Healthcare-associated Infections—Can We Do Better?

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HEALTHCARE-ASSOCIATED INFECTIONS: DEADLY, COSTLY, AND WIDESPREAD

Healthcare-associated infections (HAIs), which occur when a patient is receiving care in a hospital or other healthcare facility, are the most frequent adverse event in healthcare worldwide. HAIs cause significant increases in morbidity, mortality, length of hospital stays, and healthcare costs and have a particularly severe impact in low- and middle-income countries (LMIC).[1] In Europe, approximately 1 in 20 patients will contract an HAI leading to an annual loss of 2.5 million disability-adjusted life years (DALYs), mostly in neonates and children, and direct costs of up to €7 billion per year.[1,2] Yet research also shows that most HAIs are preventable through simple, low-cost infection prevention and control (IPC) practices. The importance of preventing HAIs is especially clear in light of the current COVID-19 pandemic, which has put healthcare systems around the globe under enormous stress, and has highlighted the role of IPC practices in protecting both the public and healthcare workers.[3]

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THE BASIC PRINCIPLES OF INFECTION PREVENTION AND CONTROL

Surveillance—Knowing Your Enemy

Robust surveillance mechanisms are a critical tool in the fight against HAIs. Data that shows who is getting infected, where infections are happening, and how many infections are occurring are essential to the design and implementation of effective interventions. In addition, an established surveillance system provides the means to assess the effectiveness of IPC programs and to invoke changes when needed. In the United States, the Centers for Disease Control and Prevention tracks HAIs through the National Healthcare Safety Network, and in Europe HAIs are tracked through the Healthcare-Associated Infections Surveillance Network. While National Healthcare Safety Network is an active surveillance network that uses mostly epidemiologic definitions, and the Healthcare-Associated Infections Surveillance Network is a point prevalence survey-based system with more clinically and laboratory-focused definitions, both aim to create metrics that allow for benchmarking and target identification.

Globally, despite some differences in terms and definitions, HAI surveillance tends to focus on the following: central line-associated bloodstream infections; catheter-associated urinary tract infections (CAUTIs); ventilator-associated events (VAEs)—the evolution of ventilator-associated pneumonia; surgical site infections; hospital-onset infections involving specific pathogens such as *Clostridium difficile* and multidrug-resistant organisms; and hand hygiene, the simplest and most effective way to prevent HAIs.

Evidence-based Practices—Fighting Your Enemy

There is a robust and expansive body of literature on the prevention of the most common HAIs,[4–6] which are focused around compliance with IPC best practices and the resultant prevention of transmission. As established and described by the World Health Organization, the core components of an effective IPC program include: establishing guidelines; supporting education and training; establishing HAI surveillance; using multimodal strategies; monitoring and evaluation of IPC practices; adequate staffing according to workload; adequate availability of materials and equipment for IPC.[6]

Table 1 shows some indicative strategies for each type of infection. As evidence is still lacking for the prevention of VAEs we have to resort to the guidelines developed for the prevention of ventilator-associated pneumonia. It is necessary to always assess the latest literature as for example previously recommended oral care with chlorhexidine was shown to increase negative outcomes for

TABLE 1. Indicative Strategies for Prevention of HAIs

CLABSIs	Standardization of processes with bundles Insertion • Optimal site selection (avoid femoral in adults) • Hand Hygiene/Aseptic Technique • Skin preparation with >0.5% CHG (not recommended under 2 mo*) • Maximal sterile barrier precautions (use cap, mask, full-body drape, sterile gloves) • Place a dressing over the insertion site (preferably sterile, transparent, semipermeable) • Implement insertion checklists • Create an open communication environment that allows staff to speak up in case of a violation of IPC practices during CL insertion • Ultrasound-guided CL placement Not recommended: routine replacement of CL Note: Femoral insertion site has not been clearly associated with increased infection risk in children as in adults. Maintenance • Daily review of necessity and prompt removal • Before accessing the CL: Scrub the access port or hub with friction for a minimum of 5 s with an appropriate antiseptic (chlorhexidine, povidone iodine or 70% alcohol) • Use sterile, transparent, semipermeable dressing (or sterile gauze) to cover the catheter site. • Replace site dressing every 7 d (every 2 d if made of gauze) or if it becomes loose, soiled or damp. In very young patients or in NICUs where lines can move when manipulated it can be reasonable to change the dressings less frequently • Use of topical antibiotic ointment or creams is not recommended unless the line is a dialysis catheter • Change administration sets for continuous infusions no more frequently than every 4 d but at least every 7 d. If blood products or fat emulsions are administered change tubing every 24 h Additional Strategies • CHG bathing (older than 2 mo) • Use of CHG-containing dressings in patients over 18 - "Not recommended to protect the site of short-term, non-tunneled central venous catheters for premature neonates due to risk of serious adverse skin reactions" - "No recommendation can be made about the use of chlorhexidine-impregnated dressings to protect the site of short-term, non-tunneled central venous catheters for pediatric patients less than 18 yr old and nonpremature neonates due to the lack of sufficient evidence" • antimicrobial-impregnated CLs for adult patients • "Remove and do not replace umbilical artery catheters if any signs of CRBSI vascular insufficiency in the lower extremities, or thrombosis are present" • "Remove and do not replace umbilical venous catheters if any signs of CRBSI or thrombosis are present" • "No recommendation can be made regarding attempts to salvage an umbilical catheter by administering antibiotic treatment through the catheter" *even though more than 50% of pediatric centers in the US do use chlorhexidine in under 2 mo with some restrictions
CAUTIs	Standardization of processes with bundles Insertion • Avoid unnecessary catheterization • Insert catheters ONLY for appropriate indications/develop indications for placement • Consider alternatives to indwelling catheters (intermittent catheterization/external condom catheters) (note: not all appropriately sized condom catheters are available for smaller children) • Hand hygiene • Aseptic technique and sterile equipment • Meatal/perineal cleansing (sterile saline vs. antiseptic: unresolved issue) • Chose catheters of appropriate size • Secure indwelling catheters to prevent movement and urethral traction • Use an insertion checklist Maintenance • Daily review of necessity and prompt removal • Do not routinely change catheters or collection systems • Nurses empowerment to remove catheters on absence of indication • Maintain a closed drainage system. • Maintain unobstructed urine flow (even though in small children tubing loops might be inevitable) • Perform meatal/perineal care at least once a day or when soiled • Empty urinary collection system when 2/3 full or every 8 h
C. difficile	Surveillance/testing • Asymptomatic colonization is common in young children and especially under 12 mo. • Positive tests for *C. difficile* in children under 2 yr old might be colonization even if diarrhea is present • Consider testing for alternative causes of diarrhea as well • Do not conduct repeat testing for CDI Reduce risk of CDI • with antimicrobial stewardship Prevent exposure • use dedicated items and equipment and private rooms • Contact precautions should be in effect. Some experts suggest at least 48 h after diarrhea resolve or until discharge • Hand hygiene to be performed preferably with soap and water as alcohol is not sporicidal • environmental decontamination CDI patients' rooms with sodium hypochlorite (household bleach) diluted 1:10 or sporicidal product
SSI	• Administer antimicrobial prophylaxis according to guidelines (for timing before incision, agent and duration). Do not prolong postoperatively for the purpose of preventing SSI • Hair should either not be removed or, if absolutely necessary, it should be removed only with a clipper. Razors not recommended. • Skin antisepsis (WHO: alcohol-based antiseptic solutions based on CHG) • Ensure normothermia (35.5 °C or more) • Optimize glucose control • Administer supplemental oxygen (during and immediately following surgical procedures involving mechanical ventilation) • Screen/decolonize selected patients with *S. aureus* • Implement the use of checklists according to WHO • SSIs surveillance, analyzed and shared

(*Continued*)

TABLE 1. (*Continued*).

VAP	Pediatric • Avoid intubation if possible • Minimize the duration of mechanical ventilation • Assess readiness to extubate daily in patients without contraindications • Avoid unplanned extubations and reintubations. • Provide regular oral care • Elevate the head of the bed unless medically contraindicated • Maintain ventilator circuits • Change ventilator circuits only when visibly soiled or malfunctioning • Remove condensate from the ventilator circuit frequently. • Suction oral secretions before each position change • Endotracheal tube selection and maintenance • Use cuffed endotracheal tubes • Maintain cuff pressure and volume at the minimal occlusive settings to prevent clinically significant air leaks around the endotracheal tube Neonatal • Avoid intubation if possible consider nasal continuous positive airway pressure ventilation with or without nasal intermittent mechanical ventilation as an alternative to intubation minimize the duration of mechanical ventilation manage patients without sedation whenever possible • Assess readiness to extubate • Avoid unplanned extubations and reintubations • Provide regular oral care with sterile water (extrapolated from studies in adults, no data in preterm neonates) • Minimize breaks in the ventilator circuit
UNIVERSAL STRATEGIES	• Hand hygiene • Perform surveillance • Have procedures and processes well defined and accessible • Be up-to-date: review guidelines, procedures and process periodically. • Educate personnel, use simulation training • Checklists can be helpful both for education but also to ensure adherence for quality tracking • Prepare carts, kits or gather all material needed before a procedure (ie, central line, urine catheter placement) • Implement multimodal, multifaceted strategies • Implement environmental cleaning and disinfection of instruments • Promote vaccination • Antibiotic stewardship
	Based on and adapted from: Yokoe DS, Anderson DJ, Berenholtz SM, et al. A Compendium of strategies to prevent healthcare-associated infections in acute care hospitals: 2014 updates. *Infect Control Hosp Epidemiol*. 2014;35:967–977. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Clinical Infectious Diseases*. 2011;52:e162–e193. Including the 2017 updates as found: https://www.cdc.gov/infectioncontrol/guidelines/bsi/updates.html; https://www.cdc.gov/infectioncontrol/guidelines/bsi/recommendations.html. Dubberke ER, Carling P, Carrico R, et al. Strategies to prevent *Clostridium difficile* infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol*. 2014;35:628–645. Bryant K, Guzmann-Cotrill JA, eds. *Handbook of Pediatric Infection Prevention and Control*. 1st ed. New York, NY: Oxford University Press; 2019. Global guidelines for the prevention of surgical site infection, second edition. Geneva: World Health Organization; 2018.

CLABSIs indicates central line-associated bloodstream infections; IPC, Infection Prevention and Control; CRBSI, Catheter related bloodstream infections; SSIs, surgical site infections; CL, central line; CHG, chlorhexidine gluconate; CDI, *Clostridium difficile* infection; VAP, ventilator-associated pneumonia; WHO, World Health Organization.

mechanically ventilated patients. Prevention in the form of care bundles, which comprise a small set of coordinated, evidence-based practices, have been successful in improving compliance with best practices and patient outcomes in a variety of countries and settings. In addition, checklists have been shown to be effective in self-training and securing correct implementation of bundles.

Above all, hand hygiene is the cornerstone of preventing transmission between patients, surfaces, devices and healthcare workers. Research consistently shows a strong association of increased hand hygiene compliance with reduced HAI rates. While gloves are essential in certain circumstances, they should be used only where appropriate and not as a substitute for proper hand hygiene; and the overuse of gloves should be seen as a "red flag" for possible lapses in hand hygiene compliance.

At every institution, IPC policies and procedures need to be designed and tailored to the specific setting, and should be reviewed and updated regularly due to frequent advancements in IPC research. At all times, these policies and procedures must be fully and easily accessible to hospital staff.

The Human Factor—Resources, Culture and Communication

Devoting sufficient time, infrastructure, staffing and other resources to IPC is critical to the success of an IPC program and to reducing rates of HAIs at a healthcare facility. The Society for Healthcare Epidemiology of America's white paper[7] on the necessary infrastructure for infection prevention and healthcare epidemiology programs emphasizes that dedicated time and qualified, appropriately compensated professionals are essential to IPC. It also identifies the physical resources required, such as office space, Information Technology systems and material for educational purposes. The use of floating or visiting nurses, or other personnel, who may not be familiar with the unit's practices and could compromise the quality of the IPC program, should be avoided.

Furthermore, HAI prevention goes beyond surveillance and education, and often requires a change of culture in an institution. For this reason, effective communication about the importance of IPC and about policies and procedures is essential. Consideration of the social, economic and cultural factors at play in a country or institution must be integral to the design of any IPC program and should also be incorporated into the analysis of outcomes and results. Newsletters, posters, screen savers, social media applications or alerts, and mobile phone messaging are just a few tools that can be used to disseminate information about IPC.

CURRENT CHALLENGES IN INFECTION PREVENTION AND CONTROL

Missing the Pediatric Focus—Surveillance and Evidence

There is a critical need for structured and uniform pediatric surveillance data on HAIs in Europe. The data that does exist on this topic are scarce and problematic, as they are usually restricted to a single hospital or ward, limited to the time frame of a research protocol, or characterized by significant methodologic differences, all of which prevent comparison and benchmarking among countries and regions, or even within the same hospital.

The common practice of extrapolating data on HAI surveillance and prevention from other populations is neither sufficient nor appropriate to accurately characterize the problem of HAIs in children. For example, the adult VAE definition is problematic when applied to children, as it excludes patients on high-frequency ventilation and thus does not consider a large proportion of pediatric ventilated patients. With respect to CAUTIs, some pediatric urologists argue that in certain scenarios, an open or low-pressure urinary drainage system might be preferable to a closed one; but the data are lacking to make this recommendation. In short, it is imperative that evidence, specific to pediatric populations, is produced for definitions and guidelines for VAE, CAUTI and other common HAIs.[5]

Missing the in Low- and Middle-income Countries Focus—Surveillance and Evidence

Globally, LMIC are the settings where HAIs constitute the greatest burden and where simple interventions have the potential to make a significant impact. However, lack of infrastructure and resources has had a negative impact on the quantity, quality and consistency of surveillance data available. Infection prevention programs designed for high-income countries may not be appropriate or effective in LMIC due to significant differences in social, economic, and cultural factors. Using techniques that have been shown to be effective in high-income countries as a starting point, evidence must be produced that shows which practices are most successful specifically in the LMIC setting.[8]

Staffing and Resources—Understaffed, Overworked, Unrecognized

IPC programs often suffer from a lack of human resources and show great variability in staffing and policies across countries.[9] In primary or community care settings, staff are frequently not familiar with IPC best practices, as a result of the coverage by IPC specialists often being poor.[10] The COVID-19 pandemic has highlighted the importance of IPC specialists and implementation science, and recognition among stakeholders has increased.[3,11] This may lead to a greater demand for professionals working in IPC. However, IPC practices and implementation skills are currently underrepresented in training programs, despite the fact that research has shown the benefit of exposing medical students to IPC as early as their undergraduate education.[11,12]

Preparing for the Unknown

The COVID-19 pandemic has shown us that in cases of infectious agents for which there is limited knowledge and no established treatment options, infection prevention is essential to maintaining the integrity of healthcare systems and ensuring patient safety to the greatest degree possible. However, even healthcare systems with an understanding and high standard of best practices can be severely disabled due to lack of personnel and resources. Healthcare systems need to be prepared, staffed and supplied not only for their regular needs, but also for a quick response and deployment in the case of an unexpected emergency.

NEW STRATEGIES TO FIGHT AN OLD PROBLEM

Technology—A Promising Ally

New technologies are being developed and marketed for the prevention of HAIs, although more research is needed to confirm the efficacy of these methods. For example, it may be possible to assess the level of cleaning in a healthcare facility by measuring adenosine triphosphate levels or using fluorescent markers, but it remains unclear which method is superior. Robots emitting UV-light or hydrogen peroxide may offer new ways to clean patient rooms after discharge, but they require trained personnel and their cost-effectiveness remains to be determined. Antimicrobial coating of surfaces with copper or silver has also been proposed and is under development; yet concerns are being investigated regarding their potential contribution to the long-term development of bacterial resistance, as well as to toxicity due to the exposure to nanoparticles of silver.[13]

Some promise is shown in textiles with antimicrobial properties, as some materials could kill bacteria within a few hours of contact and could prove useful in the production of curtains and garments. Automated monitoring systems have been developed to remove the burden of direct observations for hand hygiene and eliminate the Hawthorne effect, although most studies so far have been done as pilots in single units and the data is of low quality. New rapid diagnostic tests are constantly being developed that minimize the time to pathogen identification and even offer point-of-care solutions that impact infection control and aid antimicrobial stewardship.[14] Matrix-assisted laser desorption ionization-time of flight mass spectrometry is revolutionizing the pathogen identification process, but is costly.

New Surveillance Targets: Healthcare-associated Viral Infections

One important but poorly understood challenge in the hospital environment is healthcare-associated viral infections (HAVIs).[15] Although HAVIs constitute a major burden on both patient safety and healthcare costs, surveillance is lacking. Recently, an attempt by researchers in the United States to develop a HAVI surveillance system and a prevention bundle showed promising results. The HAVI bundle included hand-hygiene compliance and isolation precautions as well as environmental cleanliness, adherence to staff illness procedures, and year-round visitor screening.[15]

Looking Outside The Definition Box—The Hospital as a Living Organism

All HAI definitions require that the patient has been hospitalized for at least 2 days as the starting point for surveillance. Yet in some cases a patient may contract an infection within the hospital environment within an even shorter period of time; for example, in hospital waiting rooms and reception areas where there is a sizeable opportunity for child-to-child or adult-to-child transmission. In addition to implementing standard precautions, such as cough etiquette during flu season, infection preventionists should consider ideas such as redesigning a facility's waiting areas, promoting better patient flow, avoiding crowding, shortening response times, and management and filtering of airflow, to reduce the contraction of infections within the hospital setting.[16]

PUTTING ALL THE PIECES TOGETHER

Despite the paucity of pediatric-specific and LMIC-based data, there currently exists an abundance of evidence to guide the development of an effective HAI-prevention program. Adult-based surveillance systems, definitions and prevention bundles are a sufficient starting point for the development of

pediatric programs. While pediatric-specific data is critical for the long-term success of an effective IPC program, basic techniques such as hand hygiene, aseptic technique and timing of surgical prophylaxis are equally effective for both adult and pediatric patients.

IPC programs must be specific to their environment, communicated effectively to hospital staff, and accompanied by efforts to initiate cultural and behavioral changes to be successful in the fight against HAIs. The widespread lack of dedicated staff and funding, and the dearth of IPC-specific training at the undergraduate level, shows that the importance of IPC is insufficiently understood among healthcare systems, educational institutions, stakeholders, and governments. Adequate resources and robust supply chains are needed to protect populations from unexpected infectious agents.

While it is essential that we explore new options to prevent and control HAIs, any technology must be supported by evidence and shown to be cost-effective before it is widely adopted. Above all, IPC programs must set achievable goals and increase and maintain compliance to basic IPC practices, starting with the cornerstone of HAI prevention: hand hygiene.

For almost 200 years, since the time of Ignaz Semmelweis (1818–1865), the first doctor to recognize and publicize the importance of hand hygiene in preventing infections—the challenges to IPC have been fundamentally the same: to implement a change in culture and behavior by increasing awareness, to produce robust supporting evidence, and, ultimately, to limit transmission and improve patient safety. Effective IPC programs will make our healthcare systems more robust and prepared not only for the well-established dangers of common HAIs, but also for sudden and unfamiliar threats such as SARS-CoV-2. Such threats may never be fully eradicated; but the proper knowledge and resources are at our disposal and, if properly implemented, can help us to make the overwhelming crisis of HAIs a thing of the past.

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