

Chapter 11

Healthcare-Associated Infections in Pediatric Hematology-Oncology

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In the last decade, advances in cancer therapy have led to improved survival in children and adolescents with malignant disorders. As cure rates improve, treatment-related toxicity, especially infections, accounts for a greater proportion of morbidity and mortality. Pediatric hematology and oncology patients are often highly susceptible to infection. Those with medical devices, such as indwelling central catheters, and those with intermittent or chronic neutropenia are particularly at high risk of healthcare-associated infections (HAIs) such as central line-associated bloodstream infections (CLABSI), *Clostridium difficile* infections (CDIs), ventilator-associated pneumonia (VAP), catheter-associated urinary tract infections (CAUTI), and respiratory viral infections. In the past, infectious complications of therapy for oncological and hematological disorders were regarded as largely unavoidable. It is now recognized that many, although not all, of the most common infections in this population are preventable. Collaborative quality improvement efforts have led to effective strategies to reduce rates of HAI and improved outcomes in these populations.

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Healthcare-Associated Infections

Central Line-Associated Bloodstream Infections (CLABSI)

Central lines, or central venous catheters, have proved invaluable in the management of children with cancer. Indeed, the National Healthcare Safety Network (NHSN) reported that the highest permanent central line utilization rates in 2013 were in pediatric general hematology-oncology and hematopoietic stem cell transplant (HSCT) wards [1]. These units also reported substantial temporary central line use. CLABSI, however, are the most common healthcare-associated infection (HAI) affecting pediatric hematology-oncology patients. Table 11.1 lists the relative rates of CLABSI observed across different patient populations and catheter types. As in adults, these contribute significantly to mortality, hospital length of stay, and costs [1, 2].

Microorganisms colonize most central lines, often in as little as a day, by (a) migration from the skin insertion site along the external surface of the catheter, (b) introduction into the hub lumen during manipulation of the catheter or by exposure to contaminated infusates, or (c) hematogenous spread from a focal infection [3]. Thrombin covering the intravascular portion of the catheter and the biofilm produced by many microbial pathogens promotes the adhesion of pathogens. The risk of subsequent bloodstream infection is dependent on both the number of organisms and their intrinsic virulence. Host, underlying disease, and treatment characteristics also contribute to the risk of CLABSI [4, 5].

Many institutions in the United States monitor rates of inpatient central line infections and assess the effectiveness of prevention efforts through the Centers for Disease Control and Prevention's NHSN, and these data are publically reported in many states. These surveillance strategies have also been applied to infections in ambulatory pediatric hematology and oncology patients [4, 6]. Specific criteria for bloodstream infections developed by the CDC Prevention Healthcare Infection Control Practices Advisory Committee (Table 11.2) distinguish between a CLABSI, an infection occurring in a patient who has had a central line in place for >2 days, and a catheter-related bloodstream infection (CRBSI), a CLABSI for which specific laboratory testing has identified the central line as the source of the infection [7]. Practically, it is sometimes not possible to implicate or exclude the catheter because the appropriate laboratory test was not feasible (e.g., if the central line is not removed and cultures of the catheter tip, therefore, not possible) or not obtained (e.g., simultaneous blood cultures from both the central line and a peripheral vein for comparison of time to positivity). The simpler definition of CLABSI has, therefore, been used for NHSN surveillance although it is recognized that it is less specific than desirable.

Figure 11.1 the successes of early efforts to track, report, and prevent CLABSI over the last decade led to the emergence of a "zero tolerance" attitude toward CLABSI, with many organizations setting a goal of eliminating all

infections through a series of interventions that include strict adherence to hand hygiene, asepsis during catheter insertion, adherence to a maintenance bundle, and the use of an appropriate dressing [8]. More recently, it has been recognized that many bloodstream infections in persons with cancer or severe neutropenia from other causes, or who have undergone HSCT, are not CRBSI, but result

Table 11.1 Pooled means of laboratory-confirmed permanent and temporary central line bloodstream infections, by type of unit

Location	Overall pooled mean CLABSI	Pooled mean CLABSI—permanent central line days	Pooled mean CLABSI—temporary central line days
Adult general medical/surgical inpatient	0.8	NA	NA
Adult medical/surgical ICU	0.8–1.1 ^a	NA	NA
Adult general hematology-oncology ward	NA	1.4	2.0
Adult HSCT ward	NA	2.6	3.0
Pediatric general medical/surgical inpatient	0.9	NA	NA
Pediatric medical/surgical ICU	1.2	NA	NA
Pediatric general hematology-oncology ward	NA	2.1	2.1
Pediatric HSCT ward	NA	2.4	2.2

HSCT hematopoietic stem cell transplant, ICU intensive care unit, NA not available

^aRates vary by unit size and teaching status

National Patient Safety Network 2013 [1]

Table 11.2 Criteria for catheter and mucosal barrier injury laboratory-confirmed bloodstream infections

Laboratory-confirmed bloodstream infection (LCBI)	<ul style="list-style-type: none"> (1) A recognized pathogen identified from ≥ 1 blood cultures (2) Fever, chills, or hypotension in association with the same common commensal bacteria being obtained from ≥ 2 blood cultures drawn on separate occasions (3) Fever, hypothermia, apnea, or bradycardia in a patient ≤ 1 year of age in association with the same common commensal bacteria being obtained from ≥ 2 blood cultures drawn on separate occasions <p>In each case, the organism identified from blood should not be related to an infection at another site (i.e., the infection represents a primary bacteremia), and criterion elements must take place 3 days before to 3 days after the collection date of the first positive blood specimen</p>
Central line-associated bloodstream infection (CLABSI)	A LCBI that develops in a patient with a central line in place for >2 days before the onset of the infection

Catheter-related bloodstream infection (CRBSI)	A LCBI with additional laboratory evidence that identifies the central line as the source of the bloodstream infection (e.g., differential time to positivity of blood cultures)
Mucosal barrier injury LCBI	<p>A LCBI:</p> <p>(1) That meets LCBI criteria 1 and ≥ 1 blood specimen is positive for a select group of recognized intestinal organisms, in association with:</p> <ol style="list-style-type: none"> a. A history of allogeneic HSCT within 1 year and Grade III or IV gastrointestinal GVHD) or ≥ 1 liter diarrhea (≥ 20 mL/kg in patients < 18 years of age) in a 24-h period on or ≤ 7 days before the collection date of the first positive blood specimen b. A history of ≥ 2 days of an ANC or WBC < 500 cells/mm³ on or within 3 days of the collection date of the first positive blood specimen <p>(2) That meets LCBI criteria 2 and ≥ 1 blood specimen is positive for viridans group streptococci only, in association with:</p> <ol style="list-style-type: none"> a. A history of allogeneic HSCT within 1 year and Grade III or IV gastrointestinal GVHD or ≥ 1 liter diarrhea (≥ 20 mL/kg in patients < 18 years of age) in a 24-h period on or ≤ 7 days before the collection date of the first positive blood specimen b. A history of ≥ 2 days of an ANC or WBC < 500 cells/mm³ on or within 3 days of the collection date of the first positive blood specimen <p>(3) A patient ≤ 1 year of age who meets LCBI criteria 3 and ≥ 1 blood specimen is positive for viridans group streptococci only, in association with:</p> <ol style="list-style-type: none"> a. A history of allogeneic HSCT within 1 year and Grade III or IV gastrointestinal GVHD or ≥ 1 liter diarrhea (≥ 20 mL/kg in patients < 18 yrs. of age) in a 24-h period on or ≤ 7 days before the collection date of the first positive blood specimen b. A history of ≥ 2 days of an ANC or WBC < 500 cells/mm³ on or within 3 days of the collection date of the first positive blood specimen

ANC absolute neutrophil count, GVHD graft versus host disease, HSCT hematopoietic stem cell transplant, LCBI laboratory-confirmed bloodstream infection, WBC white blood cell count National Patient Safety Network 2013

from the translocation of gastrointestinal microorganisms to the bloodstream, particularly in patients with severe neutropenia or who have gastrointestinal graft versus host disease [9]. Use of CLABSI as a surveillance definition in these populations, therefore, overestimates the proportion of bloodstream infections that are attributable to central lines and has implications for whether or not these infections may be prevented by traditional approaches or, indeed, if these infections are preventable at all [10]. In 2013, the NHSN introduced a new surveillance definition of “mucosal injury-associated laboratory-confirmed bloodstream infection” (MBI-LCBI, Table 11.2). Additional studies of the impact of distinguishing MBI-LCBI from CLABSI in high-risk pediatric and adult populations are ongoing.

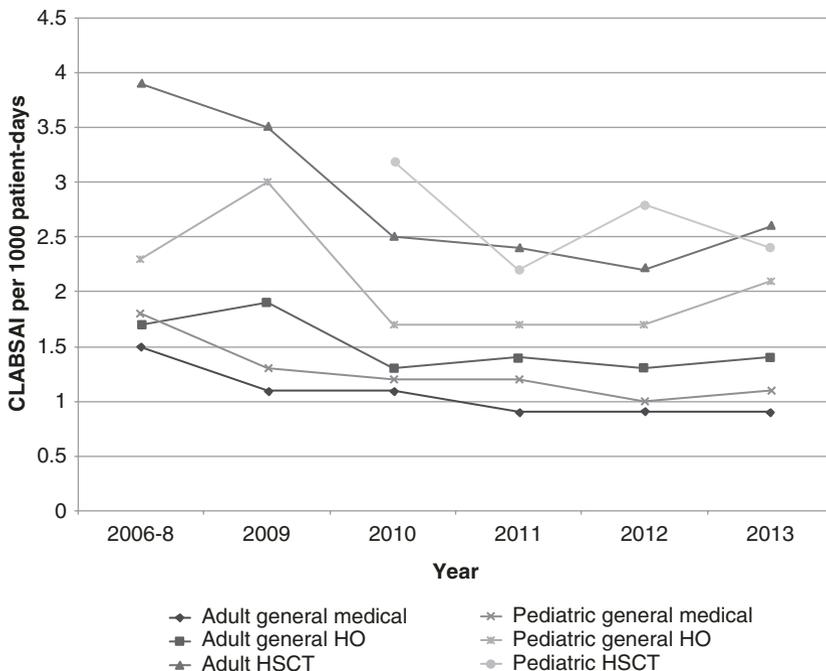


Fig. 11.1 Pooled mean rates of permanent central line-associated bloodstream infections (number of infections per 1000 patient-days) in hospitalized adults and children 2006–2013, by care unit. Data from the National Healthcare Safety Network, available at: <http://www.cdc.gov/nhsn/data-stat/index.html>

Clostridium difficile Infection (CDI)

C. difficile is the single most common organism causing HAI in the United States, with an estimated incidence of 95.3 infections per 100,000 persons overall and 6.3 per 100,000 children under 18 years of age [11, 12]. *C. difficile* is a Gram-positive, anaerobic, spore-forming bacillus. Intestinal colonization occurs when infectious spores, which may persist for long periods in the environment, are ingested. Some strains elaborate two homologous exotoxins, toxin A and toxin B, which bind to and damage intestinal epithelial cells and incite strong inflammatory responses [13]. North American pulsed-field gel electrophoresis type 1 (NAP1) PCR ribotype 027 strains of toxigenic *C. difficile*, which express more toxin A and B than other strains and an additional binary toxin, emerged in the early 2000s. Now commonly found in North America, these strains are associated with more severe disease in adults, but it is not yet clear whether they are more pathogenic in either children or cancer patients [14].

In order for CDI to occur, patients must be colonized with toxigenic *C. difficile* and undergo some alteration in the gastrointestinal microbiome that promotes decreased microbial diversity [13]. The most commonly recognized risk factor for

CDI is antibiotic use; others include antineoplastic chemotherapy, the use of proton pump inhibitors, gastrointestinal surgery, inflammatory bowel disease, and immunocompromising conditions [15]. Adults with cancer and recipients of HSCT are at significantly greater risk of CDI than the general hospital population, with rates ranging from 3.4% to 27% [16]. Disease manifestations range from mild diarrhea to fulminant pseudomembranous colitis. Complications such as toxic megacolon, bowel perforation, and sepsis are responsible for an estimated fatality rate of up to 15% in adults [12]. Malignancy is also a strong predictor of recurrent CDI. Most children with healthcare-associated CDI have underlying medical comorbidities, with malignancy being the most common. Up to 25% of cases of CDI in hospitalized children occur in those with cancer, a rate tenfold higher than that observed in children without cancer [17, 18]. Boyle reported 17% of pediatric HSCT recipients older than 1 year of age developed CDI within 100 days of transplant (20/10,000 patient days), significantly higher than that the rate observed in adult recipients [19]. Severe and complicated disease appear to be less common in children than adults, but more frequent in children with cancer than those without malignancy [15, 16, 20].

The NHSN defines healthcare-associated CDI as a positive test for toxin-producing *C. difficile* in an unformed stool specimen and/or gross anatomic or histopathological evidence of pseudomembranous colitis, with disease beginning >3 days after admission to a healthcare facility [21]. This and other clinical and surveillance definitions have significant limitations that may affect estimates of the incidence of CDI in pediatric oncology patients. Over half of young children, especially those <2 years of age, and almost a third of pediatric oncology patients may be asymptotically colonized by *C. difficile*, often for long periods of time [22–24]. Some investigators have suggested that sensitive molecular diagnostic tests, such as nucleic acid amplification of toxin A and B genes, are more likely to overestimate the incidence of CDI than older assays because these are more likely to identify the clinically inconsequential carriage of *C. difficile* [22]. Viruses and other gastrointestinal co-pathogens are also detected in as many as 80% of children, including immunocompromised children with CDI, making it difficult to judge the contribution of each potential pathogen to diarrheal disease [25, 26]. Importantly, however, patients who are colonized with toxigenic *C. difficile* may still represent a source of environmental shedding and transmission of infectious spores. Judicious use of antimicrobials, infection prevention precautions, and environmental cleaning are the mainstays of CDI prevention in healthcare settings.

Ventilator-Associated Pneumonia (VAP)

The NHSN surveillance definition for pneumonia incorporates the results of diagnostic imaging, clinical signs and symptoms, and laboratory tests [27]. A specific algorithm is available for immunocompromised patients (Table 11.3). Ventilator-associated pneumonia (VAP) is defined as pneumonia that occurs >2 calendar days after a patient is placed on mechanical ventilation; the ventilator must have been in place on the day that the first criterion for the diagnosis of VAP was met or on the previous day.

Table 11.3 National Hospital Safety Network surveillance definition for pneumonia in immunocompromised patients

Evidence	Definition
Diagnostic imaging	<p>≥2 serial chest imaging studies at a ≤ 7-day interval demonstrating at least one of:</p> <ul style="list-style-type: none"> • New or progressive and persistent infiltrate(s) • Consolidation • Cavitation • Pneumatoceles in infants ≤1 year of age <p>In patients without underlying pulmonary or cardiac disease, a single unequivocal chest imaging study is acceptable</p>
Clinical findings	<p>At least one of:</p> <ul style="list-style-type: none"> • Fever (>38.0 °C) • New onset of purulent sputum, change in character of sputum, increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough, dyspnea, or tachypnea • Crepitations or bronchial breath sounds • Hemoptysis • Pleuritic chest pain
Laboratory tests	<p>At least one of:</p> <ul style="list-style-type: none"> • Positive blood culture not related to another source of infection • Positive pleural fluid culture • Positive quantitative culture from minimally contaminated lower respiratory tract specimen • 5% BAL-obtained cells with intracellular bacteria on Gram stain • Positive quantitative culture of lung tissue • Histopathological evidence of abscess formation or intra-alveolar/bronchiolar accumulation of PMNs <p>For viral and fastidious bacterial (e.g., <i>Legionella</i>) pneumonias:</p> <ul style="list-style-type: none"> • Positive culture from respiratory secretions • Positive nonculture diagnostic test from respiratory secretions • Fourfold rise in paired acute and convalescent serum antibody titers • Detection of <i>Legionella</i> antigen in urine <p>For fungal infection:</p> <ul style="list-style-type: none"> • Matching positive blood and sputum/ET aspirate cultures with <i>Candida</i> spp. • Evidence of fungi from minimally contaminated LRT specimen by direct microscopic examination and culture or nonculture diagnostic test

Adapted from [27]

The precise incidence and clinical outcomes of VAP have been difficult to establish because studies have used diverse diagnostic criteria and inconsistently applied these criteria and because diagnostic definitions for VAP, including those reported by the NHSN, have limited sensitivity and specificity [28]. The signs and symptoms of VAP, for example, may overlap with other infections, such as tracheobronchitis, and with noninfectious pulmonary disorders [29]. Reactivation of latent pulmonary or systemic infection, such as cytomegalovirus or tuberculosis, in oncology and transplant patients, including children, may be indistinguishable from VAP. Some features of the current NHSN surveillance definition make its application to children problematic. Respiratory specimens, for example, must be obtained by methods that limit contamination, such as bronchoalveolar lavage, that may have

Table 11.4 CAUTI rates [1]

Location	Pooled mean CAUTI
Adult general medical/surgical inpatient	1.3
Adult medical/surgical ICU	1.3–2.7 ^a
Adult general hematology-oncology ward	2.1
Adult HSCT ward	2.2
Pediatric general medical surgical inpatient	1.4
Pediatric medical/surgical ICU	2.5
Pediatric general hematology-oncology ward	3.0
Pediatric HSCT ward	0.0

^aRates vary by unit size and teaching status

technical limitations and greater risks in young patients [30]. Recognizing the limitation of VAP surveillance definitions, NHSN surveillance began to assess a broader range of ventilator-associated events, including VAP, in adults in 2015 [31]. A pediatric-specific algorithm for VAP is not yet available, but one study that applied adult definitions retrospectively to PICU patients receiving mechanical ventilation suggests that this strategy may be useful [32].

Obstacles to diagnosis notwithstanding, VAP are the second most common HAI in pediatric and neonatal intensive care units. In the United States in 2012, there were 0.7 VAP per 1000 ventilator days in pediatric medical/surgical units [33]. Overall, between 3% and 10% of ventilated PICU patients develop VAP, a rate that is approximately threefold lower than that of adults (Table 11.4) [34]. Data are limited, but have suggested that VAP in children, as in adults, is associated with longer duration of mechanical ventilation and PICU stay, greater hospital costs, and increased mortality [35, 36]. The specific rates and characteristics of VAP in pediatric oncology patients have not been reported, but it is plausible that immunosuppression might predispose to infection and increase the rate and severity of VAP in this population.

The pathogenesis of VAP has not been completely elucidated. VAP may, like conventional pneumonia, result from the inhalation of infectious aerosols or complicate hematogenous bacteremia or fungemia. The presence of the same microorganisms in the oropharynx and in endotracheal aspirates, however, suggests that a frequent and potentially preventable cause of VAP is the aspiration of microorganisms colonizing the endotracheal tube (ET), oropharynx, or stomach [37]. Micro-aspiration of upper airway secretions around the uncuffed ET commonly used in infants and children or through channels formed by folds in low-pressure high-volume cuffed ET may be exacerbated by the impairment of mucociliary clearance and pooling of secretions in the subglottic airway. Risk factors for VAP in children include a prolonged duration of mechanical ventilation, prior antimicrobial exposure, and the use of immunosuppressing drugs, particularly corticosteroids [38]. Additional contributing elements may include the replacement of the usual microbiological flora of the oropharynx and stomach by more virulent species (such as *Staphylococcus aureus* and Gram-negative bacilli), the contamination of suction equipment (particularly associated

with the use of open systems and nonsterile solutions), and the presence of a nasogastric tube, enteral feeding, poor oral hygiene, gastric distension, and positioning (with the semirecumbent position associated with a lower risk of VAP than the supine position). The contribution of each of these elements to the pathogenesis of VAP in pediatric hematology-oncology patients has not been studied; most prevention strategies target multiple risk factors for infection.

Catheter-Associated Urinary Tract Infections (CAUTI)

Overall, urinary tract infections (UTI) are the fourth most common HCA infection in the United States [39]. Almost all are related to catheterization or other instrumentation. Short-term indwelling urinary catheterization may be necessary because of acute urinary retention or obstruction, or the need to monitor urinary output (especially perioperatively, during critical illness, or if receiving large volumes of fluid or diuretics). More prolonged use may be required to promote healing of sacral or perineal wounds or incisions, in incontinent patients or for comfort during end of life care.

The NHSN defines CAUTI as a UTI that occurs >2 calendar days after a urinary catheter is placed and <1 day after the catheter has been removed, if applicable [39]. Rates are generally higher in children than in adults (Table 11.4), but little has been reported on outcomes in children outside of the intensive care setting or in specific populations such as pediatric hematology-oncology and transplant recipients. CAUTI are associated with secondary bloodstream infections, increased hospital stay and costs and, in adults, increased mortality [40, 41].

Most CAUTI are ascending in origin. Uropathogens that colonize the periurethral area adhere to fibrinogen that accumulates on the catheter, multiplying and forming biofilm [41]. Thereafter, bacteria may colonize the bladder, often within days, releasing toxins and proteases that damage urinary epithelium and promote ascension to the kidney and hematogenous dissemination. Up to a third of infections may occur from contamination of the urinary collecting system from exogenous sources, such as the hands of healthcare providers [42]. Efforts to prevent CAUTI have focused on reducing the duration of catheter use and the contamination of drainage systems.

Respiratory Viral Infections

Most respiratory viruses are spread by indirect contact, droplet, or airborne transmission. Sources of infection include other patients, caregivers or visitors, and healthcare providers, who may be asymptomatic or symptomatic, and contaminated environmental sources [43]. Patient factors that increase the likelihood of healthcare-associated respiratory viral infections in pediatric hematology-oncology and transplant patients include their frequent close physical contact with caregivers, young age, lack of previous natural infection or immunization and subsequent acquired immunity, and the presence of primary or secondary immunodeficiency. In the ambulatory healthcare

setting, patients may be cared for in extended periods in common areas; the risk of infection is increased when infectious persons are not immediately recognized and when environmental cleaning is inadequate because of time constraints.

Strategies to reduce healthcare-associated respiratory viral infections include transmission-based infection, prevention, precautions, and vaccination. Institutions must provide infection prevention staff, clinical microbiology support, and the supplies and equipment necessary to assess and correct remediable causes of healthcare-associated respiratory viral infections. Risk assessment should inform the development of processes for the surveillance for and management of endemic, epidemic (e.g., influenza), and emerging (e.g., Middle East respiratory syndrome-coronavirus) respiratory infections.

Respiratory hygiene/cough etiquette strategies designed to facilitate the prompt recognition of respiratory illness in patients and caregivers have been developed with the intention of incorporating these into infection prevention standard precautions (Table 11.5) [43]. Transmission-based precautions should be implemented for hospitalized patients with any signs or symptoms of respiratory viral infections pending diagnostic tests. A single patient room with toilet and hand hygiene facilities is preferred. If this is not feasible, spatial separation of >3 ft and the use of curtains or other room dividers are recommended. Other strategies, such as cohorting patients with the same organism or the same symptoms or cohorting providers, should be considered in outbreak or other special circumstances, in consultation with infection preventionists. When patients are transferred to other facilities or departments, the presence of a potentially communicable disease and current infection prevention precautions should be communicated to the receiving providers. Viral shedding may persist for weeks to months in immunocompromised patients. Discontinuing transmission-based precautions in this population, therefore, must consider host factors, disease epidemiology, and the results of diagnostic tests.

Few high-quality randomized clinical trials have addressed the effectiveness of masks for the prevention of transmission of respiratory viruses. Existing evidence suggests, however, that both medical masks and respirators are effective. The CDC and other agencies recommend the use of these devices to protect patients and healthcare providers against seasonal influenza and tuberculosis. Clinical trials suggest that face masks provide compliance-dependent protection against

Table 11.5 Respiratory hygiene and cough etiquette components

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|--|
| 1. Education of staff, patients, and visitors regarding respiratory hygiene and cough etiquette |
| 2. Posted signs instructing patients and caregivers to make healthcare personnel aware of symptoms of respiratory illness |
| 3. Provision of materials for source control (e.g., tissues, alcohol-based hand rub or supplies for handwashing after contact with respiratory secretions) |
| 4. Masking and spatial separation of persons with respiratory symptoms from others in common waiting areas (ideally in a single room, a minimum of 3 ft from others) |
| 5. Observance of droplet and standard precautions by healthcare providers when examining patients with symptoms of a respiratory infection |

Adapted from [43]

infection in the community [44]. For healthcare providers, respirators appear to provide superior protection, but the choice of respiratory protection should be based on availability, etiology of illness, comfort, and the degree of risk.

Healthcare providers should refrain from working when ill with symptoms of a communicable respiratory infection; management policies should support and not discourage this practice. Likewise, visitors with respiratory illnesses should be discouraged from entering healthcare facilities unless this is unavoidable.

Seasonal influenza vaccination of healthcare providers reduces hospital-acquired influenza infections in cancer patients, and most evidence suggests that this practice decreases employee morbidity and absenteeism [45–47]. The Centers for Disease Control and Prevention Advisory Committee on Immunization Practices (ACIP) recommends that, unless medical contraindications exist, all healthcare personnel should be vaccinated annually to protect themselves, their families, and their patients against influenza [48]. Similar recommendations exist for the use of tetanus-diphtheria-acellular pertussis (Tdap) vaccine for the prevention of pertussis [49]. These recommendations direct organizations to provide vaccine as part of employee health programs and to make efforts to reduce administrative and financial barriers to immunization [50]. Personnel refusing influenza vaccination for reasons other than a documented medical contraindication should sign a written declination that outlines the risks of vaccine refusal. Influenza immunization of HCP is tracked by the NHSN. During the 2014–2015 season, 88.6% of employees and 84.5% of all healthcare personnel in acute care hospitals received seasonal influenza vaccination, representing a significant increase over historical rates of compliance with vaccine recommendations [51, 52]. Successful strategies to improve compliance with vaccination policies have included education and incentive-based (i.e., reward) systems, but the most effective approaches have been mandatory vaccination policies that require the use of protective face masks or antiviral prophylaxis for the duration of the influenza season or result in the suspension or termination of unvaccinated workers [53]. Some states have enacted legislation to increase healthcare provider immunization rates [54].

Measurement

Both process (important data elements related to patient care activities) and outcome data must be systematically collected to prevent HAI. Ongoing process and outcome data collection can inform the development of more effective prevention strategies or lead to the modification of suboptimal processes. The latest CDC surveillance definitions should be used to identify the occurrence and rates of HAI within an institution [6]. If ongoing surveillance reveals a sharp increase in infections, standard epidemiological investigation techniques must be used to investigate the outbreak; these methods are beyond the scope of this chapter [55]. Organizations should remain open to reevaluating and improving measures for HAI based on new knowledge. For example, the recently developed definition for MBI-LCBI, clearly differentiating these infections from other CLABSI, is a relatively new outcome measurement that has substantial importance to the pediatric hematology-oncology population.

Table 11.6 Prevention bundle elements for CLABSI, CAUTI, and VAP^a

Bundle	Standard Elements
CLABSI—insertion	Hand hygiene
	CHG scrub
	No iodine treatment
	Prepackaged or filled insertion cart, tray, or box
	Insertion checklist with staff empowerment to stop non-emergent procedure
	Full sterile barrier for providers and patients
CLABSI—maintenance	Insertion training for all providers
	Daily discussion of central line necessity, functionality, and utilization including bedside and medical care team members
	Regular assessment of dressing to assure clean/dry/occlusive
	Standardized access procedure
CLABSI—recommended element	Standardized dressing cap and tubing change procedures/timing
	Utilize a system approach to review all hospital-acquired CLABSI
CAUTI—insertion	Use aseptic technique for insertion
	Avoid unnecessary catheterization
CAUTI—maintenance	Maintain a closed drainage system
	Maintain hygiene
	Keep bag below level of bladder
	Maintain unobstructed flow of urine
	Remove catheter when no longer needed
CAUTI—recommended element	Secure catheter
VAP	Readiness to extubate—assess readiness to extubate daily
	Head of bed elevation—elevate head of bed to 30–45 degrees
	Minimize distribution of the circuit—inspect ventilator circuit for gross contamination daily, and if present, change circuit
	Oral hygiene—perform oral hygiene minimally every 12 h

^aAdapted from SPS Bundle Elements [57]

When considering process data collection, it is important to identify the methods utilized by institutions to prevent the occurrence of HAI. A common approach to infection prevention is the “prevention bundle,” designed to provide a list of elements that should be routinely implemented to prevent HAI. One identified authority for information on prevention bundles is the Children’s Hospitals’ Solutions for Patient Safety (SPS), which is an international network of over 90 hospitals that aims to reduce patient harm, including HAI, in children’s hospitals [56]. SPS provides a document that includes prevention bundle information for CLABSI, CAUTI, and VAP infections [57]. Listed in Table 11.6 are examples of elements included in these bundles that focus on standards for both insertion and maintenance of devices for CLABSI and CAUTI and important processes for the prevention of VAP. Of note, the insertion bundle elements were developed for bedside insertion in the ICU, not for line placement in an operating room. Bundle elements are stratified based on their level of evidence to provide hospitals with guidance for prioritizing their efforts.

The SPS document lists standard and recommended bundle elements and provides tools for assessing the reliability of these bundles, such as protocols for audits of performance on all SPS Prevention Bundle Standard elements [57, 58]. Institutions can choose to include additional elements if they desire to gather data on other processes, but SPS suggests limiting these to five or fewer so that healthcare staff are not overwhelmed or confused by the number of interventions [57]. For CLABSI and CAUTI, it is recommended that insertion and maintenance bundles be measured separately. SPS recommends performing a minimum of 20 audits per month in order to obtain data frequently enough to rapidly identify barriers to compliance and to make changes in the processes to eliminate these barriers [57]. A 90% compliance rate for bundle data is a common goal within SPS. Organizations using sophisticated electronic health records (EHR) with capabilities to discretely document and subsequently retrieve data may be able to gather some or all data electronically. However, this approach may not be feasible in all settings, and direct observation of bundle elements may identify additional opportunities for improvement that may not be revealed through automated retrieval of data documented in the EHR.

Recommended practices include structured investigation, data collection, and analysis of all episodes of infection. These efforts may be referred to by various names, depending on the organization [e.g., mini root cause analyses (RCA) or line rounds]. Many institutions use this approach, documented most commonly for CLABSI, to retrace every step leading up to the infection and thereby identify improvement opportunities. The goal of this approach is to allow institutions to learn from each and every infection and implement improvements based on these findings. For example, Rinke et al. used a RCA approach to systematically investigate all CLABSI in hospitalized pediatric oncology patients [59]. When a positive blood culture was reported, a multidisciplinary team interviewed care providers and analyzed 13 patient and system factors that could have contributed to the CLABSI. A similar approach was used by Bundy et al. in a multicenter quality improvement collaborative that included the implementation of a standardized bundle as well as CLABSI surveillance. This approach resulted in significant reductions in CLABSI rates among 32 pediatric hematology-oncology centers [60]. In both instances, the use of this RCA approach provided vital data elements that could then be used for system changes and the implementation of improvement strategies.

When comparing the evidence base for the prevention bundles discussed in this chapter, the most detailed and convincing data in the pediatric hematology-oncology and transplant population are available for CLABSI prevention [60]. CAUTI and VAP bundles have data supporting their effectiveness in other populations [61, 62]. Formal SPS Prevention Bundles for CDI have not been developed, and, without this guidance, other approaches must be utilized to reduce the number of these infections. One example is the guideline provided by the Society for Healthcare Epidemiology of America (SHEA); this includes strategies for prevention of CDI in adults, but can be adapted for pediatric hematology-oncology patients [63, 64]. A list of recommendations can be found in Table 11.7. Evaluating and monitoring each of these practices can provide institutions with compliance data as well as identifying areas for improvement, much like the approaches taken using the SPS bundles. If analysis is done using these approaches and the CDI incidence remains higher than the institution's goal, SHEA also provides special approaches for preventing CDI in high-risk settings [63].

Table 11.7 Basic practices for prevention and monitoring of CDI: recommended for all acute care hospitals and ambulatory care settings [63, 64]

1. Encourage appropriate use of antimicrobials
2. Initiation of contact precautions for patients with signs and symptoms consistent with CDI, single-patient room preferred
3. Implement a laboratory-based alert system to provide immediate notification about newly diagnosed CDI patients
4. Education of healthcare personnel, environmental service personnel, and hospital administration about CDI, specifically the importance of handwashing with soap and water and the use of personal protective equipment
5. Educate patients and their families about CDI as appropriate, including hand hygiene and the cleaning of cell phones and other personal effects.
6. Cleaning and maintenance of reusable medical devices according to the manufacturer's instructions and institutional policies; do not reuse single-use devices
7. Establish policies and procedures for routine cleaning and disinfection of environmental surfaces in both inpatient and ambulatory care facilities, including placing emphasis on surfaces that are most likely to be contaminated with pathogens and the use of EPA-registered detergents/disinfectants; assess adequacy of cleaning
8. Notify receiving caregivers of CDI within and outside of facility upon transfer
9. Conduct CDI surveillance and analyze and report CDI data
10. Measure compliance with CDC or WHO hand hygiene and contact precautions

Improvement

When data indicate deviations in bundle performance data, an increase in infections, or other opportunities for improvement, various actions must be taken. A wide variety of causes and contributing factors must be considered, including staff, patient, and family practices, equipment and supply changes, the environment of care, and others. Similar to other areas of patient safety, actions must focus on high leverage changes that provide fundamental and lasting changes in the process of care. Simple actions such as education and policy changes may provide value in some situations, but rarely provide lasting change and improvement. Iterative, ongoing improvements will often be needed to embed lasting change into practice, and leaders must be nimble and responsive to promote changes in practice.

Participation in formal collaborations across children's hospitals focused on reducing HAI has become a core technique. The Quality Transformation Network, managed by the Children's Hospital Association (CHA), unified pediatric hospitals to work together in order to deliver high-quality, reliable, and safe care for pediatric patients [56]. Initial collaborative efforts to prevent HAI in children's hospitals were focused on CLABSI in the pediatric intensive care unit (PICU). The successful PICU work prompted CHA to expand these efforts to inpatient pediatric hematology-oncology units in 2009, and to the ambulatory setting in 2011, by creating the Hematology-Oncology CLABSI Collaborative, later renamed the Childhood Cancer and Blood Disorders Learning Network (CCBDN) [56, 60, 65]. Recently, the CHA collaborative has worked with SPS [56]. SPS now collects data on inpatient

CLABSI for pediatric oncology/hematology units, and CCBDN has concentrated efforts on reducing CLABSI in ambulatory patients with cancer and blood disorders, recognizing that the majority of these children and adolescents receive much of their care outside the hospital and that CLABSI occur more than twice as frequently in the ambulatory setting than in hospitalized children in this population [56, 65, 66].

Ultimately, preventing HAIs is a team effort that requires sustained involvement and engagement across the entire healthcare team as well as patients and families. For example, the entire team should routinely discuss the continuing need for intravenous and urinary catheters. In the pediatric hematology-oncology population, however, care may require a central venous catheter for months to years at a time. Further, to reduce line accesses, nurses and physicians will need to work together to bundle lab draws, and nurses, pharmacists, and physicians will need to work together to switch from intravenous to oral therapy. All of this ongoing communication must occur in an environment with a positive patient safety culture that encourages team members and families to speak up to make changes for patient care.

Sustainability

Sustaining the improvements achieved after reducing healthcare-associated infections is necessary to continue to obtain successful outcomes in pediatric hematology-oncology patients, given the high rates of infections in this population and the associated morbidity and mortality [2, 67–69]. Although sustainability has been recognized as a key practice in quality improvement and safety work, including the reduction of HAI in pediatric hematology-oncology patients, it does not occur automatically [70]. The Institute for Healthcare Improvement refers to sustainability as locking in the progress that groups have made already and continually building upon it [71]. In pediatric hematology-oncology patients, sustaining reductions in HAI implies adoption and long-term implementation of the established evidence-based practices that are known to result in infection rate reductions, such that these become the norm within a group and ideal adherence is accomplished (i.e., strict compliance with the central line care bundle to reduce CLABSI). The goal is to develop a change to reduce pediatric HAI with enduring impact, even after the initiative is no longer the top priority for a group, and it begins to function without additional dedicated resources. Yet, maintaining a positive change long-term is known to have a high rate of failure, and only limited reports exist of sustained healthcare improvements [72].

Some of the factors associated with difficulty achieving sustainable change are not specific to efforts aiming to reduce HAI in pediatric hematology-oncology patients, but certainly apply. These include incorporation of new staff unaware and/or untrained in best practice and the development of new projects that create distraction or shift the focus away from infection reduction, complacency, and the commonality of emergencies and complex cases in this group of patients, which can at

times justify the lack of adherence to best practice [73]. Therefore, a specific focus on sustainability is necessary in order to hold on to the gains achieved.

Strategies for sustainability must be incorporated early on and embedded into the process as it occurs, such that it is inseparable from the process of designing, testing, and implementing change. Some of the improvement strategies utilized to achieve reductions in HAI can also lead to sustainability independently, but a formal focus on this aspect through careful planning increases the chances of maintaining improvements. A number of approaches to foster sustainability after change based on high reliability principles have been described in other chapters of this book and elsewhere [71]. Many of these are applicable to preserving the changes after reductions in pediatric hematology-oncology HAI are obtained, but limited evidence exists that is unique to sustainability in this particular area. Rather, efforts have primarily been concentrated on achieving improvements and reducing HAI in this vulnerable population, rather than on upholding gains.

Organizing children's hospitals around the United States into large-scale pediatric collaborative improvement networks has been an overarching principle in successful and sustainable pediatric quality improvement and safety efforts. These efforts have paved the way for additional healthcare improvement and safety initiatives in pediatric hospitals. These, in turn, have led to sustainable reductions in patient harm, including fewer pediatric HAI [47, 49, 54]. The first visible success story in sustainable improvements specific to pediatric cancer and blood disorder patients resulted from the CHA CCBDN effort to reduce inpatient CLABSI in pediatric hematology-oncology patients; this has successfully achieved and maintained an inpatient CLABSI rate reduction of approximately 28% for years [60].

Collaboration has been central in sustaining reductions in CLABSI rates in pediatric hematology-oncology patients and spreading change. Hospitals collaborating in networks are being encouraged to share success stories and helpful tools and strategies in achieving and maintaining reductions in CLABSI rates. In addition, networking provides a platform for spread and expansion. The success of networking and collaboration is based on providing a common forum to work, learn, and improve together [60, 74].

The collaborative success in pediatric hematology-oncology CLABSI reduction highlights a number of strategies that are central in sustaining change within this complex population. These can be summarized into three categories: People, Process, and Place (the three Ps).

People

Similar to the importance it has in achieving improvement, a strong leadership that is visible and effective is central to sustaining change. The collaborative has provided this at a high level, but individual institutions also require the presence of strong leaders locally in order to maintain the changes achieved. A large majority of successful efforts in reducing CLABSI in pediatric hematology-oncology patients have emphasized the importance of a dedicated team with direct leadership, central

to maintaining hospital-wide support even after the goal has been achieved, such that efforts can be continued [60, 68, 75].

One of the main strategies of sustaining a change that is primarily reliant on staff consistently performing all aspects of a bundle, as is the case with many pediatric HAI prevention efforts, is ensuring formalized ongoing staff education and training of newcomers on best practice. This requires high-quality training of staff, where multidisciplinary teamwork and communication are key to successfully holding on to the gains achieved [73]. Formal competency testing processes are essential. One recommended approach is to have ongoing formal competency testing through fidelity simulation, which has been associated with assuring competency in care delivery of aspects such as central line care [70, 71].

Process

Standardization and spreading of change are both key aspects to sustainability [71]. These aspects were also observed as a result of the large-scale collaboration to reduce CLABSI in pediatric hematology-oncology patients. Participating children's hospitals across the nation were required to continuously report rates of infection and compliance with the central line care bundle [60]. The collaborative reproduced detailed data about CLABSI and bundle compliance rates for participating centers, allowing for transparency, visibility, and the ability to generate benchmarking data facilitating comparison among centers. Furthermore, the process of monitoring and reporting continued even after a reduction in CLABSI rates was observed, thus serving as a main strategy in sustaining gains. Monitoring and reporting of infection rates incentivizes adherence to best practice and, therefore, leads to sustained reductions in rates. Similarly, connecting teams at other hospitals reduces trial and error to find effective solutions. Also central to sustainability is the fact that these initiatives were expected to be long term and were built to persist until goals were achieved and quality improvement was maintained [60, 66, 67].

In pediatric hematology-oncology CLABSI reduction, the collaborative's use of self-audit not only served as a measurement tool but also as a reminder to staff regarding best practices when caring for central lines. This strategy encourages strict compliance with evidence-based practice, standardization, ongoing monitoring of performance, and incorporation into the daily routine, all of which are aspects central to maintaining change [60, 74]. Other strategies that have been used include the development of processes to learn from outstanding scenarios by RCA and identifying local barriers through methodology such as failure modes and effects analysis, a strategy used to prospectively identify areas of risk. One group specifically described the importance of ongoing monitoring of infection rates and the need to have a process in place to respond to unexpected changes in the face of an observed rise in CLABSI rates. Their strategies included preemptively identifying patients with CLABSI-specific risk factors, identification of variables associated with increased CLABSI rates directly from frontline staff, and the evaluation of variables associated with increased micro-system stress [76].

Place

Embedded in every improvement process that is meant to last is the need to promote culture change [71]. In pediatric hematology-oncology, reducing HAI has required both a national and international focus that has helped identify the severity of the problem and concluded that improvements are achievable. The large-scale collaboration that has led to sustainable reductions in pediatric hematology-oncology CLABSI both directly and indirectly contributed to culture change [60, 66]. An emphasis on reducing HAI collectively led to increased awareness of the problem. This key step in developing culture change also indirectly led to increased attention to detail, and both contributed to a focus on safety culture and changes in belief systems [60, 66, 71].

In summary, attitudes toward infectious complications of pediatric hematology-oncology care have evolved over the past decade from the belief that these illnesses were largely inevitable to the understanding that, with diligent adherence to best practices, the incidence of many common infections in pediatric hematology-oncology patients and transplant recipients can be significantly reduced. The efforts of individual institutions are critical to identifying risks for infection in these populations and new strategies for infection prevention and ensuring that the organization itself maintains compliance with standards. Large-scale collaborations have provided forums for testing of new interventions; for disseminating standardized, evidence-based infection prevention methods; and for developing measurement and monitoring processes and benchmarks for improvement. Although still a relatively new effort, the systematic incorporation of quality improvement strategies has already demonstrated great promise in reducing the morbidity and mortality associated with infection in children and adolescents with cancer and improving disease outcomes.

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