are negative	—
Tuberculosis, latent (skin-test positive with no evidence of current pulmonary disease)	Standard	Ongoing	—
Varicella zoster (chickenpox)	Airborne, Contact		Until all lesions are crusted (10 to 21 days) Susceptible healthcare staff should not enter the room if immune caregivers are available.
Whooping cough (pertussis)	Droplet	Until 5 days after initiation of effective therapy	—
Source: [22; 313]			*Table 20*

Group A Streptococci

Most outbreaks of group A streptococci involve surgical wounds, and the source can usually be traced to an asymptomatic carrier in the operating room or on the wound care team [87; 316]. Standard Precautions are sufficient if the wound is minor; if it is major, Contact Precautions should be instituted and followed for 24 hours after initiation of effective therapy [22]. The healthcare worker should receive antimicrobial therapy as appropriate and leave the setting until completion of therapy.

Pulmonary Tuberculosis

Dealing with pulmonary tuberculosis involves prompt identification of the disease and determining the susceptible individuals who were exposed to the patient before isolation [87]. Airborne Precautions should be instituted and remain in place until the patient is receiving effective therapy, is improving clinically, and the culture results for three consecutive sputum specimens, collected on different days, are negative. Comprehensive information is available in the CDC guidelines for preventing the transmission of tuberculosis in healthcare facilities [317].

Legionella

The source of HAI with *Legionella* pneumonia is usually contaminated water [87]. Implementation of Standard Precautions for the patient is sufficient [22]. Laboratory-based surveillance for nosocomial *Legionella* should be performed, and samples of tap water should be obtained for culture. If the culture is positive, it is best to obtain cultures from patients who have healthcare-associated pneumonia. There are more than 40 known types of *Legionella* species, but most outbreaks are caused by *Legionella pneumophila* serotypes 1 and 6.

Antibiotic-Resistant Micro-Organisms

Outbreaks of antibiotic resistance have involved MRSA, VRE, and, most recently, vancomycin-resistant *S. aureus* [318]. In such outbreaks, it is important to identify patients with colonization or infection early and isolate them or cohort them. Contact Precautions should be implemented and carried out until antibiotic therapy has been completed and cultures are negative [22]. The importance of adhering to proper hand hygiene and other elements of Contact Precautions should be emphasized. Healthcare workers who were involved with patients before isolation should be evaluated for colonization and infection and treated appropriately.

Other Outbreaks

The potential for other outbreaks or epidemics vary, and the CDC website, http://www.bt.cdc.gov, offers resources on emergency preparedness for outbreaks or epidemics caused by potential agents of bioterrorism, including anthrax and viral hemorrhagic fever. A Bioterrorism Readiness Plan template is also available (https://emergency.cdc.gov/bioterrorism/pdf/13apr99APIC-CDCBioterrorism.pdf). Many aspects should be considered when planning for bioterrorism preparedness, and each department of a healthcare facility can play an important role.

CONCLUSION

Infections acquired in the healthcare setting raise a great risk for patients, leading to high rates of morbidity and mortality. Many of the deaths caused by HAIs could be prevented by following evidence-based guidelines and consensus statements on prevention strategies. Several institutions have implemented campaigns to enhance the quality of health care and patient safety by focusing on measures to reduce the most common HAIs: catheter-associated urinary tract infection, surgical site infection, pneumonia, intravascular device-related bloodstream infection, and *C. difficile* infection. The single most effective infection control measure is appropriate hand hygiene, and all efforts to reduce the rate of HAIs must focus on enhancing compliance with this measure in conjunction with other prevention strategies. Along with hand hygiene, meticulous attention to aseptic technique when preparing for invasive procedures or using invasive devices is also essential for reducing the prevalence of HAIs. Prevention measures specific for each of the most common types of HAIs have been recommended in evidence-based guidelines and consensus statements (***Table 21***).

The common pathogens, diagnosis, and treatment vary among these infections and even within each type of infection. The CDC has detailed diagnostic criteria for each type of infection, and consensus statements and guidelines have also proposed such criteria. The treatment of HAIs varies according to the pathogen and the anatomic site. The prevailing principle is to use antibiotics judiciously, as the inappropriate use of antibiotics has led to an increasing number of resistant strains of bacteria. When using empiric antibiotic therapy, physicians should select an antibiotic on the basis of known pathogens in the healthcare facility as a whole, as well as on the specific unit within the facility.

An effective infection control team is critical to reducing the incidence of HAIs in a healthcare facility. All departments within a healthcare facility should be represented on this team to ensure widespread adherence to prevention measures. The responsibilities of an infection control team are to conduct surveillance of infections; ensure compliance with infection control guidelines, including those for management of drug-resistant organisms; and establish response and control plans for outbreaks and epidemics. Most important is the development of an organizational culture that fosters a focus on patient safety and emphasizes education on HAIs and infection control for healthcare workers and patients and their families.

SUMMARY OF PREVENTION MEASURES FOR THE MOST COMMON HEALTHCARE-ASSOCIATED INFECTIONS		
Type of Infection	**Evidence-Based Recommended Measures**	**Other Suggestions**
All infections	Appropriate hand hygiene Meticulous aseptic technique for devices and equipment	—
Catheter-associated urinary tract infection	Indwelling catheters only when needed Proper securing of catheter Closed sterile drainage system Unobstructed urine flow Removal of catheter as soon as possible	Alternative to indwelling catheter (suprapubic, condom) Antimicrobial-coated catheter Hand-held bladder scanners
Pneumonia (without mechanical intubation)	Deep breathing Frequent coughing Early movement (in bed and/or walking) Limited use of narcotic agents Incentive spirometry (for patients at high risk)	—
Ventilator-associated pneumonia	Elevation of the head of the bed (30 degrees)[a] Daily interruptions of sedation and assessment of readiness to extubate[a] Prophylaxis of peptic ulcer disease[a] Prophylaxis of deep venous thrombosis[a]	Endotracheal tube with a dorsal lumen Noninvasive ventilation
Surgical site infection	Appropriate antibiotic prophylaxis Avoidance of preoperative shaving Maintaining adequate glycemic control Maintaining a warm body temperature	Performance feedback to surgeons
Intravascular device-related bloodstream infections	Maximal barrier precautions[a] 2% chlorhexidine solution for skin antisepsis[a] Selection of optimal site for the catheter (subclavian vein preferred for nontunneled catheters)[a] Daily review of the need for the line, with prompt removal if line is deemed unnecessary[a]	Catheter with antimicrobial coating Performance feedback to personnel
Clostridium difficile-associated diarrhea	Judicious use of antibiotics Barrier precautions (gowns and gloves, dedicated or disposable equipment, cohorting of patients and/or staff) Handwashing with soap and water (alcohol is not effective against C. *difficile* spores) Appropriate disinfectant for surfaces and devices	—
[a]Component of a bundle of interventions that, when implemented together, has lowered the rate of infection.		
Source: Compiled by Author		*Table 21*

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