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Hospital Epidemiology and Infection Control in Acute-Care Settings

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INTRODUCTION

The Centers for Disease Control and Prevention (CDC) defines health care-associated infections (HAIs) as infections acquired while in the health care setting (e.g., inpatient hospital admission, hemodialysis unit, or same-day surgery), with a lack of evidence that the infection was present or incubating at the time of entry into the health care setting (139). These definitions need to respond to a changing medical environment. Modern medical care has become more invasive and therefore associated with a greater risk of infectious complications. An aging population, the AIDS epidemic, the growth of chemotherapeutic options for cancer treatment, and a growing transplant population have expanded the population at an increased risk for infection as a consequence of interactions with the health care system. Both surgical care and medical care that are increasingly complex and invasive are being provided in non-acute-care settings, making the definition of a health care setting more problematic. Finally, patients move freely within sometimes loosely defined elements of the health care system: between long-term care or rehabilitation facilities, to acute-care facilities, to free-standing surgical care providers.

In 1980, the Study on the Efficacy of Nosocomial Infection Control (SENIC) demonstrated that surveillance for nosocomial infections and infection control practices that included trained professionals could prevent HAIs (122). As a result, an important role developed for hospital epidemiologists and infection control practitioners (298). As medical care has become more complex, antimicrobial resistance and HAIs have increased, as have their attributable morbidity and mortality (362). Additionally, HAIs increase hospital lengths of stay and health care expenditures (247). In response to patient risks and growing costs, in 2008 the Centers for Medicare and Medicaid Services (CMS) implemented a strategy of withholding reimbursement for certain HAIs such as catheter-associated urinary tract infections (CA-UTIs) and central line-associated bloodstream infections (CLABSIs) (336). Now more than ever, institution-specific surveillance driven by hospital epidemiologists and infection preventionists (IPs) is needed in order to enact early detection and prevention strategies to curtail HAIs.

This review is intended for general internists and infectious diseases physicians and provides a general overview of hospital epidemiology and infection control in acute-care settings. This review summarizes some of the challenges and opportunities faced by the health care epidemiology community. We discuss HAIs in the broadest sense to include all health care-associated infections, communicable diseases, and multidrug-resistant (MDR) and epidemiologically significant organisms.

HISTORY

Semmelweis

Ignaz Semmelweis is credited with first discovering that health care providers could transmit disease, as he described the mode of transmission of puerperal sepsis. Semmelweis was a Hungarian obstetrician at the Maternity Hospital in Vienna, Austria, who in 1847 noted higher rates of maternal mortality among patients cared for by obstetricians and medical students than among those cared for by midwives. At that time he also witnessed a pathologist die of sepsis after sustaining a scalpel wound while performing an autopsy on a patient with puerperal sepsis. He noted that the pathologist's clinical illness mimicked that of women with puerperal sepsis and identified that not only a scalpel but also physicians' hands contaminated after an autopsy could transmit contaminated material or organisms to mothers in labor. He introduced chlorinated lime hand washing into the clinic staffed by obstetricians and medical students, with drastic improvements in rates of maternal mortality (232). However, Semmelweis' theories were dismissed by most of the medical establishment. When Koch's postulates were published in 1890, the germ theory of disease and Semmelweis' theory of transmission from patient to patient were considered plausible. In essence, Semmelweis gave us the first description of an HAI and an intervention to prevent its development through his demonstration of the benefits of hand hygiene.

Discovery of Penicillin

While studying color variants of *Staphylococcus aureus* on petri plates, Alexander Fleming noted the growth of a contaminating mold with an associated zone of bacterial clearance (20). He demonstrated that the active substance causing bacterial lysis could be found in the filtrate of the contaminating mold culture, and the fungus was discovered to be a species of

the genus *Penicillium* (81). Through the publication of his findings and Fleming's persistence, in 1940 chemists were able to isolate, concentrate, and purify the substance that came to be known as penicillin (81). Penicillin G was first used in clinical practice in 1942. Penicillin's lack of reliable activity against Gram-negative bacteria led to the search for other novel antibiotics, and cephalosporins were subsequently discovered in the 1950s.

Staphylococcal resistance to penicillin increased during the 1950s, fueling the discovery of antistaphylococcal penicillins and aminopenicillins (e.g., ampicillin) (81). Since that time we have seen continually increasing rates of antimicrobial resistance among organisms infecting patients, with subsequently more-difficult-to-treat infections. Many of these resistant pathogens develop in health care settings and cause HAIs.

Growth of Infection Control Programs

Public health officials in the 1970s took notice of increasing numbers of HAIs, with their resultant increased morbidity, mortality, and hospital costs. Simultaneously, hospitals began implementing infection surveillance and control programs; however, their efficacy was unproven. In 1974, Haley and others at the CDC designed a nationwide study, the SENIC Project, to examine whether infection surveillance and control programs could lower the rates of HAIs (122). This study, performed over a 10-year period (1975 to 1985), examined HAI rates in a sampling of U.S. hospitals before and after the implementation of infection control programs (120, 122). The SENIC study demonstrated that four components were essential to an effective infection prevention and control program. These included (i) surveillance with feedback of infection control rates to hospital staff, (ii) enforcement of preventative practices, (iii) a supervising IP to collect and analyze surveillance data, and (iv) the involvement of a physician or microbiologist with specialized training in infection prevention and control (120). Programs with these elements reduced rates of the four most common HAIs by 32% (120, 146). This and subsequent studies have confirmed the effectiveness of infection surveillance and control programs and have stimulated an increase in numbers of infection control programs throughout hospitals in the United States.

The Joint Commission on Accreditation of Healthcare Organizations (JCAHO), now named the Joint Commission, was formed in 1976 in an effort to promote hospital reform based on patient-centered outcomes (159a). This private-sector nonprofit organization accredits health care institutions, which is necessary in order to meet requirements for Medicare reimbursement. Even before the results of the SENIC study were published, the Joint Commission began requiring certain components of infection prevention and control programs in the United States, including detailed surveillance systems.

After the results of the SENIC study were reported, infection surveillance and control programs expanded across the country. Using a standard surveillance methodology, infection surveillance and control programs reported infection rates through databases such as the National Nosocomial Infection Surveillance (NNIS) system. In 2005, the NNIS system was replaced by the National Health Safety Network (NHSN) based at the CDC and continues to be a voluntary reporting system that monitors components of HAIs, including those in acute-care settings. Elements of this novel system have been emulated worldwide. This reporting system requires the use of strict definitions, standard case-finding procedures, and risk stratification to generate data that are fed back to participating institutions and later used as benchmarks.

In 1991, the Occupational Safety and Health Administration (OSHA), an agency of the U.S. Department of Labor, released the Bloodborne Pathogens Standard, aimed at minimizing occupational exposures to blood-borne pathogens (236). The Bloodborne Pathogens Standard implemented measures that employers must take in order to minimize the transmission of pathogens such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) to their employees. Such measures include providing education, HBV vaccination, use of personal protective equipment, and ensuring institutional medical surveillance. The Bloodborne Pathogens Standard both enforced the need for infection control programs and expanded their role within hospitals to include issues related to occupational health and health care worker (HCW) protection.

In 2000, the Institute of Medicine published *To Err Is Human*: *Building a Safer Health System* and subsequently drew attention to preventable medical errors, including HAIs and patient safety (172, 362). The Joint Commission issued the first-ever National Patient Safety Goals in 2003. Each accredited hospital was required to demonstrate programs that addressed the reduction of HAIs as a goal toward improving patient safety. Specifically, they recommended compliance with CDC or World Health Organization (WHO) hand hygiene guidelines and reporting death or major disability secondary to HAIs as sentinel events (159).

External Influences

In response to the passage of the Deficit Reduction Act of 2005, the CMS began requiring hospitals to submit data on 10 quality measures, including measures to prevent HAIs. Finally, in 2008 the CMS began withholding reimbursement for patients readmitted with certain HAIs, including CA-UTIs, CLABSIs, and surgical-site infections (SSIs) (336). This change in reimbursement, coupled with public reporting, heightened public awareness, and the increasing accountability of health care systems has forced hospitals to expand infection prevention and control practices focusing on the prevention and monitoring of HAIs (139).

Today, there is a myriad of external influences impacting infection control programs. These external influences include legislative mandates, industry, accrediting agencies, payers, professional societies, and consumer advocacy groups (89). These groups are often at odds with each other and propose conflicting recommendations.

Methicillin-resistant *Staphylococcus aureus* (MRSA) surveillance is one example of these competing interests. The CDC recommends MRSA surveillance strategies be decided locally and does not recommend routine MRSA surveillance cultures (301). The Society for Healthcare Epidemiology of America (SHEA) recommends obtaining MRSA surveillance cultures from high-risk patients upon admission and then periodically (43); however, these guidelines are controversial because the

effectiveness of active MRSA surveillance is debated (127, 191, 277, 317). Despite controversy over the effectiveness of MRSA surveillance, the Department of Veterans Affairs has mandated hospital-wide MRSA surveillance in its facilities; several states now mandate MRSA surveillance (343), and the CMS is considering withholding reimbursement for MRSA infections (89).

The interest of the media in HAIs has had an immense effect on consumer advocacy groups, legislative bodies, and accrediting organizations (89). This effect has been seen in the form of increasing legislative mandates. Multiple states now mandate the public reporting of HAI rates (89) despite a lack of evidence supporting public reporting (355). Federal legislation which would require all hospitals to report HAIs has also been introduced (329). In addition to mandates for public reporting, interest has grown in withholding payment for HAIs. Like the CMS, commercial payers have initiated programs that would withhold reimbursement for some HAIs (89).

Growing mandates and restrictions on payments have the potential to lead to increased unnecessary antimicrobial use in an effort to prevent infections, lack of time and resources to address other potentially preventable infections, and instances of individuals gaming surveillance systems (i.e., falsifying data) in order to lower reported infection rates (89). Broad mandates also impose a one-size-fits-all strategy, when in reality local epidemiology varies, and infection control programs need flexibility to address local problems. We also need to beware of mandating and implementing practices that are not evidence based, and we should focus our energies on developing the best evidence-based practices.

More resources and trained individuals are needed to enable infection control programs to respond to growing requirements. In this age of increasing external pressures, strong leadership is needed within infection prevention and control programs to develop research programs, promote evidence-based practices, educate the public, and set national priorities.

DEFINING THE NEED FOR HOSPITAL EPIDEMIOLOGY AND INFECTION CONTROL

HAIs are the most common complication seen in hospitalized patients. HAIs increase morbidity, mortality, costs, and length of stay even after adjustment for underlying illness (63) (Table 1). The term nosocomial infection encompasses a narrower spectrum. Nosocomial infections are HAIs acquired in an acute-care setting that were neither present nor incubating at the time of admission (139). Based on data for 2003, 5 to 10% of patients admitted to acute-care hospitals or approximately 2 million patients per year in the United States acquire a nosocomial infection. At least 90,000 deaths per year are a result, making nosocomial infections the fifth leading cause of death in acute-care hospitals (40, 314). These infections are estimated to add an extra $4.5 billion to $5.7 billion per year to the cost of patient care (40). Roughly 25% of nosocomial infections occur in intensive care units (ICUs), which have been estimated to increase ICU length of stay by 4.3 to 15.6 days and account for more than 20% of total ICU costs (63, 64).

Risk factors for all HAIs include those associated with the host, those associated with treatment strategies, and those associated with HCW behaviors. Most HAIs are associated with devices such as urinary catheters, intravascular catheters, and mechanical ventilators that disrupt normal host protection mechanisms such as intact skin or mucosal membranes. However, the patient immune status also impacts the risk of HAIs. For example, immunocompromised patients represent a patient population at an increased risk of HAIs, given compromised immune systems, frequent contact with the health care system, and increased rates of invasive procedures. Beyond these risk factors, exposure to the ICU; use of other devices (nasogastric tube, etc.); antimicrobial exposure, including type, duration, and number of agents used; extremes of age; and underlying illness all increase the risk of HAIs (96, 322). Specific infections or organisms have unique risk factors that are outlined below. Three specific patient populations deserve special focus: (i) those with HIV infection, (ii) patients with significant immunosuppression due to hematological malignancies and/or hematopoietic stem cell or solid-organ transplants, and (iii) those with cystic fibrosis.

At-Risk Patient Populations

The expanded availability of highly active antiretroviral therapy (HAART) has improved the survival of HIV-positive patients, with an increasing prevalence of chronic diseases associated with HIV and long-term HAART use (38, 104, 226, 319). The now-chronic nature of this disease increases patient interaction with the health care system.

Three prospective studies have estimated that approximately 8% of HIV-related admissions were complicated by nosocomial infections (102, 255, 318). Stroud et al. found a nosocomial infection incidence rate among HIV-positive patients of 6.1 per 1,000 patient days compared to a hospital-wide incident rate of 3.5 per 1,000 patient days (318). $CD4^+$ T-lymphocyte counts less than 200 cells/μl, chronic wasting, and worse performance status tended to be associated with a greater risk of HAIs in HIV-positive patients (254).

BSIs are the most common HAI in HIV-positive patients, with *S. aureus* being the most commonly isolated pathogen, compared to coagulase-negative staphylococci in HIV-negative patients (318). Petrosillo and colleagues showed an almost-4-fold increase in mortality between disease-matched HIV-positive patients with BSIs and those without BSIs (24.6% versus 7.4%) (256).

Similarly to HIV, patients with hematological malignancies and solid-organ and bone marrow transplants represent unique populations at an increased risk of HAIs due to neutropenia, mucosal disruption, immunosuppressant exposure, as well as extensive exposure to the health care environment (91, 147). These patients frequently become colonized with antimicrobial-resistant organisms that may take on the role of a pathogen after the patient becomes immunosuppressed (99).

Cystic fibrosis is a complex genetic disease often leading to recurrent pulmonary infections and significant contact with the health care system. These patients often develop colonization and infection with resistant Gram-negative organisms. Antibiotic exposure promotes resistant organisms; however, there is increasing evidence of patient-to-patient transmission of resistant organisms among this population (239). In response, the Cystic Fibrosis Foundation has developed infection control

TABLE 1. Epidemiologically significant HAIs[b]

Infection	Risk factor	Impact[a]			Preventative strategy	Reference
		Excess LOS (days)	Excess cost (dollars)	Mortality (%)		
CLABSI	Prolonged hospitalization prior to catheterization Prolonged duration of catheterization Microbial colonization at insertion site Microbial colonization at catheter hub Internal jugular catheterization Femoral catheterization Neutropenia Total parenteral nutrition Substandard care of catheters	10–20	3,700–29,000	35	Infection prevention and control program to identify patients with CLABSI Information technology to calculate rates of CLABSI Implementation of catheter insertion checklist Establish catheter insertion kits/carts Educate all health care personnel on basic practices to prevent CLABSI Hand hygiene prior to insertion Avoid femoral and internal jugular access sites Use maximal sterile barrier precautions during insertion Use chlorhexidine-based antiseptic for skin prepn in those older than 2 mo of age Disinfect all hubs, connectors, and ports prior to accessing the catheter Change catheter dressing and perform site care every 5–7 days Remove nonessential catheters	84, 204, 261
CA-UTI	Duration of catheterization Open drainage system Female sex Older age Diabetes mellitus Impaired renal function Poor quality of catheter care	10	500–3,000		Minimizing catheter use Closed drainage system Use of written protocol for catheter care Minimize urethral trauma at time of placement Provide reminders to clinicians to reevaluate need for urinary catheter Surveillance with unit-specific feedback on infection rates	11, 185, 321, 324
VAP	Intubation Duration of ventilation Sedation Supine positioning Aspiration Enteral nutrition Oropharyngeal colonization Risks for MDR pathogens Risks for MDR pathogens with prior/prolonged hospitalization Risks for MDR pathogens with prior antibiotic exposure Nursing home residence Age >65 yr	4.3	40,000	10–50	Isolation of patients with MDR pathogens Alcohol-based hand hygiene Semirecumbent positioning Microbiological surveillance of MDR pathogens Early removal of invasive devices Avoid sedation Antibiotic management programs Oropharyngeal decontamination Airway humidifiers Subglottic secretion suction systems Maintain endotracheal cuff pressure ≥20 cm H_2O Endotracheal tube with polyurethane cuff Silver-coated endotracheal tubes	7, 8, 71, 135, 242, 262, 285
HAP/HCAP	Sedation Supine positioning Aspiration Enteral nutrition Oropharyngeal colonization Risks for MDR pathogens Prior/prolonged hospitalization Prior antibiotic exposure Nursing home residence Age >65 yr		40,000	10–50	Isolation of patients with MDR pathogens Alcohol-based hand hygiene Semirecumbent positioning Microbiological surveillance of MDR pathogens Early removal of invasive devices Avoid sedation Antibiotic management programs	7, 29, 262
SSI	Diabetes mellitus Smoking Obesity Immunosuppression Hair removal Preoperative infections Inadequate physician/nurse surgical scrub Inadequate skin prepn Unsterilized surgical equipment Operative time Surgeon skill/technique	7–10	3,000–29,000	75	Control glucose Encourage smoking cessation 30 days prior to surgery Adjust prophylactic antibiotics for wt Avoid immunosuppressants if possible Use clippers (not razors) if hair removal is necessary Enforce appropriate scrub technique/duration Appropriate preoperative cleansing agents (chlorhexidine-alcohol) Enforce judicious skin prepn Antimicrobial prophylaxis prior to surgery Minimize operating room traffic Ventilate according to American Institute of Architects' recommendations Use EPA-approved disinfectant to clean surfaces Sterilize all equipment according to published guidelines	10, 80

[a] Estimated per infection.
[b] LOS, length of stay; CLABSI, central line-associated bloodstream infection; CA-UTI, catheter-associated urinary tract infection; VAP, ventilator-associated pneumonia; MDR, multidrug resistant; HAP, hospital-acquired pneumonia; HCAP, health care-associated pneumonia.

recommendations that stress standard precautions, hand hygiene, care of respiratory equipment, and cohorting of patients with resistant organisms (288).

Effective Prevention Measures

Given the increasing numbers of HAIs and MDR organisms, several other factors are important to consider in defining the need for health care epidemiologists. One example is that of interventions that improve compliance with evidence-based practices. Studies have shown that compliance with infection prevention measures such as hand hygiene decreases the transmission of MRSA and that the use of evidence-based bundled prevention measures decreases rates of CLABSIs (260, 264). These effective prevention measures emphasize the need for well-developed and focused infection prevention and control programs and the continued development and implementation of interventions and prevention measures aimed at HAIs.

Pandemic Preparedness

Recent experience with the 2009-2010 novel H1N1 influenza virus pandemic has also emphasized the role that health care epidemiologists play in preventing the transmission of communicable diseases among high-risk patients. Influenza viruses commonly cause seasonal epidemics that can spread rapidly and dramatically in health care settings. Their impact can lead to patient illness and altered hospital operations. As evidenced during the recent novel H1N1 pandemic, hospital epidemiologists and IPs tracked influenza trends, educated staff, and performed risk assessments to best disseminate and implement prevention measures. The United States developed a multilayered national strategy for pandemic influenza, including various governmental, health department, civilian, and hospital roles. The three main goals of the national strategy were to limit the impact of influenza by (i) preparedness and communication, including the stockpiling of vaccine and antiviral medications; (ii) surveillance and detection; and (iii) response and containment (217). In health care settings, health care epidemiologists and IPs are needed to coordinate preparedness planning, conduct surveillance, oversee case finding and treatment, and orchestrate complex strategies such as the cohorting of patients and antiviral and vaccine distribution (217). Documents such as that outlining the national strategy for pandemic influenza do not anticipate the challenges that hospital and health care epidemiologists will face in supporting the mission of health care institutions, managing the influx of patients with a highly transmissible disease, and caring for the worried well.

Our health care system is continually becoming more intricate owing to more complex patient populations, increasing antimicrobial-resistant pathogens, increasingly invasive procedures and treatments, and the challenges of emerging pathogens. Hospital epidemiologists and IPs with training in these complex interactions are needed to protect patients and HCWs. By developing accurate surveillance of HAIs, studying and implementing the best practices to prevent and treat HAIs, and educating health care personnel regarding their role in the transmission and prevention of infections, hospital epidemiologists and IPs aim to decrease HAI rates and improve patient outcomes. Table 1 provides detailed information on risk factors, impacts, and prevention strategies for important HAIs. Organisms most commonly causing HAIs will be discussed below.

EPIDEMIOLOGICALLY SIGNIFICANT PATHOGENS

A total of 28,502 HAIs, including CLABSIs, CA-UTIs, and ventilator-associated pneumonias (VAPs), were reported to the NHSN between January 2006 and October 2007 from 621 U.S. hospitals (90) (Table 2). Of the 33,848 pathogens reported, 87% were bacteria and 13% were fungi. Over 15% of infections were polymicrobial. The most commonly isolated pathogens were coagulase-negative staphylococci (CoNS), *S. aureus*, *Enterococcus* species, *Candida* species, *Escherichia coli*, and *Pseudomonas aeruginosa* (136). With public reporting, increasing numbers of health care institutions participate in the NHSN, making comparisons of data more generalizable.

The human and financial costs of antimicrobial-resistant organisms are enormous. A recent study from Chicago, IL, found 13.5% of inpatients to have infections due to antimicrobial-resistant organisms (276). The cost attributed to these infections ranged from $18,588 to $29,069 per patient. The excess length of hospitalization ranged from 6.4 to 12.7 days. The excess societal cost ranged from $10 million to $15 million. In order to understand the scope of this problem, we must first briefly review the key pathogens.

Staphylococcus aureus

S. aureus causes a variety of infections ranging from skin and soft tissue infections to BSIs, pneumonia, meningitis, endocarditis, and toxic shock syndrome (27, 28, 170, 192, 250, 251, 347, 365, 369). MRSA emerged as a significant problem in the 1980s. In the 10 years that followed, MRSA infection rates rose dramatically (228). In 2004, the NNIS reported that 59.4% of *S. aureus* infections in U.S. ICUs were methicillin resistant, a 29% increase over the preceding 5 years (227, 228). Interestingly, recent data have shown a decrease in the rates of invasive health care-associated MRSA infections between 2005 and 2008, possibly due to an expansion of MRSA prevention programs among U.S. hospitals (161). Several studies have demonstrated increased mortality from infections due to MRSA compared to that from infections due to methicillin-susceptible *S. aureus* (MSSA), which persists after controlling for the severity of underlying illnesses (77, 92, 299). MRSA also increases length of hospitalization and hospital costs compared with those associated with MSSA (76).

MSSA and MRSA are normally found colonizing the nares and skin of healthy humans (250, 292). Approximately 20 to 30% of persons are colonized with *S. aureus* in the nares; the rate of MRSA colonization is lower, at around 1.5% (115). However, higher rates of nasal MRSA colonization are seen among those with diabetes mellitus, intravenous drug users (IVDUs), patients undergoing hemodialysis, and those with AIDS (344). Carriage of *S. aureus* is an important risk factor for infection, especially among surgical patients and those in the ICU (214, 265, 334). In addition to colonization, risk factors for MRSA infection include recent hospitalization or sur-

TABLE 2. Epidemiologically significant pathogens[b]

Pathogen	Risk factors for colonization and/or infection	Commonly associated infections	Impact[a]
HA-MRSA	Recent hospitalization, hemodialysis, diabetes mellitus, IVDU, surgery, AIDS	BSIs, pneumonia, SSI, endocarditis, skin and soft tissue infection, osteomyelitis	Increased cost, $6,916; increased LOS, 2 days; increased attributable mortality compared to MSSA, OR of 1.93
CA-MRSA	Contact with someone known to have CA-MRSA, IVDU, incarceration, MSM, participation in contact sports	BSIs, pneumonia, SSI, endocarditis, skin and soft tissue infection, osteomyelitis	Similar to those of HA-MRSA
VRE	Sharing a hospital room with patient colonized or infected with VRE, older age, duration of antibiotic use, increased no. of antibiotics used, urinary catheter	BSIs, CA-UTI, endocarditis, SSI	Increased cost, $33,000; increased LOS, 22 days; increased mortality, variable
Acinetobacter species	Residence in nursing home, residence in long-term care facility, hospitalization in the previous 3 mo, hospitalization ≥5 days, antibiotic use in the previous 3 mo, hemodialysis, home infusion therapy or wound care in the last 30 days, immunosuppression, family member with MDR pathogen	BSIs, VAP, HAP, SSI, CA-UTI	Increased cost, $50,000; increased LOS, 6–16 days; attributable mortality, 7–15%
Pseudomonas aeruginosa	Residence in nursing home, residence in long-term care facility, hospitalization in the previous 3 mo, hospitalization ≥5 days, antibiotic use in the previous 3 mo, hemodialysis, home infusion therapy or wound care in the last 30 days, immunosuppression, family member with MDR pathogen	BSIs, VAP, HAP, SSI, CA-UTI	
ESBL-producing *Enterobacteriaceae*	Residence in nursing home, residence in long-term care facility, hospitalization in the previous 3 mo, hospitalization ≥5 days, antibiotic use in the previous 3 mo, hemodialysis, home infusion therapy or wound care in the last 30 days, immunosuppression, family member with MDR pathogen	BSIs, VAP, HAP, SSI, CA-UTI	
Carbapenemase-producing Gram-negative organisms	Residence in nursing home, residence in long-term care facility, hospitalization in the previous 3 mo, hospitalization ≥5 days, antibiotic use in the previous 3 mo, hemodialysis, home infusion therapy or wound care in the last 30 days, immunosuppression, family member with MDR pathogen	BSIs, VAP, HAP, SSI, CA-UTI	
Clostridium difficile	Antibiotic use, hospitalization	CDI, pseudomembranous colitis, toxic megacolon	Increased cost, $15,000; increased LOS, 3 days
Candida species	Intravascular catheter use, increased length of hospital stay, broad-spectrum antibiotic use, burns, ICU stay, parenteral nutrition, neutropenia	BSIs, SSI, disseminated candidiasis	Increased cost, $2–4 billion/yr
Aspergillus species	Immunosuppression, neutropenia, exposure to construction and renovation	Pulmonary aspergillosis, tracheobronchial aspergillosis, sinus disease, disseminated aspergillosis	Crude mortality, 45–80%
Nosocomially acquired respiratory viruses	Residence in long-term care facility, immunosuppression, extremes of age, contact with infected or unvaccinated health care worker	RSV, influenza virus, bronchiolitis	Increased cost, $3,860; increased LOS, 5 days
Nosocomially acquired gastrointestinal viruses	Older age, immunocompromised	Norovirus, rotavirus	Outbreak cost, $650,000

[a] Estimated per infection unless otherwise stated.
[b] HA-MRSA, health care-associated methicillin-resistant *S. aureus*; CA-MRSA, community-associated methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*; BSI, bloodstream infection; LOS, length of stay; IVDU, intravenous drug user; SSI, surgical-site infection; MSM, men who have sex with men; VRE, vancomycin-resistant *Enterococcus*; CA-UTI, catheter-associated urinary tract infection; VAP, ventilator-associated pneumonia; HAP, hospital-acquired pneumonia; ESBL, extended-spectrum beta-lactamase; MDR, multidrug resistant; CDI, *Clostridium difficile* infection; ICU, intensive care unit; RSV, respiratory syncytial virus.

gery, dialysis, residence in a long-term care facility, and the presence of percutaneous devices and catheters (39, 189).

Cases of MRSA infection in previously healthy individuals without established risk factors, namely, no contact with the health care system, have been increasingly reported over the last decade (55). These cases have been coined community-associated MRSA (CA-MRSA). Cases of CA-MRSA are classically caused by microbiologically distinct strains of MRSA (most commonly pulsed-field gel electrophoresis type USA300) different from those strains associated with health care-associated MRSA (HA-MRSA) (303). Similarly, risk factors for CA-MRSA infection are distinct. Notable risk factors for CA-MRSA infection include close contact with someone colonized or infected with CA-MRSA strains, being an IVDU, incarceration, participation in contact sports, and being a man who has sex with men (30, 176). Recent data suggest the rectum and inguinal area, in addition to the nares, are important ecological niches for CA-MRSA strains (359). In fact, one study found that patients with CA-MRSA strains were colonized at sites other than the nares 25% of the time, compared to only 6% among those with HA-MRSA (359).

Recent studies demonstrated that CA-MRSA strains are increasingly responsible for HAIs (263). Popovich et al. found from 2000 to 2006 that the proportion of CA-MRSA strains causing hospital-onset MRSA BSIs increased from 24% to 49% (263). While CA-MRSA strains may represent an increasing proportion of HAIs due to MRSA, there is currently no evidence that HAIs due to CA-MRSA strains have different outcomes than those caused by HA-MRSA strains (263).

Infection prevention. Hospitalized patients colonized with MRSA are at an increased risk of developing MRSA infections (142). In response to increased risks associated with colonization, poor outcomes due to MRSA infection, and pressure from outside groups, many states and the Department of Veterans Affairs are now requiring routine MRSA surveillance cultures for high-risk patient populations. Active MRSA surveillance and the isolation of MRSA-colonized patients have been shown to control MRSA transmission and decrease MRSA infection rates when applied to high-risk patient populations or in outbreak settings (144, 191, 286, 350). Active surveillance is currently recommended for the prevention of MRSA transmission; however, surveillance frequency and target populations are debated (43). Patients found to be colonized with MRSA should be placed into contact isolation to decrease the risk of transmission to other patients. The routine use of clinical cultures alone does not identify the full reservoir of patients asymptomatically colonized with MRSA (143, 290).

The evidence for universal MRSA surveillance is conflicting (127, 277), and at this time there is no recommendation for universal MRSA screening in the United States (43). Several uncontrolled trials have noted that patients placed in isolation are examined less frequently (167, 289) and exhibit higher rates of depression and anxiety (50). Another study reported an association between contact isolation for MRSA and the incidence of preventable adverse events such as falls and pressure ulcers (312). While these studies are not conclusive, they highlight the need for a thoughtful examination of the risks and benefits of MRSA screening. In order to decrease MRSA rates, active surveillance must be combined with HCW education, hand hygiene, environmental cleaning, contact precautions, and antimicrobial stewardship (43).

There is recent increased interest in MRSA decolonization. An added benefit to decolonization may be to decrease MRSA transmission among patients. Various decolonization regimens have been tried in general medical patients, with mixed results (126, 278, 302). Although patients may be successfully decolonized in the short term, well-designed studies outside the perioperative setting have not demonstrated that decolonization of general medical patients prevents subsequent infections, and there is evidence to suggest that widespread decolonization may promote resistance to mupirocin (278). In contrast, preoperative decolonization of surgical patients colonized with *S. aureus* decreases rates of surgical-site infections (26, 249). Some institutions are now instituting this practice and recommending surveillance and decolonization prior to surgery.

Coagulase-Negative Staphylococci

Colonization with CoNS occurs in all humans shortly after birth, and multiple strains inhabit human skin and mucous membranes (140, 169). Thirty-two species of CoNS are recognized, with *Staphylococcus epidermidis* being the most common species isolated from humans. CoNS are readily able to form biofilms, and for this reason, they most commonly cause infections associated with indwelling foreign devices such as intravenous catheters, shunts, prosthetic joints, and pacemakers (62).

CoNS were the most commonly isolated pathogens from HAIs reported to the NHSN in 2006 and 2007: 5,178 of 33,848 (15.3%) pathogens from 28,502 infections (136). CoNS are the most common cause of CLABSIs and the second most common cause of SSIs (18, 136). Less commonly, CoNS infection is the etiology of CA-UTIs and ventilator-associated pneumonias (VAPs) (136).

The true impact of CoNS infections was unrecognized for years, until Martin et al. reported a CoNS BSI-attributable mortality rate of 14% (205). As it is now recognized as more than a contaminant, the incidence of CoNS infections has risen with the increasing use of intravascular catheters, prosthetic devices, and invasive procedures in combination with increasingly vulnerable hosts (145). Although CoNS infections may be due to endogenous strains from the patient's native flora, there is emerging evidence that strains are often transmitted among hospitalized patients. These nosocomial strains are increasingly antibiotic resistant, and strains with vancomycin resistance have been reported (145).

Vancomycin-Resistant *Enterococcus*

Enterococci, formerly classified as group D *Streptococcus*, have innate antibiotic resistance, with emerging antibiotic resistance related to antimicrobial pressure in and outside health care settings. *Enterococcus faecalis* and *Enterococcus faecium* are common enteric flora in humans and represent the two most clinically significant species. *E. faecalis* tends to be susceptible to ampicillin, with a low percentage of strains being resistant to vancomycin. *E. faecium* is more resistant to ampicillin and more commonly associated with vancomycin resis-

tance (117, 353). Vancomycin resistance is most commonly mediated by the *vanA* gene, which produces altered amino acid residues at the normal site where vancomycin binds to inhibit cell wall synthesis (274). Vancomycin-resistant *Enterococcus* (VRE) infection was first reported in the 1980s but did not become a significant problem within the health care setting until the 1990s, as resistance and infection rates rose rapidly (275).

In the United States, hospitalizations attributable to VRE infections increased from 9,820 in 2000 to 21,352 in 2006 (271). Surveillance data from 1995 to 2002 revealed that 9% of CLABSIs were caused by *Enterococcus* species, of which 2% of *E. faecalis* isolates and 60% of *E. faecium* isolates were vancomycin resistant (353). In a prospective cohort of ICU patients, VRE was associated with increased ICU costs ($33,251), in-hospital mortality (75% versus 24%), and length of stay (22 days) compared to uninfected patients (246). Similarly, a separate study assessing the effect of nosocomial VRE bacteremia on mortality, length of stay, and hospital costs compared to matched controls found an odds ratio (OR) of crude mortality of 2.52 when those with VRE bacteremia were compared to controls (309). Those authors also found a VRE-attributable excess length of stay of 17 days and excess charges of $81,208. Other studies have found similar results (48). While some studies have shown increased mortality due to infections caused by VRE compared to vancomycin-susceptible *Enterococcus* (VSE) (83), other studies have found conflicting results (106, 177, 190, 196, 246, 330), and this point remains debated.

Risk factors for colonization and subsequent infection with VRE include having a hospital roommate colonized or infected with VRE, older age, duration of antibiotic use, specific types and numbers of antibiotics used, and the presence of a urinary catheter (320, 368). Molecular and epidemiological data suggest that VRE may be transmitted to patients directly from contact with infected or colonized patients, from the hands of HCWs, or from contact with contaminated equipment or environmental surfaces (320). Results for the effectiveness of antibiotic stewardship in curtailing VRE transmission, colonization, and infection among groups of patients are mixed (266, 304, 320).

Infection prevention. Increased mortality, longer duration of hospitalization, and increased costs are the basis of recommendations for surveillance for VRE and contact precautions recommended by the Healthcare Infection Control Practices Advisory Committee (HICPAC) (368). Also influencing these recommendations are reports of two VRE outbreaks in the early 1990s that were aborted after contact precautions were instituted, including the mandatory use of gowns and gloves by anyone in contact with infected or colonized patients (32, 33, 275).

Current guidelines for the prevention of nosocomial transmission of VRE recommend (i) active surveillance and contact precautions for colonized or infected individuals, especially in populations with high prevalence or where transmission has been documented; (ii) appropriate hand hygiene by HCWs, with monitoring and feedback of hand hygiene compliance to HCWs; (iii) antimicrobial stewardship to avoid inappropriate or excessive antibiotic use; and (iv) aggressive cleaning and methods to verify the adequacy of environmental cleaning (224, 301). The use of active surveillance should target patients at a high risk of colonization, and the frequency of obtaining surveillance cultures is debated. When instituted, the use of surveillance cultures should be based on the institutional prevalence of VRE and patient risk factors for colonization. Antimicrobial stewardship programs should focus on restricting the use of implicated antibiotics, including those with anaerobic activity, broad-spectrum cephalosporins, and vancomycin, in an effort to decrease selective pressure for vancomycin resistance (224). Routinely used disinfectants such as quaternary ammonium, phenolic, and iodophor germicidals are active against VRE (224). However, several studies have shown improved rates of VRE surface eradication with enhanced disinfection involving a more thorough application of the disinfectant to the surface by drenching either the surface or the cleaning rag (42, 305).

Antibiotic-Resistant Gram-Negative Organisms

Many Gram-negative bacteria are implicated in the most common HAIs, including CLABSIs, CA-UTIs, VAPs, and SSI (136). In 2006 to 2007, NHSN data demonstrated that *E. coli* and *P. aeruginosa* were the Gram-negative organisms most frequently isolated from HAIs, with other frequently isolated organisms including *Klebsiella pneumoniae*, *Enterobacter* species, *Acinetobacter baumannii*, and *Klebsiella oxytoca* (136). These data and others suggest that the proportion of HAIs due to Gram-negative bacteria has increased (179). In fact, the authors of a recent publication from a major university medical center described an increase in primary health care-associated BSIs caused by Gram-negative bacteria from 15.9% in 1999 to 24.1% in 2003 (3).

The proportion of Gram-negative bacteria resistant to available antibiotics is increasing (245). National data demonstrate a significant increase in multidrug resistance (defined as resistance to three or more antibiotic agents from three different antibiotic classes) among several species, including *Klebsiella*, *Acinetobacter*, and *Pseudomonas* spp. (227). In a recent analysis of isolates of *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* reported to the NHSN from January 2006 through December 2008, up to 60% of isolates were found to be MDR (160). In one hospital, susceptibility to ciprofloxacin, an agent with broad Gram-negative coverage, fell from 86% to 76% over 5 years (230). Antibiotic resistance due to extended-spectrum beta-lactamase (ESBL)-producing organisms and carbapenemase-producing *Enterobacteriaceae* has now been reported globally (132).

The most significant risk factors for colonization or infection with MDR Gram-negative bacteria among children and adults are residence in a long-term care or rehabilitation facility, antibiotic treatment in the last 3 months, and hospitalization within the last 3 months (233). Additional risk factors for colonization or infection with MDR Gram-negative bacteria include immunosuppression, hospitalization for 5 days or longer, participation in chronic dialysis, and home infusion therapy or wound care in the last 30 days (7). In the modern health care structure, patients often transition between multiple facilities, and long-term acute-care hospitals have been implicated as the source of regional outbreaks of MDR Gram-negative infections (222).

Infections due to antibiotic-resistant bacteria lead to increased morbidity, mortality, and hospital costs (75, 137). A

cohort study of surgical patients compared patients with resistant Gram-negative infections to those with susceptible Gram-negative infections and found that resistant Gram-negative infections were associated with higher median costs ($80,500 versus $29,604) and longer lengths of stay (29 versus 13 days) (94). Another study estimated mortality attributed to infection with Gram-negative organisms to be 6.5% overall (137). It is worth discussing a few salient examples that are increasingly encountered and are notable for significantly impacting morbidity, mortality, and health care costs.

Extended-spectrum beta-lactamase- and carbapenemase-producing *Enterobacteriaceae*. ESBLs are enzymes produced by Gram-negative organisms, commonly of the family *Enterobacteriaceae*, that hydrolyze the beta-lactam ring of beta-lactam antibiotics, yielding them inactive. ESBLs have become a worldwide problem, and studies have shown that these organisms are associated with increased mortality rates and lengths of hospital stays (112). ESBLs, first described in 1983, are commonly found in *E. coli* and *Klebsiella* species. ESBLs inactivate broad-spectrum cephalosporins and beta-lactamases, and they are associated with beta-lactam resistance and frequent resistance to fluoroquinolones, aminoglycosides, and trimethoprim-sulfamethoxazole (112, 231). Based on a well-designed case-control study, common sites of infection include the urinary tract (51.5%), wounds (15%), catheters (12%), blood (9%), respiratory tract (9%), and intra-abdominal sources (3%) (178). Total antibiotic exposure was the only independent predictor for ESBL production in *E. coli* or *K. pneumoniae.* This study also demonstrated that infections with an ESBL-producing organism increased mortality 1.9-fold, ICU length of stay 1.2-fold, and mean hospital charges 1.7-fold.

Another emerging and concerning resistant class of organisms are those that produce carbapenemases, which are carbapenem-hydrolyzing beta-lactamases. Carbapenemases are classified based on amino acid homology. Class A and D beta-lactamases are referred to as serine beta-lactamases, and this group contains enzymes that function as carbapenemases.

Klebsiella pneumoniae was the first clinically significant organism identified that produced a carbapenemase. These organisms were originally named *Klebsiella pneumoniae* carbapenemase (KPC)-producing organisms. KPC-type carbapenemases are class A serine beta-lactamases. These enzymes reside on transmissible plasmids, and carbapenemases have now been identified in several species of the family *Enterobacteriaceae*. These organisms are now referred to as carbapenemase-producing *Enterobacteriaceae*. The first carbapenemase-producing *Klebsiella* species were reported in the late 1990s (360); however, these organisms did not gain notoriety until outbreaks of KPC-producing *Klebsiella* species were reported around the world (34, 36, 180, 306, 332). Carbapenemases have also been identified in non-*Enterobacteriaceae* species such as *Pseudomonas aeruginosa* (367).

The most recently emerged carbapenemase is the New Delhi metallo-beta-lactamase (NDM-1). This carbapenemase is a member of class B, the metallo-beta-lactamases. NDM-1 was first reported in 2009 in a patient who traveled to New Delhi, India, and acquired a urinary tract infection due to a carbapenem-resistant *K. pneumoniae* strain (364). The strain was found to be resistant to all antibiotics except colistin. The NDM-1 gene is located on a plasmid and is easily transferrable to other organisms. These plasmids also often harbor genes conferring resistance to other classes of antibiotics. NDM-1 has already been reported in other *Enterobacteriaceae* and non-*Enterobacteriaceae* Gram-negative organisms from around the world (53, 165, 175, 220). NDM-1 has now been reported from nearly every continent, with the majority of patients having traveled to India or Pakistan, reflecting worldwide dissemination from a local source (279). The emergence of the NDM-1 strain is alarming given its rapid worldwide spread and the association with other genes conferring antimicrobial resistance, rendering strains carrying the NDM-1 gene resistant to almost all currently available antibiotics.

***Pseudomonas aeruginosa*.** *P. aeruginosa* is ubiquitous in health care settings and is an important pathogen in the immunocompromised and among the critically ill. *P. aeruginosa* becomes resistant to antimicrobials through a variety of mechanisms that lead to MDR *Pseudomonas*, defined as resistance to three or more classes of antipseudomonal antibiotics (112). The increasing use of fluoroquinolones has led to increasing resistance, with 97.1% of MDR *Pseudomonas* strains being resistant to fluoroquinolones (231). One-quarter of 52,637 *P. aeruginosa* isolates reported from 1999 to 2002 were MDR (100). *P. aeruginosa* is a significant nosocomial pathogen. In a cohort of 489 patients, one-third of *P. aeruginosa* infections were nosocomial (49). Sites of infection included wound (41%), urine (22%), respiratory tract (21%), effusion (5%), blood (4%), and tissue (4%). This study revealed a relationship between increasing *P. aeruginosa* resistance and increasing mortality and length of stay.

Water is one of the main environmental reservoirs of *P. aeruginosa*. Outbreaks of *P. aeruginosa* in ICUs have been associated with water faucets colonized with *P. aeruginosa* and tap water used to clean bronchoscopes (24, 273). This organism is a concern due to its associated morbidity, mortality, impact on health care costs, and increasing prevalence; the lack of currently effective antimicrobials for MDR strains; and the absence of new antimicrobials in development for MDR Gram-negative infections.

***Acinetobacter* species.** *Acinetobacter* species have become a growing cause of HAIs with increasing antibiotic resistance (110, 179). *Acinetobacter* species are not only ubiquitous in the environment, they can also live for long periods on equipment and surfaces and are frequent patient colonizers. Due to these characteristics, *A. baumannii* frequently causes outbreaks in hospital settings. Traditionally, these outbreaks are associated with ICUs, respiratory equipment, or water sources and have been difficult to contain because of the associated environmental contamination (101, 199, 331). Surveillance methods used to identify carriers of *Acinetobacter* are insensitive, further hindering infection control and prevention efforts. Resistance profiles of isolates collected during outbreaks show high rates of antibiotic resistance, and in 2003, nearly 70% of isolates were resistant to amikacin (179). Growing numbers of *A. baumannii* strains are MDR, thereby limiting therapeutic options.

Infection prevention. Standard infection control practices should be used for MDR Gram-negative infections. Hand hygiene is imperative when one comes into contact with patients, their secretions, and the environment. Patients should be isolated, and the use of gowns and gloves (contact precautions) is recommended. In some cases, the cohorting of patients with similar organisms is used to prevent transmission (56). The

role of active surveillance is less clear for MDR Gram-negative organisms; however, active surveillance has been effective in controlling outbreaks of carbapenemase-producing *Enterobacteriaceae* (223).

Few studies aimed at estimating the proportion of resistant Gram-negative organisms due to antibiotic use compared to the proportion due to patient-to-patient transmission have been conducted in nonoutbreak settings, with a significant variability in reported estimates (22, 107, 130, 131, 156, 219, 238, 241). Harris and colleagues have provided evidence that some strains of *Klebsiella* are transmitted in ICU patients (129). Of the 27 patients who acquired *Klebsiella pneumoniae* infection, 52% were transmitted from patient to patient. These data suggest that in the setting of outbreaks and in certain high-risk groups, there may be a role for case finding and active surveillance.

Due to the growing challenge of carbapenem-resistant and carbapenemase-producing *Enterobacteriaceae*, the CDC and HICPAC recently provided updated infection prevention and control guidelines for these organisms in acute-care facilities (56). The guidelines recommend the strict use of hand hygiene when one comes into contact with patients and/or the environment and recommend that all acute-care facilities implement contact precautions for all patients colonized or infected with carbapenem-resistant and carbapenemase-producing *Enterobacteriaceae*. Clinical microbiology laboratories should establish a protocol, consistent with Clinical and Laboratory Standards Institute (CLSI) guidelines (69), for the detection of carbapenem-resistant and carbapenemase-producing *Enterobacteriaceae*.

In areas where these organisms are endemic, facilities should monitor clinical cases due to carbapenem-resistant and carbapenemase-producing *Enterobacteriaceae* and consider intensifying infection control strategies if rates are not decreasing. The guidelines also recommend facilities where carbapenem-resistant and carbapenemase-producing *Enterobacteriaceae* are not endemic review microbiology records at least semiannually. If previously unrecognized cases are found, a single round of active surveillance should be conducted to identify unrecognized sources of colonization where infection control strategies may be targeted. Of note, other experts advocate for a hierarchical and aggressive approach to isolating patients, identifying cases, cohorting, and cleaning the environment (47, 56, 171). An outbreak with a carbapenemase-producing organism requires more aggressive surveillance and case-finding activities.

Not only are antimicrobial-resistant Gram-negative organisms responsible for a significant proportion of HAIs, they are also a group of bacterial organisms becoming more resistant to available antimicrobials, with no new antimicrobials in sight. The recognition of risk factors for infection with these organisms can guide institutional practices to ensure the prevention of colonization and infection.

Clostridium difficile

C. difficile is ubiquitous in nature and is a part of the normal intestinal flora of 1 to 3% of the healthy human population (87). *C. difficile* has a spectrum of clinical presentations, ranging from asymptomatic carriage to mild diarrhea, severe colitis, toxic megacolon, and death.

Clostridium difficile infections (CDIs) are increasing in incidence worldwide (86). The number of U.S. hospital discharges for which CDI was listed as a discharge diagnosis doubled from 82,000 in 1996 to 178,000 in 2003 (208). Early studies identified hospitalization as an additional risk factor for *C. difficile* infection. Studies in the 1980s showed high rates (20% to 40%) of colonization with *C. difficile* in hospitalized adults, as opposed to lower rates (1% to 3%) of colonization in healthy adults (209, 333). Studies have estimated the length of stay related to CDIs to be approximately 3 days longer than the length of stay for patients without CDIs, with a mean incremental cost per stay of $14,507.47 (235).

C. difficile may exist as normal commensal colonic bacteria, able to replicate and cause infection when antibiotics disturb the normal colonic flora. As *C. difficile* replicates, it produces an enterotoxin (toxin A) and a cytotoxin (toxin B). Recent data suggest that toxin B is primarily responsible for colonic injury and the well-recognized manifestations of infection (193).

In the early 2000s, clinicians around the world noted an increased severity among patients with CDIs (15, 207). The pronounced form of the disease seen was more refractory to therapy; was more commonly associated with toxic megacolon, necessitating colectomy; and led to death in increased numbers. The elderly were affected in increased numbers. The strain of *C. difficile* responsible for this more severe presentation was termed the BI/NAP1 strain. This hypervirulent strain produces substantially larger amounts of toxins A and B than other strains of *C. difficile* (338), is associated with a deletion in the gene responsible for the downregulation of toxin production, and is highly resistant to fluoroquinolones (15, 86, 87). Severe CDI (with and without the epidemic BI/NAP1 strain) was also recently reported for previously healthy individuals with no health care exposure as well as peripartum women (60, 108).

C. difficile is the consummate nosocomial pathogen. This organism quickly contaminates the environment. In one recent study, researchers sampled the air and environmental surfaces adjacent to patients with symptomatic CDI and found *C. difficile* isolated from the air and environmental sources near a majority of the patients (23). Molecular testing established a link between airborne spread, environmental contamination, and CDI cases. This finding emphasizes the need for contact isolation and private rooms for patients with confirmed or suspected CDI.

C. difficile spores can survive for up to 70 days on surfaces and are resistant to traditionally used cleaning solutions and alcohol-based hand hygiene products (87, 358). Because of the resistance of the spores of *C. difficile* to alcohol, the use of alcohol-based hand hygiene products is not recommended (67). Hand washing with soap and water is recommended after contact with a patient with CDI (86). The increased use of alcohol-based hand hygiene products has not been identified as a risk factor for increasing rates of CDI (114); however, soap and water are still recommended over alcohol-based hand hygiene products.

Diagnostic modalities for CDI are changing as molecular methodologies are replacing older techniques such as toxin enzyme immunoassay (EIA), direct cytotoxin testing, and two-

step algorithms, including glutamate dehydrogenase (GDH) screening followed by direct cytotoxin testing. Compared to the "gold standard" of enrichment culture, PCR-based molecular testing has a sensitivity and specificity of 94% (325). The sensitivity of EIA is 60%, and that of combined GDH algorithms is 73% (325). One limitation of newer molecular diagnostics is the possibility of false-positive diagnoses, as patients may carry toxigenic strains of *C. difficile* but not have CDI. Test results must be combined with clinical information for appropriate interpretations. Where available, newer molecular diagnostic methodologies are likely to replace EIA and GDH-based testing.

Infection prevention. Recently reported updated clinical practice guidelines for the prevention of CDI recommend employing standardized case definitions for the surveillance of both health care facility (HCF)-onset and HCF-associated CDIs in all inpatient health care facilities (72). These guidelines do not recommend the routine identification of asymptomatic carriers. The guidelines recommend placing patients with CDI in contact isolation for the duration of diarrhea. HCW compliance with hand hygiene using soap and water should be encouraged. In addition, chlorine-containing cleaning agents or other sporicidal agents should be used for environmental decontamination. The guidelines also recommend implementing an antimicrobial stewardship program in order to minimize the frequency and duration of antimicrobial agents that increase the risk of CDI (72).

Mycobacterial Pathogens

***Mycobacterium tuberculosis*.** *Mycobacterium tuberculosis* is a small organism spread from person to person via airborne droplet nuclei. Organisms can linger for up to 30 min in the air in poorly ventilated areas. Interest in the transmission of *M. tuberculosis* within health care settings increased during the late 1980s and 1990s with the growing HIV epidemic and an increase in reported cases of tuberculosis (212, 307). Reports of several health care-associated transmissions of MDR *M. tuberculosis* strains prompted the CDC to publish guidelines for the prevention of *M. tuberculosis* infections in health care settings (155).

(i) Infection prevention. These guidelines recommend a hierarchy of control measures, including administrative controls, environmental controls, and respiratory protection for HCWs and patients. Administrative controls include policies and procedures to guarantee that patients that are likely to have tuberculosis are rapidly identified, placed into appropriate airborne isolation, diagnosed, and appropriately treated. Other administrative control measures include surveillance for latent tuberculosis infection in HCWs with a comprehensive tuberculin skin testing program and HCW education on the components of and their role in an effective tuberculosis control program. Environmental controls include ensuring that airborne isolation rooms have negative air pressure compared to the surrounding corridor and an appropriate number of air exchanges through adequate ventilation systems.

It is recommended that HCWs wear personal respiratory protection when entering areas where exposure to *M. tuberculosis* may occur. OSHA's minimum requirement for personal respiratory protection is the N95 particulate respirator (155). Despite limitations of N95 fit testing (70, 97), OSHA requires fit testing be performed annually for HCWs. HEPA respirators and powered air-purifying respirators (PAPRs) are other forms of personal respiratory protection that may be needed for those performing high-risk procedures, such as bronchoscopy, on patients suspected of having tuberculosis.

This hierarchy of control measures has been effective in terminating outbreaks of tuberculosis and preventing nosocomial transmission (25, 97). These guidelines buttressed the nation's tuberculosis control programs, which decreased *M. tuberculosis* rates to 3.2% in 2004, the lowest case rate since reporting began in 1953. Simultaneously, transmission rates of *M. tuberculosis* fell within the health care setting (155). The primary lessons learned were the importance of case identification and early isolation. For this reason, clinical diligence and caution are necessary to identify potential new cases of *M. tuberculosis*.

Nontuberculous mycobacteria. Nontuberculous mycobacteria (NTM) can rarely cause HAIs. NTM have been associated with both outbreaks and pseudo-outbreaks in health care settings (111). Primary sites of infection include the respiratory tract, bloodstream secondary to hemodialysis or intravenous catheters, surgical sites, and soft tissue (258). The common source of all of these infections was a contaminated water source or contaminated solutions used during procedures.

Interpretation of the significance of NTM from clinical specimens is difficult, as the organism can colonize, contaminate specimens, or represent true infection. The significance of NTM in a specimen must be evaluated based on the patient's signs and symptoms. NTM infections tend to be more indolent, more difficult to culture, and harder to diagnosis than other bacterial HAIs. In some situations, they may not be diagnosed until the patient has left the health care setting, and commonly, two positive microbiological samples must be obtained. Finally, in order to confirm the diagnosis, the clinician must have a high index of suspicion of mycobacterial disease.

(i) Infection prevention. These organisms exist everywhere in the environment, including soil and water. NTM are widely known to colonize drinking water systems, and up to 60 to 100% of drinking water systems in hospitals and hemodialysis units are colonized by NTM (258). The prevention of health care-associated NTM infections is difficult, as these organisms are hardy and resistant to standard disinfection methods. Disinfectants such as glutaraldehyde, peracetic acid, iodophors, isopropyl alcohol, chlorine, and formaldehyde, which are mycobactericidal, should be used to disinfect contaminated surfaces and instruments that come into contact with mucosal surfaces (i.e., endoscopes). Water systems colonized with NTM can be cleaned with high concentrations of chlorine or temporary increases in water temperature to >70°C. The control of outbreaks in the health care setting requires diligent surveillance, identification of the source, and effective control measures such as the disinfection of equipment and cleaning of water systems (258).

Health Care-Associated Fungal Infections

The incidence of health care-associated invasive fungal infections has risen over the last 10 years (252). This increase is likely due to an aging population, increases in cancer inci-

dence, the broader use of myeloablative therapies, and growing numbers of solid-organ and hematopoietic stem cell transplants. *Candida* species are the most common cause of these HAIs (152). Minimal immune suppression is needed to predispose an individual to infections with *Candida* species. *Aspergillus* species are the second most common cause of health care-associated invasive fungal infections, as they tend to occur in patients with more significant immunosuppression and prolonged neutropenia (152, 202). Other mold infections such as *Fusarium* and mucormycosis are seen in the most severely immunocompromised patients and are relatively uncommon. Endemic mycoses such as *Histoplasma*, *Coccidioides*, and *Blastomyces* are rarely acquired in health care settings. For the purposes of this review, we will focus on health care-associated *Candida* and *Aspergillus* infections.

***Candida* species.** *Candida* species are the third most common nosocomial bloodstream isolates (353, 354). The incidence of invasive candidiasis increased 15-fold between the 1970s and the 1990s (164, 257), and it has been estimated that the health care costs associated with invasive candidiasis in the United States total $2 billion to 4 billion per year (352, 366). Rates of invasive *Candida* may be leveling off, possibly due to the increased use of prophylactic and empirical antifungal therapy in immunocompromised hosts; however, data are conflicting (16, 295). *Candida albicans* has historically been the predominant species causing invasive *Candida* infections. Since the 1990s, there has been an increase in the proportion of non-*C. albicans* species causing invasive candidiasis (252, 354). The most common non-*C. albicans* species causing invasive candidiasis include *Candida glabrata*, *C. tropicalis*, *C. krusei*, and *C. parapsilosis*. Whether exposure to azole antifungals is a risk factor for invasive candidiasis due to non-*C. albicans* species is debated (148, 182, 313).

Unlike other fungal infections, immunosuppression is not the predominant risk factor for invasive candidiasis. Identified risk factors for health care-associated invasive candidiasis include the presence of a central venous catheter, prolonged length of hospitalization, broad-spectrum antibiotic use, burns, ICU stay, and parenteral nutrition (118, 152, 351, 353). Host colonization by *Candida* species is a precursor and risk factor for invasive candidiasis (203, 206). Broad-spectrum antibiotic use has been associated with increases in *Candida* colonization and the risk of disseminated candidiasis (152, 200). Similar to burns and percutaneous catheter placement, which disrupt skin barriers, chemotherapy and radiation induce the disruption of gut mucosal barriers and increase the risk of invasive *Candida* infections (270, 291). Neutropenia is associated with an increased risk of invasive candidiasis and increased mortality due to invasive candidiasis (234). Other etiologies of impaired phagocyte activity, such as corticosteroid use and diabetes mellitus, are also associated with an increased risk of invasive candidiasis (234).

(i) Infection prevention. The CDC published recommendations for preventing opportunistic infections among hematopoietic stem cell transplant patients in 2000 (57). These guidelines can be applied to immunocompromised hosts in all health care settings. This document recognizes hand washing as the single most effective procedure for preventing HAIs and recommends encouraging proper HCW hand hygiene, given that *Candida* species can be carried on the hands. The guidelines also recommend administering fluconazole prophylaxis during neutropenia to prevent invasive disease with fluconazole-susceptible *Candida* species. This practice is usually reserved for patients undergoing allogeneic hematopoietic stem cell transplantation or those with prolonged neutropenia and mucosal damage from intensive-conditioning chemotherapeutic regimens.

***Aspergillus* species.** *Aspergillus* species are the second most common cause of health care-associated fungal infections. The estimated incidence of invasive aspergillosis is 5 cases per 100,000 population, with an associated crude mortality rate of 45% to upwards of 80% (73, 82, 151, 352).

Unlike invasive *Candida* infections, which usually arise from a patient's endogenous flora, *Aspergillus* infection is most commonly acquired by inhaling spores (119, 221). *Aspergillus* is a genus consisting of several hundred molds, which are ubiquitous in the environment. *Aspergillus* species are abundant in soil and grow on many plants, trees, fruits, and vegetables. Health care environmental sources of inhaled *Aspergillus* spores include dust from construction and renovation and water droplets. Dry mopping and the use of non-HEPA-filtered vacuums have also been associated with a greater spread of *Aspergillus* spores (326). Hospital water systems have been implicated as sources of *Aspergillus* spores (9), and high spore counts in the air have been found during facility construction and renovation and were associated with outbreaks of invasive aspergillosis (12, 138, 168, 188, 253). The most common species causing invasive aspergillosis in health care settings are *Aspergillus fumigatus*, *A. flavus*, and *A. niger* (35).

Aspergillus rarely causes invasive disease in immunocompetent patients and is more commonly seen in those with severe immunocompromising conditions such as hematological malignancies, solid-organ or hematopoietic stem cell transplants, and prolonged high-dose steroid use. Invasive *Aspergillus* is less common in patients with HIV. When invasive *Aspergillus* does occur in those with HIV, it is usually among those with $CD4^+$ T-lymphocyte counts less than 50 cells/μl and those who are severely neutropenic (225, 337). In those having undergone hematopoietic stem cell transplants, the incidence of invasive *Aspergillus* infections is bimodal, with increased rates of infection seen at 2 weeks and then again at 3 months posttransplant (201, 335).

(i) Infection prevention. To prevent nosocomial invasive *Aspergillus* infections, the CDC and others recommend that severely immunocompromised patients avoid hospital construction or renovation areas (57, 361). These patients should wear masks when outside inpatient rooms in order to reduce potential exposure to spores (267). Per the guidelines, the following measures should be implemented during construction and renovation in order to minimize fungal spore counts and potential exposure to severely immunocompromised patients: (i) HEPA filtration, (ii) positive air pressure in patient rooms in relation to the corridor so that air flows out of patient rooms, (iii) positive air pressure in ward corridors in relation to corridors outside the ward so that air flows from the ward into the surrounding area, (iv) correctly sealed rooms and windows, (v) high rates of room air exchange (at least 12 air changes/h), and (vi) placement of sealed plastic barriers between patient care and renovation or construction areas to prevent dust from entering patient rooms (57, 361). Having patients wear masks,

laminar airflow, and HEPA filtration systems have all been associated with lower rates of nosocomial invasive aspergillosis (14, 267, 297). The infection control team must collaborate with engineers, architects, and construction personnel to complete an infection control risk assessment (ICRA) before a construction or renovation project begins in order to ensure that the above-mentioned measures are in place. The role of the infection prevention team in construction and renovation will be discussed in greater detail in the latter part of this review.

Respiratory Infections

Respiratory syncytial virus. Respiratory syncytial virus (RSV) is a single-stranded RNA virus of the family *Paramyxoviridae*. RSV causes a spectrum of illness from asymptomatic carriage to minor upper respiratory tract symptoms similar to those of the common cold. However, in certain hosts such as young children, RSV causes bronchiolitis and occasionally progresses to a severe respiratory illness requiring hospitalization. RSV infection and subsequent outbreaks are well described for infants and children; however, other populations at risk of acquiring and transmitting the virus include neonates, medical personnel, older adults with comorbidities, and immunocompromised patients of all ages. RSV has been estimated to cause 27% of viral respiratory illnesses in institutionalized adults (123). Immunocompromised patients are at risk of severe infection. Investigators have reported that RSV caused 31% of viral respiratory illnesses among adult cancer patients (78). Over 50% of the infections were acquired nosocomially, and among transplant patients, the mortality rate was 20% to 100%.

RSV is easily transmitted in health care settings. Patients and visitors within the health care setting are capable of acquiring, shedding, and transmitting infection. Medical personnel frequently have asymptomatic infection, and 15% to 20% of asymptomatically infected hosts shed significant amounts of RSV in their respiratory secretions (123). Young children and immunocompromised individuals shed virus for extended periods of time, leading to an increased potential for transmission (124, 125). RSV in secretions remains viable in the environment for up to 6 to 12 h on fomites, and this may be a source of transmission (123). In addition to fomites, RSV may spread by large-particle droplets as well as small-particle aerosols generated by coughing or sneezing. These small particles may travel more than 1.8 m and therefore do not require close person-to-person contact for transmission (123). Although RSV may spread by the droplet and aerosol routes, direct contact with infected respiratory secretions is the most common mode of transmission (123, 300). Finally, RSV infection is not followed by protective immunity, and repeated infections are possible (123). This again leads to a large population of susceptible individuals, as no one is completely protected from prior infections.

(i) Infection prevention. The prevention of health care transmission of RSV requires a multimodal strategy (163). The detection of patients with respiratory viral infections requires a high level of suspicion during characteristic times of the year. By detecting RSV arrival in the health care setting, infection control practitioners can then proactively implement educational and infection control procedures to curtail spread. While individual hospitals may manage RSV surveillance differently, most hospitals institute RSV surveillance when the first seasonal case has been identified and continue surveillance until 2 weeks after the last case is identified. Strict and effective hand hygiene is paramount to the prevention of spread. The CDC recommends that infants, young children, and immunocompromised adults with RSV infection be placed in contact precautions and that masks be worn by HCWs as a part of standard precautions (181, 194, 300). Many facilities also place patients with RSV infection under droplet precaution conditions, given the potential for droplet transmission; however, this recommendation is controversial. During the respiratory virus season, all patients with characteristic symptoms and potential or proven RSV infection are either cohorted into rooms with other infected patients or placed into private rooms. To limit the introduction of infection, hospitals can limit the number of visitors to the health care setting during the RSV season. Screening of visitors for respiratory symptoms is limited by the potential for asymptomatic infection; therefore, transmission may still occur (123). Programs that include case finding, preventing new cases from entering the system, and the isolation and cohorting of patients can prevent nosocomial transmission.

Influenza virus. Influenza virus is an RNA virus from the family *Orthomyxoviridae*. It infects birds and mammals and causes an illness commonly more severe than RSV, with high fever, headache, myalgias, sore throat, and cough. Severe cases can be complicated by secondary bacterial infections. Nausea, vomiting, and diarrhea are occasional presenting symptoms, especially in children. Influenza is transmitted through the inhalation of large particle droplets as well as through direct contact, as the virus can remain viable on the skin for at least 5 min (197). Healthy adults generally shed virus for an average of 4 days, and infants, children, and immunocompromised patients shed virus for longer, often weeks (197).

The WHO estimates that worldwide annual influenza epidemics affect 5% to 10% of the population, with between 250,000 and 500,000 deaths annually (197). Annual influenza epidemics increase health care utilization in the United States and result in 3.1 million hospital days and a total economic burden of $87.1 billion (218).

Nosocomial influenza virus infection occurs during annual influenza epidemics, as incoming patients and HCWs provide a continuous reservoir for the spread of influenza virus. Because of its short incubation period and the potential for asymptomatic shedding of virus, influenza virus transmission is commonly unrecognized. Patients may transmit influenza to uninfected patients; however, unvaccinated HCWs are most commonly linked to the nosocomial spread of influenza (197, 198). Only 40% of HCWs receive an annual influenza virus vaccine due to concerns about adverse side effects, the perceived low risk for contracting influenza, and the perceived lack of vaccine effectiveness (197). Because of the risks to patients and the costs to the health care sector, many groups are embracing the strategy of mandatory influenza virus vaccination as a condition for employment in health care settings. Those groups who have championed mandatory influenza virus vaccination have shown sustained HCW influenza virus vaccination rates of more than 98% (13, 269).

(i) Infection prevention. Much like RSV, the prevention of health care-associated influenza outbreaks requires a knowledge of community influenza activity, surveillance, the identification of patients at risk for respiratory disease, isolating or cohorting of patients, and the use of droplet precautions. Many IPs and public health authorities recommend aggressive testing once influenza activity is noted in the local community or in the health care setting. Diagnosis has become relatively simple, with several rapid antigen detection tests being available, which are performed on nasopharyngeal samples; however, the sensitivities of these tests range from 40% to 70%. Therefore, these tests cannot rule out influenza virus infection with 100% accuracy (79, 128, 149, 268). If the direct antigen test is negative, most laboratories will perform a subsequent direct immunofluorescence assay (DFA), followed by a viral culture if the DFA is negative (197). Recently, multiplex PCR assays are being introduced into clinical laboratories and replacing culture techniques. Testing is stopped and influenza virus is reported when any test in the algorithm is positive.

When a patient presents with clinical symptoms consistent with influenza, the patient should be placed into a private room or cohorted with other probable or confirmed influenza cases and placed on droplet precautions. All HCWs and visitors should wear gowns, gloves, and a respiratory mask with eye protection to prevent transmission by direct contact or through respiratory droplets from the patient (197).

The 2009-2010 influenza A(H1N1) pandemic rejuvenated controversy over which type of respiratory protection, surgical mask or N95 respirator mask, is necessary to prevent the transmission of influenza virus to HCWs. The prevention of spread to HCWs is important given that HCWs are a significant reservoir for transmission to patients. The controversy stems from data suggesting the influenza virus can be transmitted by smaller particles that would not be filtered by surgical masks (323). During the 2009 influenza A(H1N1) pandemic, the WHO and SHEA recommended the use of surgical masks for most patient care activities, while the CDC and the Institute of Medicine (IOM) recommended N95 respirators (58, 184, 308, 356). A recent multicenter randomized clinical trial compared surgical masks to N95 respirators for the prevention of transmission of influenza among HCWs in acute health care settings. That study found that surgical masks were noninferior to N95 respirators in preventing influenza virus infection (23.6% versus 22.9%; $P = 0.86$) (186). More recently, the CDC currently recommends that HCWs wear a surgical mask when entering the room of a patient with suspected or confirmed seasonal influenza virus infection and the equivalent of an N95 respirator for those HCWs participating in aerosol-generating procedures such as sputum induction and intubation (59).

In the event of a health care-associated influenza outbreak, exposed patients with high-risk conditions and unvaccinated HCWs should be vaccinated with influenza virus vaccine and receive appropriate prophylaxis with anti-influenza virus antiviral agents (adamantanes or neuraminidase inhibitors as appropriate) (197). Antiviral agents should be administered for at least 2 weeks if the transmission of influenza virus continues to be documented (197). Because unvaccinated HCWs are the main source of transmission in this setting, education and annual influenza virus vaccination campaigns as well as the consideration of a mandatory employee influenza virus vaccination policy should be infection control priorities.

Pertussis. Pertussis, or whooping cough, is caused by the bacterium *Bordetella pertussis*. Two closely related organisms are *Bordetella parapertussis*, which causes a pertussis-like syndrome in humans, and *Bordetella bronchiseptica*, which produces respiratory tract illness in animals. *Bordetella bronchiseptica* has occasionally been reported in humans, including several recent case reports of HIV-infected patients (88).

This highly transmissible infection is seriously underreported, especially among adults (229). The lack of awareness and diagnosis of adult pertussis in patients with prolonged cough and the high incidence of subclinical disease (40%) result in intrafamilial and nosocomial disease. This is a major factor in the increase in rates of pertussis currently seen among infants. Infants, particularly those less than 6 months of age, are at the highest risk for pertussis and its complications (pneumonia, seizures, encephalopathy, and death). The widespread use of pertussis vaccines in the United States has reduced the number of reported pertussis cases and deaths by 95%. Despite increasing vaccine use among preschool children (61) and mandatory vaccination among school-age children, pertussis remains endemic in the United States.

The transmission of pertussis in hospital settings has been documented by numerous reports (65, 183). In a 1993 Cincinnati, OH, outbreak, 195 employees were evaluated for suspected pertussis; 78 were placed on 5-day furloughs and erythromycin therapy for 14 days. In addition, postexposure prophylaxis was recommended for 505 employees. The costs of control measures were estimated at $85,000 (65). These outbreaks have resulted from the failure to recognize and isolate infected infants and children, the failure to recognize and treat disease in staff members, and the failure to institute control measure rapidly (341). The cornerstone of prevention is having a high index of suspicion and isolation. Because of the risk of transmission to and from HCWs, the CDC now recommends acellular vaccination for pertussis (Tdap) for all HCWs (174). Exposed personnel who have not received Tdap should receive prophylaxis with erythromycin, clarithromycin, or azithromycin.

Gastrointestinal Viruses

Several viruses are important causes of gastrointestinal infection in health care settings, including norovirus and rotavirus. Noroviruses are RNA viruses of the family *Caliciviridae* and are a leading cause of viral gastroenteritis. They infect roughly 23 million people annually in the United States, but this number likely underestimates the true incidence (157). Community-based outbreaks are notable, but in the health care setting, the disease can be explosive (157, 287). Historically, the United States has not supported a national surveillance system for viral gastroenteritis because of diagnostic challenges and the minor impact of infections. In 2008, the CDC requested a voluntary reporting of all acute gastroenteritis outbreaks to the National Outbreak Reporting System (287).

Infections can affect people of all ages; however, those most susceptible and at risk for severe complications include the elderly and immunocompromised individuals. Norovirus causes a spectrum of illness but is characterized by diarrhea, abdominal pain,

nausea, vomiting, and fever. The diagnosis of this infection is probable for someone with these symptoms for 12 to 60 h, a documented sick contact, and stool cultures negative for bacterial pathogens (287). Stool PCR testing is available in most state and national public health laboratories and is useful in the setting of an outbreak to guide prevention, control, and treatment strategies.

Norovirus is highly transmissible. Fewer than 10 to 100 virions are sufficient to cause infection, and these heat- and cold-resistant virions can persist for weeks on environmental surfaces. Norovirus is classically transmitted in a fecal-oral fashion, and spread occurs through contaminated food or water or contact with contaminated surfaces or fomites. Vomiting leads to the aerosolization of particles and has been proposed to be an additional mechanism of transmission.

Rotavirus is the leading cause of viral gastroenteritis in infants and young children and rarely affects adults (98). Rotavirus is a member of the *Reoviridae* family of viruses. Much like norovirus, most rotavirus infections are contracted in the community, but HAIs have been documented as well. One study estimated that 25% of hospital admissions for rotavirus in the United States were due to health care-associated rotavirus infection (98). Manifestations of rotavirus infection can range from a mild diarrheal illness to severe dehydration and death, which is more common in developing countries. Rotavirus is highly transmissible at low doses and can survive for extended periods on environmental surfaces. Both the CDC and the Advisory Committee on Immunization Practices (ACIP) recommend the routine vaccination of infants with rotavirus vaccine (74).

Infection prevention. These and related viruses are highly resistant to standard disinfectants. Bleach solutions or hydrogen peroxide-based disinfectants must be used. Commonly used alcohol-based hand cleaners are also insufficient for the removal of norovirus, and patients and HCWs must wash their hands with soap and water for 1 min and rinse for 20 s for adequate decontamination (162). Measures to prevent the spread of norovirus should be aggressive and focus on the identification and isolation of infected patients, proper disinfection of rooms or wards, and education of HCWs about the spread of the virus and precautions needed. Health care-associated outbreaks of norovirus are costly and difficult to eradicate. For example, at the Johns Hopkins Hospital a norovirus outbreak affected over 500 patients and HCWs and ultimately cost an estimated $650,000 (157). After the outbreak was recognized, patients were cohorted and isolated, units were cleaned and disinfected using strict protocols, and ill HCWs were furloughed. However, it was not until visitors were prohibited, affected wards were closed, and nurses were cohorted that the outbreak was terminated (157, 287).

Nosocomial Blood-Borne Pathogens

In the health care setting, blood-borne pathogens pose a threat to patients and HCWs. HBV, HCV, and HIV represent the three most commonly transmitted blood-borne viruses in health care settings (19). Percutaneous injuries commonly occur via needle sticks or contact with sharp objects such as a scalpel. Surgeons are at the greatest risk of percutaneous injuries. During surgery, most (73%) injuries are related to suturing, operations lasting longer than 1 h, and procedures with more than 250 ml of blood loss (244, 327). Blood-borne pathogens are generally transmitted from patient to provider, with fewer infections being transmitted from patient to patient and even fewer being transmitted from provider to patient. However, increased awareness and the implementation of preventative measures suggest that HCWs are less frequently exposed to blood-borne pathogens than they were 10 to 15 years ago (68). Still, a risk exists for blood-borne infection, and the likelihood of infection after exposure to a blood-borne pathogen is multifactorial and differs for each virus.

Patients are also at risk of acquisition of blood-borne pathogens once they come into contact with the health care system. This risk has fallen significantly in developed countries since 1985, when widespread HIV, HBV, and HCV testing became available; however, the nosocomial spread of blood-borne pathogens remains a problem in developing countries. In this setting, transmission to patients occurs following transfusion of infected blood or blood products, the use of infected transplanted organs, or invasive procedures performed without sterile needles or syringes and rarely occurs through transmission from an infected HCW (105).

It is estimated that approximately 5% of worldwide AIDS cases are acquired through the transfusion of contaminated blood products (105). The screening of blood donors for HIV has not been universally adopted around the world despite the demonstration that this practice reduces transfusion-related transmission. In fact, it is estimated that 40% of donated blood in Kenya is not screened for blood-borne pathogens, and in 2007, the transmission of HIV to 103 children through unscreened blood products was reported in Kazakhstan (1, 105).

The reuse of needles and syringes is a practice still reported in resource-limited settings, many of which have a high prevalence of HIV and hepatitis viruses. The transmission of HIV and HCV has been linked to the contamination and reuse of multidose medication vials (52, 166). The transmission of all three primary blood-borne pathogens to patients with chronic renal failure through the reuse of hemodialysis filters, reused needles, and a lack of infection control practices has been documented.

Lastly, HCWs rarely transmit HIV or hepatitis viruses to patients (19, 46). Mathematical modeling suggests that 2 to 24 patients per million procedures will be infected if the procedure is performed by an HIV-positive surgeon (105). The most famous account of HIV transmission from an HCW to a patient occurred in 1995, when an HIV-positive dentist reportedly infected six patients (66). Several outbreaks of HCV and HBV have been associated with infected surgeons, although the precise mode of transmission is disputed (46, 93). In general, these transmissions involve health care providers performing invasive and "exposure-prone" procedures where blind suturing and other practices occur. Furthermore, these transmissions occurred prior to the widespread use of standard precautions and other barrier precautions such as single or double gloving.

Reducing nosocomial blood-borne pathogen transmission requires education, infrastructure, and resources. In 1991, the CDC published guidelines for the prevention of transmission of HIV and HBV to patients (51). Since that time, recommendations have expanded. In all settings, the public and HCWs

need to be educated about the risk of transmission of HIV and hepatitis viruses from unsanitary and unsafe health care practices. This will encourage transparency in hospitals. Surveillance for blood-borne pathogen exposures among HCWs is not mandatory in many countries. All countries should screen blood and organ donors for blood-borne pathogens. Other necessary prevention strategies include (i) standard precautions, (ii) adequate and low-cost disinfectants, (iii) proper sterilization of equipment, and (iv) policies limiting the reuse of certain supplies and equipment. Single-use safety injection devices have revolutionized modern medicine and should be made available at a low cost in resource-limited settings.

HIV. Although it is the most commonly feared blood-borne virus, the nosocomial transmission of HIV is less commonly reported than HBV and HCV. This is likely due to the lower global burden of HIV than HBV or HCV and lower blood titers of HIV (105). Based on prospective studies of HCWs, the average risk of transmission of HIV after occupational percutaneous exposure is 0.3%, with the risk of transmission after mucosal exposure being much lower, at 0.09% (19). No transmission of HIV through the contact of blood with nonintact skin occurred in these studies. Therefore, the risk of HIV transmission appears to be low (113). Similarly, the risk of HIV transmission after exposure to other potentially infectious body fluids or tissues has not been well studied. In one study, 559 HCWs reported cutaneous exposure to different potentially infectious body fluids from patients presumed to have HIV, and no HCW became infected (95).

Four factors increase the risk of HIV transmission after percutaneous exposure. These include (i) deep injury, (ii) visible blood from the source patient on the device that caused the injury, (iii) injury from a large-gauge hollow-bore needle placed directly into a vein or artery of the source patient, and (iv) exposure to blood from a patient known to have a high plasma HIV viral load or symptomatic AIDS (19, 105). The risk is higher in an area with a high prevalence of HIV. Patients taking and responding to antiretroviral therapy with lower plasma viral loads are less likely to transmit HIV (19). *In vitro* models have demonstrated that wearing gloves directly reduces the amount of blood transferred from a device to the site of injury (19).

As of 2001, 57 confirmed cases of occupationally acquired HIV infection and 138 possible occupational HIV infections had been reported to the U.S. National Surveillance for Occupationally Acquired HIV Infection (85). The reporting of possible occupational exposure to HIV is voluntary, and available data likely underrepresent the total number of cases.

(i) Infection prevention. Since 1996, the U.S. Public Health Service has issued guidelines for occupational HIV exposure that are used in most health care settings (243). Health care facilities should have a system in place that includes a protocol for reporting exposures followed by evaluation, counseling, and treatment by a provider trained in postexposure prophylaxis and counseling regarding blood-borne pathogens. After exposure, HCWs should be advised to immediately clean the exposed site. Skin wounds should be cleaned with soap and running water. Exposed mucous membranes should be flushed with copious amounts of water. HCWs should be counseled to immediately notify occupational health authorities because the sooner they receive postexposure prophylaxis, the better.

Postexposure prophylaxis is recommended on an individual basis based on the type of exposure (percutaneous versus mucosal), characteristics of the patient (high versus low HIV plasma viral load), and risk of exposure to drug-resistant virus. Retrospective case-control studies of HCWs, animal data, and data from pregnant women have all shown that zidovudine reduces the risk of HIV transmission after exposure by up to 81% (19, 44). Zidovudine is the only antiretroviral that has been shown to prevent HIV transmission in humans; however, due to ethical reasons and the lack of adequate case numbers, no prospective studies have evaluated other antiretrovirals. Combination postexposure regimens directed at drug-resistant viruses may be needed, and this decision should be made in concert with an HIV specialist with expertise in postexposure prophylaxis.

HBV. HBV was the first recognized occupational blood-borne pathogen, as it was recognized that HCWs had a 10-times-greater risk of HBV infection than did the general population. In the early 1980s, the incidence of HBV in HCWs was 386 cases per 100,000 population. The risk of transmission of HBV from a percutaneous exposure is approximately 6% to 30%, well above the risk of transmission of HIV (0.3%) (19). As with HIV, the risk of HBV transmission varies depending on the characteristics of the source virus. The risk of infection increases when exposed to HBeAg-positive blood and some variant HBV strains (4, 116, 349). HBV has been isolated from saliva, urine, and other body fluids but usually in much lower titers than in plasma (113). An amazing success story is the introduction of the HBV vaccine in 1991. Since that time, the incidence of HBV infection has fallen over 90% to 1.6 cases per 100,000 population in 2006 (339).

(i) Infection prevention. OSHA requires that all employers offer the HBV vaccine to employees exposed to blood or other potentially infectious materials as part of their job (237). Postexposure prophylaxis for HBV is based on immunity in the exposed worker. A nonimmune HCW who sustains a percutaneous injury from a patient with an unknown HBV serostatus should be immunized with the HBV vaccine. If the patient is HBsAg positive or at high risk of being HBV infected, the exposed worker should receive HBV immunoglobulin in addition to the HBV vaccine (19). If the HCW has been vaccinated and has a documented antibody response, no postexposure prophylaxis is necessary.

HCV. HCV is now the most commonly transmitted blood-borne pathogen. Rates of transmission range from 1 to 22%, with a rate of risk per exposure of 1.9% (133). There is currently no effective vaccine or postexposure prophylaxis for HCV. Studies do not support the use of immunoglobulin as prophylaxis against HCV infection (5). Data evaluating the use of immunoglobulin in the HCV postexposure setting are lacking, and animal data have not shown that immunoglobulin with high-titer anti-HCV antibodies given 1 h after exposure to HCV prevents infection (173). Currently, the use of pegylated alpha interferon as postexposure prophylaxis to reduce the risk of HCV transmission is not recommended (19).

(i) Infection prevention. After exposure to blood or potentially infectious body fluids, it must be determined whether the patient is HCV positive. If exposed to an HCV-infected patient, the HCW must be monitored serially to watch for HCV

seroconversion. If seroconversion occurs, the HCW should be evaluated to determine the role of treatment for acute HCV with pegylated alpha interferon and ribavirin (195). Follow-up is critical in order to conduct counseling, allay fears, and assess for any symptoms of acute viral hepatitis.

HCWs infected with blood-borne viruses. The CDC guidelines for the prevention of transmission of HIV and HBV to patients recommend that HIV- and HBV-infected providers should not perform exposure-prone procedures unless they have obtained counsel from an expert review panel and have been advised under what circumstances they may continue to perform procedures (51). The SHEA recently updated a position paper addressing the management of HCWs infected with HBV, HCV, and HIV (2, 134). SHEA guidelines state that HBV-, HCV-, and HIV-infected HCWs should not be prohibited from practicing solely based on their infection status. Rather, characteristics of the HCW's viral infection should be taken into account.

The guidelines recommend that HBV-infected providers who are either HBeAg positive or have circulating HBV DNA levels greater than or equal to 10^4 genome equivalents (GE)/ml should refrain from conducting procedures for which there is a definite risk of blood-borne virus transmission. This category of procedures includes most surgical procedures and emergent procedures.

Similar recommendations are made for HCV-infected providers with circulating viral burdens greater than or equal to 10^4 GE/ml and HIV-infected providers with circulating viral burdens greater than or equal to 5×10^2 GE/ml. HBV-, HCV-, and HIV-infected providers with circulating viral levels less than the cutoffs listed above should be allowed to perform at-risk procedures as long as the provider (i) is not known to have transmitted viral infection to patients; (ii) obtains advice from an expert review panel about continued practice; (iii) undergoes routine follow-up by occupational health authorities, with semiannual viral load testing; (iv) receives follow-up by a personal physician with expertise in the management of blood-borne viral infections; and (v) consults with an expert about optimal infection control procedures (134). Another recent set of guidelines similarly highlights the role of standard precautions, safer devices, attention to detail of infection control procedures, and treatment of provider infection as strategies for the prevention of provider-to-patient transmission (216).

ROLE OF HOSPITAL EPIDEMIOLOGY AND INFECTION CONTROL

In 1958, nationwide epidemics of nosocomial *Staphylococcus aureus* infection in newborn nurseries were recognized. The American Hospital Association's Advisory Committee on Infections within Hospitals subsequently recommended routine surveillance for nosocomial infections (294). In the 50 years since then, the role of infection control and hospital epidemiology has expanded, and its contribution to the quality of health care is highlighted. In 1976, the Joint Commission included requirements for infection control and prevention in its requirements for hospital accreditation (294). Finally, in 1985, the SENIC Project provided scientific evidence that infection control programs with qualified IPs and hospital epidemiologists could prevent 32% of nosocomial infections. This and other studies have found that infection control programs prevent infections and lead to decreased morbidity, improved survival, and shorter hospital stays, and they are cost-effective (121, 345).

Since their inception in the 1960s and 1970s, the role and responsibilities of infection control programs have grown substantially. This growth has been fueled by more complicated cases and an intricate health care system but also due to an increased awareness of patient safety and medical accountability and the need for mass infectious disease casualty planning and delivery of high-quality clinical care. Given this trend, the SHEA created a consensus panel to help define the infrastructure and activities of hospital epidemiology and infection control programs (294). Foremost, the SHEA laid out the goals for infection control programs as (i) to protect the patient, (ii) to protect HCWs and all others in the health care environment, and (iii) to accomplish the first two goals in a cost-effective manner (294). Infection control and hospital epidemiology programs obtain their goals through many activities. We will discuss the main roles and activities of an infection prevention and control program.

Surveillance

Surveillance in hospital epidemiology and infection control is the process of identifying rates of HAIs, rates of infection or colonization with epidemiologically important organisms (e.g., MRSA, VRE, and *Legionella*), and rates of relevant processes of care such as compliance with hand hygiene (248). The SENIC investigators found that surveillance was the one essential component of an infection prevention and control program necessary to reduce rates of HAIs (122, 248). Surveillance data are used to identify problem areas where infection prevention and control measures should be instituted, with the goal of improving patient safety. Surveillance is truly the cornerstone of hospital epidemiology and infection control programs, as it highlights where these programs should focus their energies and allows programs to evaluate the effectiveness of their infection control efforts.

Given the growing pressure for transparency in the health care system, several countries and multiple states within the United States have passed legislation requiring that health care facilities report rates of HAIs, rates of infection and colonization with epidemiologically significant organisms, and rates of process-of-care measures to public health authorities or other agencies that can publicly display the data (248). The ultimate goal of reporting these rates is an increased public awareness and improvements in health care quality and patient safety. With increased interest in the public reporting of HAI rates and rates of epidemiologically significant organisms, proper surveillance techniques are imperative in order to make data from different health care facilities meaningful and comparable (210, 211).

In addition to meeting regulations and guidelines, surveillance serves multiple other roles important for an infection prevention and control program. Surveillance can be used to establish baseline infection rates, detect outbreaks, convince clinicians and administrators of potential problems, affect hospital policy, assess the impact of interventions, guide antimicrobial stewardship practices, conduct research, reduce HAI rates, and make comparisons of rates and practices within and between hospitals (248). Another important application of sur-

veillance is the monitoring of process measures. Process measures are evidence-based interventions or procedures known to decrease HAIs. Examples of surveillance based on process measures include vaccination rates among HCWs, rates of compliance with recommended hand hygiene, and rates of compliance with surgical antibiotic prophylaxis. Process measure surveillance provides information on what infection control measures should be the focus of prevention efforts (328).

There are several necessities for a productive surveillance program. A surveillance program must first set clear goals and objectives. Undoubtedly, resources will be scarce and should be focused where they can have the most effect. An infection prevention and control program should focus surveillance efforts on specific pathogens, infections, and patient populations. Surveillance programs should be tailored to infections or pathogens that frequently occur in the facility, cause morbidity and mortality, and can be prevented (248). Second, surveillance programs must apply standardized case definitions. The CDC HAI definitions are widely used and accepted (109). These definitions have been used for years and are well understood in the health care epidemiology community. Third, rates must be calculated using appropriate numerator and denominator data that have been validated. Correct numerator and denominator data are imperative in the setting of public reporting and comparison of rates between health care facilities. Surveillance programs must also have easy access to computer and medical records, and data should be collected with a standardized method. There must be a mechanism in place to report surveillance results. This includes not only required reporting to public health officials and other agencies but also a productive forum in which to report results to clinicians and administrators. Finally, a surveillance program must have strong leadership and human and financial resources. A leader needs the ability to set goals and objectives for the program as well as a vision for the future and the changing needs of a surveillance program.

Several surveillance methods exist, and infection prevention and control programs must decide which method is best suited to their facility. The most common surveillance methods include hospital-wide surveillance, prevalence surveys, targeted surveillance, and periodic surveillance (248). Hospital-wide surveillance is the most comprehensive and includes the prospective continuous survey of all areas to identify HAIs or epidemiologically significant organisms (248, 346). Hospital-wide surveillance is costly and may identify infections that cannot be prevented. This method is not commonly recommended. A prevalence survey determines the number of active cases (new and existing) of a particular infection or organism in a given area during a specified time period (259). Prevalence surveys can be applied to individual wards or an entire health care facility. Prevalence surveys can be used to determine the burden of a particular HAI or epidemiologically significant organism as well as assess risk factors for a particular infection within a given population. Targeted surveillance is focused on selected areas of the hospital, selected patient populations, or selected organisms (e.g., VRE, MRSA, or *C. difficile*). Examples of targeted surveillance include MRSA surveillance for ICU patients only or surveillance of infections associated with specific devices, such as VAP. By performing targeted surveillance, infection prevention and control programs can focus on patients at increased risk and areas with high infection rates where interventions are proven to be beneficial. Periodic surveillance is used when surveillance methods are done only during specified time intervals. Examples would be hospital-wide surveillance 1 month every quarter or targeted surveillance rotating among different units. Periodic surveillance is less time-intensive and less expensive (248).

New surveillance technologies are emerging. Computer software that integrates microbiological, clinical, radiographic, and pharmacy data has been developed. This new technology allows automated surveillance for HAIs and has been shown to be more efficient at identifying outbreaks than routine surveillance (357). Automated surveillance systems should free up time for IPs to focus on rounding on units, infection prevention, policy implementation, and educational activities.

The future for infection prevention and control programs will require automated surveillance systems as information technology is expanding. In addition, IPs will need to communicate with those in the outpatient setting and IPs at outside institutions as the health care system grows more complex and patients need to be tracked within this complex system. With increasing emphasis on public reporting, the importance of standardized definitions and standard approaches for identifying infections cannot be overemphasized. Surveillance is the cornerstone of infection control and prevention programs; however, to be most effective, surveillance must be individualized to the needs of the facility and performed in a methodical and efficient manner.

Outbreak Investigations

An outbreak is defined as an increase in the incidence of a particular disease over the baseline expected incidence (311). Five percent of HAIs occur as epidemics or outbreaks (348). During outbreaks of HAIs, the infection either is usually spread from a common source or from person to person or is associated with specific procedures. Outbreak investigations often provide critical information about the epidemiology of important pathogens (153, 207). They have led to the identification of new routes of infection transmission in health care settings and enhanced measures to improve patient safety (54, 150). Electronic data and surveillance systems and expanded molecular typing methods that determine organism relatedness have improved our ability to recognize outbreaks of HAIs.

The first step when an outbreak is suspected is to review all available information and confirm the presence of an outbreak. This requires comparing current rates with previous rates and determining if there is clustering in time or space. If an outbreak is confirmed, the next step is to create a case definition, verify the diagnosis, and then determine the nature, location, and extent of the problem. All cases need to be identified and aggregated into a line list, which is a summary of all affected patients and important case data such as location, demographic data, signs and symptoms, underlying diseases, and procedures which the patient has undergone. This information will ultimately help with one's investigation and will be used to identify case risk factors and define outbreak epidemiology. As in other settings, the organism identified can commonly provide clues as to additional steps to be taken to identify the source (Table 3.) An epidemic curve should also be graphed,

TABLE 3. Organisms identified in outbreaks and their reservoirs[a]

Organism (type of infection often associated with outbreak)	Common reservoir(s)	Reservoir(s)/site(s) associated with outbreaks	Method of detection	Description
Aspergillus spp. (blood, lower respiratory tract)	Air, dust, mold	Building renovation or construction sites, ventilation systems, dust-generating activities	P,[b] micro cultures; E,[b] air sampling, surface samples	Often pathogenic in immunocompromised populations
Staphylococcus aureus (surgical site, blood)	Human skin, anterior nares, upper respiratory tract, perirectal area, throat	Nasal/skin carriage in health care workers, increased nurse-to-patient ratios	P,[b] micro cultures; E,[b] settle plates, hand cultures	Usually associated with SSI; PFGE can be helpful to determine whether point source or technical; point source may suggest carrier and would require nare cultures
Staphylococcus species (coagulase negative) (blood)	Human skin	i.v. fluids, instrumentation, contaminated hands of health care workers, implanted devices	P,[b] micro cultures; E,[b] not known to be useful	Pathogenic in immunocompromised hosts and premature infants; commonly a contaminant
Salmonella species (GI tract infections)	Gastrointestinal and biliary tract	Contaminated food, dairy, eggs/poultry; contaminated blood products	P,[b] stool, blood cultures; E, not known to be useful	Not normal flora; cross-contamination reported
Streptococcus pyogenes (group A streptococcus) (deep wounds or intra-abdominal abscess)	Upper respiratory tract, perianal area (rectum and vagina)	Carriage among health care workers	P,[b] wound, stool cultures; E,[b] settle plates	Not commonly normal flora; threshold for investigation, 1 case
Enterococcus faecalis and *E. faecium* (enterococcus or group D streptococcus) (neonatal sepsis, cystitis, bacteremia)	Vaginal/perianal area, colon	Neonates/surgical patients	P,[b] stool, vaginal cultures; E, not known to be useful	
Pseudomonas cepacia and other *Pseudomonas* species[c] (blood)	Skin	Water, contaminated solutions and skin disinfectants, contaminated equipment	P, micro cultures, stool; E,[b] cultures of potentially implicated items	Associated with disinfectants (especially those containing iodine), water, solutions
Pseudomonas pickettii[c] (blood)	Skin	Water, skin disinfectants, sterile water	P,[b] micro cultures, stool; E,[b] cultures of potentially implicated items	Deliberate contamination of sterile fluids has been reported
Stenotrophomonas maltophilia (blood)	Skin	Water, contaminated anticoagulant, and other solutions	P,[b] micro cultures, stool; E,[b] cultures of potentially implicated items	Cross-contamination reported
Pseudomonas aeruginosa (burns, wounds, urinary tract, pneumonia)	Gastrointestinal tract	Ventilators, whirlpools, sitz baths, solutions (mouthwash), any other water sources	P,[b] micro cultures, stool; E,[b] cultures of potentially implicated items	Can be normal flora
Escherichia coli (epidemic diarrhea, wounds, urinary tract, neonatal sepsis or meningitis)	Colon	Equipment or fluids contaminated with organisms from lower GI tract	P,[b] micro cultures, stool; E,[b] cultures of potentially implicated items	Very common normal flora
Klebsiella pneumoniae (urinary tract, pneumonia)	Colon, nose, mouth, skin	Urinary catheters, hand lotions, contaminated fluids, ventilators, eczema	P,[b] micro cultures; E,[b] cultures of potentially implicated items	Cross-contamination described
Enterobacter species (urinary tract, i.v.-associated bloodstream infections)	Colon	Contaminated i.v. fluids, TPN, hands/dermatitis	P,[b] micro cultures; E,[b] cultures of potentially implicated items	Intensive care units, reuse of calibrated pressure transducers
Acinetobacter species	Vaginal/perianal area/skin	Instrumentation, burns, surgery, respiratory equipment, gloves, parenteral nutrition, water	P,[b] micro cultures; E,[b] cultures of potentially implicated items	Immunocompromised population and patients in intensive care units at increased risk
Haemophilus influenzae (infant meningitis, conjunctivitis, respiratory tract infections)	Upper respiratory tract	Contaminated medications/equipment, eye drops	P,[b] cultures of potentially implicated items, micro cultures; E,[b] cultures of potentially implicated items	Nontypeable species are most common
Candida species (blood, urinary tract)	Air, endogenous flora	Hands, oncholysis, devices	P,[b] micro cultures; E,[b] cultures of hands and nail beds	Immunocompromised population at increased risk
Hepatitis A virus	Gastrointestinal	Hands/foods, transfusion	P, serology; E, not known to be useful, testing of potentially implicated personnel	Cross-contamination described
Hepatitis B virus	Blood	Blood and secretions, transfusions, improperly cleaned equipment	P, serology, PCR; E, not known to be useful, testing of potentially implicated personnel	Patients on dialysis, patients in psychiatric units, contaminated devices
Hepatitis C virus	Blood	Blood and secretions, transfusions, improperly cleaned equipment, multidose vials	P, serology, PCR; E, not known to be useful, testing of potentially implicated personnel	Patients on dialysis, patients in psychiatric units, contaminated devices, multidose vials
Mycobacterium tuberculosis (respiratory)	Lungs	Airborne, improperly cleaned equipment	P,[b] micro cultures; E,[b] not known to be useful, cultures of potentially implicated personnel	Health care transmission suggests poor infection control

Atypical mycobacteria (*Mycobacterium avium*, *M. gordonae*)	Lungs, skin	Contaminated water, improperly cleaned and sterilized equipment	P,[b] micro cultures; E,[b] cultures of potentially implicated items	Associated with pseudo-outbreaks, reuse of improperly cleaned dialyzers, contaminated ice machines and other equipment
Campylobacter fetus	Gastrointestinal	Food	P,[b] micro cultures; E,[b] cultures of potentially implicated items/personnel	Neonatal intensive care unit patients at risk
Legionella pneumophila and other species	Water	Potable water, air-conditioning units, cooling towers, construction	P,[b] micro cultures; E,[b] cultures of potentially implicated items/personnel	Can be associated with intense scrutiny by the media
Streptococcus viridans (blood, skin)	Skin	Colonized health care workers, eczema	P,[b] micro cultures; E,[b] cultures of potentially implicated items/personnel	
Achromobacter xylosoxidans (blood)	Water	Contaminated water	P,[b] micro cultures; E,[b] cultures of potentially implicated items	Immunocompromised patients and those on dialysis, reuse of pressure transducers
E. coli O157:H7 and other hemorrhagic species (diarrhea and hemorrhagic colitis)	Gastrointestinal tract of animals	Contaminated water, and foods (meat, salads)	P,[b] micro cultures; E,[b] cultures of potentially implicated items	HUS and TTP are sequelae; high mortality among elderly and extremely young; cross-contamination described
Herpesvirus infection (skin, pneumonia)	Secretions and lesions	Patients and health care workers	P,[b] Tzanck prep and viral cultures, PCR, immunofluorescence staining, or serology; E,[b] not known to be useful	Outbreaks reported when patients shed or with lesions in health care workers
Varicella infections (disseminated or localized infection)	Secretions and skin lesions	Poor ventilation	P,[b] Tzanck prep and viral cultures, PCR, immunofluorescence staining or serology; E,[b] not known to be useful	Children and immunocompromised patients at risk, poor ventilation or poor infection control practices
Adenovirus (EKC)	Oral pharyngeal secretions	Equipment (tonometers) and health care workers	P,[b] viral cultures, PCR; E,[b] not known to be useful	Ophthalmologic patients, NICU patients, immunocompromised patients
Norovirus	Stool	Patients, health care personnel, and visitors, environment	P, stool EM, PCR; E, not known to be useful	Dramatic spread in any health care population; shedding can persist for days
Serratia marcescens (urinary tract, bloodstream)	Gastrointestinal and urinary tracts	Solutions, inhalation therapy equipment, disinfectants, plasma, EDTA collection tubes, air-conditioning vents, improperly cleaned equipment	P,[b] micro cultures; E,[b] cultures of potentially implicated items	Cross-contamination well described; reuse of calibrated pressure transducers
Listeria monocytogenes (bloodstream and central nervous system infections)	Food	Contaminated foods	P,[b] micro cultures; E,[b] cultures of potentially implicated items	Immunocompromised and mother-infant pairs at highest risk
Vancomycin-resistant *Enterococcus*	Gastrointestinal tract	Hands of health care workers, contaminated equipment and environment	P,[b] micro cultures; E,[b] cultures of potentially implicated items	Cross-contamination well described; immunocompromised patients and those in intensive care units at highest risk
Polymicrobial infections	Depends on setting	Contaminated i.v. solutions or medications	P,[b] micro cultures; E,[b] cultures of potentially implicated items	Suggests technical problems, increased nurse-to-patient ratios
Yersinia enterocolitica	Gastrointestinal tract	Packed red blood cells	P,[b] micro cultures; E,[b] cultures of potentially implicated items	

[a] P, in patients; E, in the environment; micro, microbiological; PFGE, pulsed-field gel electrophoresis; i.v., intravenous; GI, gastrointestinal; TPN, total parenteral nutrition; HUS, hemolytic-uremic syndrome; TTP, thrombotic thrombocytopenic purpura; EKC, epidemic keratoconjunctivitis; NICU, neonatal ICU; EM, electron microscopy.

[b] Molecular typing available.

[c] Some species are now *Burkholderia* species.

with time along the "*x*" axis and the number of cases along the "*y*" axis. The shape of the epidemic curve may suggest the source and mode of transmission. Infection control personnel should request that the microbiology laboratory save and store all isolates from case patients for possible molecular typing. Finally and concomitantly, emergency control measures need to be instituted (311).

After the initial investigation is under way, the next steps involve generating hypotheses about disease transmission and risk factors. These hypotheses should then be tested with comparative studies and supported by using microbiological studies. The final step in an outbreak investigation is communicating the results of the outbreak investigation to involved departments and implementing definitive control measures (311).

Outbreaks are almost always politically charged. Key in health care settings is keeping all parties informed, including the administration, the unit involved, and any personnel involved. Risk management and the microbiology laboratory should also be involved. Most states or provinces require notification of the public health authority. Outbreaks of HAIs increase morbidity, mortality, hospital costs, and liability (348). The recognition and investigation of outbreaks of HAIs are two of the most important activities of a hospital epidemiology and infection prevention and control program. Such investigations can lead directly to improved patient care and patient safety by assessing practices and policies while simultaneously expanding medical and epidemiological knowledge.

Policies and Procedures

In response to endemic or epidemic HAIs, IPs implement evidence-based infection control policies and procedures aimed at the prevention of future events. Policies and procedures are written and developed based on scientific evidence of benefit, legal requirements, state and federal regulatory standards, as well as guidance from professional society guidelines such as HICPAC (294). Infection control programs also work closely with their institution's occupational health program to institute policies for diagnosing and monitoring infectious diseases in HCWs as well as setting work restrictions for ill employees and instituting vaccination programs. This partnership is imperative, as HCWs represent a potential source of infections transmissible to patients.

Infection Prevention

An imperative function of infection control and hospital epidemiology programs is the prevention of disease transmission. Infection prevention is a priority, with initiatives being led by health care organizations, government and accrediting agencies, legislators, regulators, payers, and consumer advocacy groups. Infection prevention is accomplished through surveillance, outbreak investigation, instituting control measures to stop transmission and abort outbreaks, education and training of health care providers, and instituting effective HAI prevention measures.

In 2008, the SHEA and the Infectious Diseases Society of America (IDSA) Standards and Practice Guidelines Committee assembled a task force to create a compendium of evidence-based recommendations for the prevention of the most common HAIs (363). The compendium includes recommendations for the prevention of SSIs, CLABSIs, CA-UTIs, VAPs, *C. difficile*, and MRSA (10, 43, 71, 86, 185, 204). These guidelines present practical recommendations for the prevention of HAIs, and they are an invaluable resource for the development and implementation of HAI prevention. The SHEA/IDSA compendium also recommends performance measures for internal monitoring in order to assess the effectiveness of a facility's HAI prevention program. These documents aim to assist infection control and prevention programs in focusing and prioritizing their HAI prevention efforts.

Recent attention has turned to the implementation of a bundle or package of evidence-based interventions to prevent HAIs. Three bundles have been implemented by the Institute for Healthcare Improvements (IHI) as part of the Save 100,000 Lives campaign. The bundles are aimed at preventing CLABSIs, VAPs, and SSIs. As an example, the CLABSI bundle includes (i) HCW education, (ii) hand hygiene, (iii) maximal barrier precautions during catheter insertion, (iv) chlorhexidine skin antisepsis, (v) optimal site care, (vi) catheter removal, and (vii) practices monitoring CLABSI rates (154). The implementation of the CLABSI prevention bundle has significantly reduced CLABSI rates at multiple institutions (21, 264). The use of a VAP prevention bundle has also led to significant reductions in VAP rates in ICU patients (41, 272). In an effort to reduce SSIs, the CMS has instituted the Surgical Care Improvement Project (SCIP). SCIP measures emphasize a bundle of evidence-based interventions, including (i) improving surgical antimicrobial prophylaxis, (ii) glucose control in cardiac surgery patients, (iii) proper hair removal, (iv) urinary catheter removal, and (v) normothermia (37).

Hospital epidemiology and infection control and prevention programs have an important role in working together with health care providers to implement and monitor these evidenced-based practices. (See Table 1 for a detailed description of specific prevention measures.)

Disinfection, Sterilization, and Cleaning

Invasive medical and surgical procedures have the potential to expose patients to pathogenic microbes and lead to infection. If not properly disinfected or sterilized, medical devices and surgical instruments used in invasive procedures may be the carrier of infectious organisms and may lead to infection. Failure to comply with disinfection and sterilization guidelines has contributed to outbreaks associated with contaminated medical devices and surgical instruments (215, 310, 340).

Sterilization kills all microorganisms and high levels of bacterial spores. Sterilization can be performed with steam (autoclave machine), dry heat, or chemical sterilants for heat-sensitive items (284). High-level disinfection kills all microorganisms but does not kill high numbers of bacterial spores. High-level disinfection techniques include pasteurization and chemical sterilants used for heat-sensitive items (284). Intermediate-level disinfection destroys bacteria in the growth phase, mycobacteria, and most viruses and fungi but not bacterial spores. Chlorine-based products, phenolics, and accelerated hydrogen peroxide are all used for intermediate-level disinfection (284). These agents must have documented tuberculocidal activity to be used for intermediate-level disinfection.

Low-level disinfection kills bacteria in the growth phase and some fungi and viruses but does not kill mycobacteria or bacterial spores. Nontuberculocidal chlorine-based products, phenolics, accelerated hydrogen peroxide, and quaternary ammonium compounds are used for low-level disinfection (284).

Given the importance of disinfection and sterilization in the prevention of the transmission of infectious organisms, guidelines for disinfection and sterilization methods have been created and adopted by infection prevention programs (282, 283). Recommended disinfection and/or sterilization is based on the risk of infection associated with exposure to particular instruments. Items are categorized as being critical, semicritical, or noncritical.

Critical items are those at a high risk of transmitting infection. These objects are those that enter sterile tissue or the vascular system. Examples of critical items include surgical instruments, cardiac catheters, implants, and ultrasound probes that enter sterile body sites. Critical items should be purchased sterile or undergo sterilization after use. Steam is the preferred sterilization technique (284).

Semicritical items are those that come into contact with nonintact skin or mucous membranes. Examples include respiratory therapy items, anesthesia equipment, and endoscopes. Semicritical items should undergo high-level disinfection in order to destroy all pathogenic organisms and a majority of bacterial spores (283).

Noncritical items are those that come into contact with intact skin. These include virtually all inanimate objects in the health care environment. Examples include blood pressure cuffs, bed rails, linens, countertops, and floors. Noncritical items are unlikely to transmit infectious agents directly to patients (342); however, they contribute to secondary transmission by contaminating HCW hands. Noncritical items should undergo low- to intermediate-level disinfection (283).

In addition to the sterilization and disinfection of equipment, cleaning of the environment is also important. Numerous environmental surfaces exist in patient rooms, and studies have documented that a large proportion of these surfaces are missed during routine and terminal cleaning between patients (45). Studies have also shown that patients admitted to hospital rooms previously occupied by patients colonized or infected with *C. difficile* and drug-resistant organisms are at an increased risk of acquiring these organisms (141; M. Shaughnessy, et al., presented at the 48th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy-Infectious Diseases Society of America 46th Annual Meeting, Washington, DC, 25 to 28 October 2008). Interest has shifted to alternative methods of environmental cleaning due to the limitations of current methods. Hydrogen peroxide vapor and UV light are two techniques being explored. Hydrogen peroxide vapor is increasingly employed in health care facilities, as it has been effective in eradicating various pathogens from environmental surfaces and has been associated with a reduced incidence of *C. difficile* (17, 31, 103). Automated UV light systems have also been associated with decontamination of environmental surfaces (284).

Disinfection and sterilization are imperative to prevent the transmission of infectious organisms contaminating invasive medical devices and surgical instruments. Infection prevention and control programs should be actively involved in recommending appropriate disinfection methods and overseeing disinfection and sterilization in their facility. Similarly, programs need to be involved in decisions regarding environmental cleaning techniques. Infection prevention programs need to be aware of disinfection methods used in their facility in order to understand the risk of infection associated with procedures and identify areas for improvement.

Facility Construction and Renovation

Construction, renovation, and maintenance in health care settings can increase the risk of certain HAIs (281). Immunocompromised patients and staff are most at risk for these HAIs. The most common organisms involved are *Aspergillus* and *Legionella* species. Everything from large construction and renovation projects to daily maintenance must be assessed for its potential impact and risk of leading to HAIs. Construction and renovation projects must meet guidelines established by government, regulatory, and accreditation agencies. Infection prevention programs should be involved in every step of the process and must work closely with engineers, architects, administrators, clinicians, construction personnel, and maintenance staff (281).

Aspergillus and *Legionella* species are the leading causes of construction-related HAIs (213, 240, 281). *Legionella* species are ubiquitous aquatic organisms commonly isolated from water (281). *Legionella* can be introduced into water systems during construction if pipes become contaminated with soil. Changes in water system pressure, the disruption of water flow, and blind loops can lead to the release of *Legionella* species growing within biofilms inside pipes. The organism is then transmitted to susceptible individuals by inhaled aerosols or drinking water (281). The most commonly seen clinical manifestation is pneumonia.

Aspergillus species are ubiquitous in soil. Dust and dirt from construction projects harbor *Aspergillus* spores that can be released into the air and inhaled by susceptible individuals. Other fungi and molds can also grow behind walls or in areas with water damage or high humidity. Molds can cause influenza-like illnesses or hypersensitivity reactions if inhaled, and mold remediation must be undertaken if mold is found (281). More serious complications include lung and sinus infections that are difficult to treat.

The Joint Commission recommends that health care facilities follow American Institute of Architects guidelines (6) when undergoing construction or renovation projects (158). When accrediting health care systems, the Joint Commission assesses whether health care facilities comply with guidelines for protecting patients, visitors, and HCWs during construction and renovation (158). It is the responsibility of infection prevention programs, architects, engineers, and administrators to ensure that these guidelines are followed.

The most important means to ensure that guidelines are followed is the performance of an infection control risk assessment (ICRA) before construction, renovation, or maintenance projects begin. A multidisciplinary team with expertise in infection prevention, facility design, construction, ventilation, and heating and air-conditioning systems should perform the

ICRA for all renovation and construction projects (6, 281). This involves a multistep process that identifies the magnitude of the project and the patient population at risk and then helps identify necessary preventative measures. Examples of prevention measures include protective barriers to minimize dust, HEPA filtration units, and protective attire for construction workers. The team performing the ICRA must also assess whether essential services such as power, gas, water, and sewer might be disrupted and provide contingency plans. The ICRA must also evaluate how patients in adjacent areas will be affected, whether patients in the affected or nearby units should be relocated, and how the project will affect ventilation systems (281). The ICRA process is formalized in the ICRA matrix, a tool that guides the multidisciplinary team to systematically evaluate all issues (281). Prior to opening a newly completed construction or renovation area, infection prevention personnel should inspect the area to ensure that all requirements have been met.

Infection prevention expertise is needed for all stages of building and renovation projects to ensure that measures are in place to prevent HAIs. Construction and renovation projects are continuous in most health care settings and another role in which infection prevention personnel must work closely with a multidisciplinary team to protect patients.

Providing Education

IPs also serve an educational role, as they educate and train staff in infection control practices such as isolation precautions, personal protection, and aseptic techniques. IPs are often responsible for infection control training of employees, as required by regulatory agencies such as the Joint Commission and OSHA (294). One of the most effective forms of education is by providing HCWs with surveillance data from their particular unit. This often serves as a catalyst for employee-driven quality improvement programs to decrease HAIs.

Future Directions

Hospital epidemiology and infection control programs have grown over the last 30 years and will most certainly continue to do so. Many programs have taken on new functions with the ultimate goal of patient and HCW safety. For example, many infection control programs have teamed with antimicrobial stewardship programs to improve antimicrobial use. Antimicrobial stewardship programs work with the microbiology laboratory to monitor antimicrobial-resistant organisms and work with clinicians to curtail excessive antimicrobial use as well as educate clinicians on safe antimicrobial practices. Research has also become a large component of infection control programs as we look to better define the epidemiology of HAIs and search for evidence-based interventions to improve patient care. Given the national interest in cutting health care costs and improving patient safety, hospital epidemiology and infection control represent a much-needed practice that will continue to grow.

ORGANIZATION OF HOSPITAL EPIDEMIOLOGY AND INFECTION CONTROL

The basic structure of a hospital epidemiology and infection control program includes either a trained infection control professional or a hospital epidemiologist in charge of the program, IPs, surveillance personnel, secretarial staff, and computer support personnel for the management and analysis of data (294). Microbiology laboratory support is crucial to the functioning of an infection control program. If the microbiology laboratory is unable to perform molecular typing of organisms, a reference laboratory is needed. The hospital epidemiology and infection control program must work with a multidisciplinary infection control committee comprised of leadership from different departments within the health care facility. Support from hospital administration and the executive board is imperative to the success of a hospital epidemiology and infection control program. Similarly, there must be an infection control culture and enthusiasm at all levels of the institution.

The Hospital Epidemiologist

The SENIC study found that infection control programs headed by physicians with interests in hospital epidemiology had overall lower rates of HAIs (120, 122). Current participation in the NHSN requires that hospital epidemiology and infection control programs be headed by a trained infection control professional or a hospital epidemiologist (315). Most hospital epidemiologists are physicians trained in internal medicine or pediatrics with subspecialty training in infectious diseases (294). In a recent survey of 289 hospitals participating in the NHSN, registered nurses led 66% of infection control programs, and physicians led only 12% of programs. Of those programs with hospital epidemiologists (49% of programs), the majority were physicians, but only 10% reported working full time as a hospital epidemiologist (315). These findings coupled with results of the SENIC study and an ever-expanding and more complex health care system suggest a great need for hospital epidemiologists in order to achieve significantly lower rates of HAIs.

Infection Preventionists

The SENIC study found IPs to be an integral part of a successful infection control program and suggested that 1 IP per 250 occupied beds was effective (120). In the last 30 years the health care system has become more complex, with the expansion of health care services outside the hospital, sicker and more complex patients, and increases in numbers of drug-resistant organisms. The suggested ratio of 1 IP per 250 beds likely no longer applies, as IPs are responsible for a broader range of tasks and more complex patients. IPs are most often registered nurses, many with bachelor's degrees or master's degrees in epidemiology. Many professional organizations offer training courses in surveillance and infection control, and many IPs are obtaining certification in infection control by the Certification Board of Infection Control (293). A recent survey by Stone et al. found that IPs spend the majority of their time collecting and analyzing data (315). This suggests that less time

FIG. 1. Recommended infection control committee. ‡, physician and nursing leadership recommended.

and fewer staff are available for the education of providers and intervention and policy implementation aimed at the prevention of infections. IPs are on the front lines of infection prevention and control and represent the manpower fueling these programs. IPs are imperative to the functioning of these programs, and there is a growing need for more personnel trained in infection prevention and control.

Infection Control Committee

The infection control committee is made up of individuals with leadership and clinical positions within the health care institution, and the committee serves as a liaison between the infection control and prevention program, hospital patient care and supporting departments, and the hospital administration. Each infection control and prevention program should meet regularly with the infection control committee, and the committee should report to the medical board or medical advisory committee. Ideally, a physician leader should chair the infection control committee. The hospital epidemiologist often fills this role. Committee membership should be multidisciplinary (Fig. 1) and include representation from IPs, the microbiology laboratory, the pharmacy, operating room staff, occupational and employee health, environmental services/housekeeping, engineering facilities, central processing, hospital administration, and physician and nursing leadership from various clinical and support departments.

Roles of the infection control committee include (i) reviewing surveillance data and drafting intervention plans where necessary, (ii) formulating and approving infection control policies, (iii) reviewing outbreaks and formulating a response, (iv) approving the yearly goals and objectives of the infection control program, (v) developing policy regarding public reporting, and (vi) advising the medical and senior administration of the facility (280). The infection control committee is truly the voice of the infection control and prevention program within the health care facility.

Computer Support Personnel

Computer support personnel are a key component of the operations of an infection control program. They are necessary for data management, statistical analysis, and information technology management. In a survey by Stone et al., only 32% of hospitals reported having an electronic surveillance system. Only 35% had personnel responsible for data management, and only 13% had a hired statistician (315). Personnel skilled in data management and analysis are a requisite for the infrastructure of infection control programs. Without them, analyses of surveillance data as well as analyses of outcomes of interventions aimed at improving patient safety become impossible. As more health care systems move to electronic medical records and advanced surveillance software systems become available, it is imperative that infection prevention and control programs have adequate information technology support.

FUTURE CHALLENGES

The need for hospital epidemiology and infection control programs has grown since its inception, and the need for hospital epidemiologists and IPs will continue to expand as out-of-hospital care increases, new invasive procedures and technologies are introduced, patients become more complex, and the scope of antimicrobial-resistant organisms broadens. As hospitals and health care institutions look to reduce costs and improve the quality of patient care, they will turn to hospital epidemiologists and infection control programs for strategies to conserve resources, prevent infections, and control outbreaks.

Moving forward, the challenges facing infection control programs will be many. These programs must take on new roles to curtail the expansion and spread of antimicrobial-resistant organisms within and between health care institutions. Recent literature has highlighted the role that long-term acute-care hospitals play in HAIs (222). Given that long-term care facilities have been implicated as the source of regional outbreaks of MDR organisms (187), it is now necessary for IPs to work closely with IPs at surrounding facilities in order to understand the spread of MDR organisms and define the local epidemiology of HAIs.

Infection prevention and control programs must work to expand HCW vaccination programs to reduce the risk of spread of pathogens such as influenza virus from HCWs to patients. Infection control programs will be handed the task of eliminating HAIs, which are seen as "never" events: those that should never occur and for which a health care institution will not be reimbursed. Infection control programs will grow beyond the walls of the hospital and work to understand the epidemiology and prevention of infections at all steps of the health care process, as patients move between the community and the hospital and between multiple health care institutions. Hospital epidemiologists and infection control practitioners will be charged with the task of investigating the next generation of technology and prevention strategies aimed at tackling HAIs. Finally, needs will broaden not only in the developed world but also in developing countries, where technology is

growing and health care is modernizing, increasing the opportunities for HAIs.

Available data point to a lack of health care epidemiologists and other key members of the infection control team, such as data managers and statisticians (315). These roles are imperative to performing all the functions of an infection control program. Future directions must focus on expanding and increasing not only the numbers of members within the infection control team but also the expertise and experience of its leaders.

CONCLUSION

From Semmelweis to the SENIC study, evidence has evolved to support both the role of certain infection prevention and control practices and the role of trained professionals studying the transmission and prevention of infections in the health care setting (122, 232). While our knowledge of epidemiologically significant transmissible organisms and infections in the health care setting has grown, these pathogens are an increasing threat to patient safety as health care extends from inpatient hospitals to community health care settings, antimicrobial-resistant organisms have flourished, and our patients and health care practices have become more complex. Now more than ever, well-structured infection control programs, with the expertise of a hospital epidemiologist and support of IPs, support of a microbiology laboratory, data managers, and statisticians, are imperative to the prevention of HAIs.

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