PART ONE

Introduction to Healthcare-Associated Infections and their Control

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CHAPTER ONE

The Hospital and Ambulatory Care Environment

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Introduction

HEALTHCARE-ASSOCIATED INFECTIONS (HAIs): THE EVOLUTION

Although the modern-day concepts of prevention and control of hospital-associated infections originated in the middle of the nineteenth century, the history regarding knowledge about hospital-related infections dates back to the sixteenth century. Ambroise Pare (1517–1590), a surgeon at Hotel-Dieu in Paris, was one of the first physicians to describe increased frequency and severity of wound infections in hospitalized patients compared to nonhospitalized patients. The phrase "hospital disease" was first used in the eighteenth century. Hungarian physician Ignaz Philipp Semmelweiss (1818–1865) introduced the concept of hand washing while Sir Joseph Lister (1827–1912), a British surgeon, pioneered the concept of asepsis. Over the years, the Center for Disease Control and Prevention (CDC) has published several sets of definitions for Nosocomial Infections. Definitions used during the Comprehensive Hospital Infections Project (CHIP) (1969–1972) and in the National Nosocomial Infectious Study (NNIS) (1970–1974) were first used in the *Proceedings of the First International Conference on Nosocomial Infection* organized by CDC in 1970 (1). Definitions were further extended in 1974 for hospitals participating in NNIS (2). Definitions for nosocomial infections were again modified by CDC in 1988 (3). The term HAI (4) was officially introduced in 2008 to reflect infections

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acquired by patients while receiving treatment for any surgical or medical conditions. It was defined as a localized or systemic condition resulting from an adverse reaction to the presence of an infectious agent(s) or its toxin(s) without any evidence that the infection was present or incubating at the time of admission to the acute care setting. HAIs can occur in acute care settings within hospitals or in ambulatory outpatient care settings, including same-day surgical centers or dialysis center. HAIs are increasingly associated with long-term facilities such as nursing homes and rehabilitation centers.

Healthcare-associated infections (HAIs) are a major cause of morbidity and mortality in the United States. It is estimated that there were 1.7 million HAI in 2002 which resulted in around 99,000 deaths, making it among the most common healthcare-associated adverse event (5). HAIs can occur in patients at any age and in any healthcare setting, but the most common infections are seen among adults and children in the non-ICU setting. According to National Nosocomial Infections Surveillance (NNIS) system data from 1990 to 2002, out of an estimated 98,987 deaths associated with HAI in the United States hospitals, 35,967 were due to pneumonia, 30,665 were related to bloodstream infections, 13,088 were related to UTIs, 8205 were due to for surgical site infections (SSI), and 11,062 due to infections from other sites.

HAIs have significant economic implications as well. They increase the healthcare burden on the society by $35.7–45 billion every year (6).

PATHOGENS

Bacteria remain the most common pathogens and source of HAIs (7, 8). HAI are typically associated with Gram-positive pathogens including methicillin-resistant *Staphylococcus aureus* (MRSA) (9–13), coagulase-negative *Staphylococci* (14), and glycopeptide (vancomycin)-resistant *Enterococci* spp. (15–20). More recently, there are increasing reports of glycopeptide intermediate and glycopeptide-resistant *S. aureus* (21). *Clostridium difficile*, a normal intestinal flora in 3% of healthy adults and 20–30% of hospitalized adults (22), is responsible for 25–30% of antibiotic-associated diarrhea and is being increasingly recognized as a major nosocomial pathogen (23–27). There is increasing resistance among Gram-negative organisms. Among *Enterobacteriaceae* pathogenic isolates, resistance to fluoroquinolones, extended-spectrum cephalosporins, and carbapenems is increasing (14). There is also an increasing carbapenem resistance among *Acinetobacter* spp. (14, 28) and *Klebsiella pneumoniae* (14). MDR *Pseudomonas* spp., *Klebsiella* spp. *and Enterobacter* spp. are concerning as well. Emerging resistance to carbapenems conferred by New Delhi metallo-B-lactamase 1 (NDM-1) in countries such as India, Pakistan, and United Kingdom is a potential global health problem that will require coordinated international surveillance (29).

Candida species remain the most common healthcare-associated pathogens among fungi (14, 30); and although less common, viruses including Adenovirus, Rotavirus, Norovirus, and hepatitis B have been recognized as nosocomial pathogens.

Common HAIs

URINARY TRACT INFECTION (UTI)

UTIs are the most common HAIs in both acute care setting and long-term care facilities. A major cause of septicemia and mortality, rates are similar in adult and pediatric patients (31)

and account for 36% of all HAIs (5). Intrinsic risk factors associated with UTIs include: advanced age, female gender, and severity of underlying illness (e.g., diabetes mellitus (DM)) (32). Duration of indwelling catheterization is by far the most important extrinsic risk factor for UTIs (33). Indwelling urinary catheters are used in nearly all hospital nursing units, unlike ventilators and many other devices. Various studies have emphasized that catheter use is frequently inappropriate; inattention to both the proper indications for catheter use and catheter status in patients seems to be an important factor (34–39).

The most common etiologic agents for catheter-associated UTI (CAUTI) as reported to the NHSN at CDC, 2006–2007, are *E. coli* (21%), *Candida* spp. (20%) [*C. albicans* (14%)], *Enterococcus* spp. (15%), *P. aeruginosa* (10%), *K. pneumoniae* (8%), *Enterobacter* spp. (4%), coagulase-negative *Staphylococci* (3%), *S. aureus* (2%), *A. baumannii* (1%), and *K. oxytoca* (1%) (14).

Hospitals and Long-Term Care Facilities (LTCF) should develop, maintain, and propagate policies regarding indications for catheter insertion and removal. Education of staff, use of condom catheters where appropriate, and consideration of intermittent catheterization and suprapubic catheterization as an alternative to short-term or long-term indwelling urethral catheterization have all been recommended to reduce the risk of nosocomial UTIs (40).

PNEUMONIA

Pneumonia is the third most common HAI, the second most common in the ICU, and the most common cause of mortality among all HAIs (5). It is associated with considerably increased healthcare costs and hospitalization days (32, 41). Hospital-acquired pneumonia (HAP) is defined as pneumonia that occurs 48 hours or more after admission, which was not incubating at the time of admission (42, 43). Ventilator-associated pneumonia (VAP) refers to pneumonia that arises more than 48–72 hours after endotracheal intubation (44, 45). Healthcare-associated pneumonia (HCAP) includes any patient who was hospitalized in an acute care hospital for two or more days within 90 days of the infection; resided in a nursing home or long-term care facility; received recent intravenous antibiotic therapy, chemotherapy, or wound care within the past 30 days of the current infection; or attended a hospital or hemodialysis clinic (43, 45, 46). Most current data, including microbiological, have been collected from patients with VAP but can be extrapolated to HAP and HCAP patients as well (47). Tracheal intubation and mechanical ventilation are the strongest risk factors, with 3- to 21-fold increase in risk for nosocomial pneumonia (48).

Among etiologic agents, *S. aureus* (24%) is the most common pathogen, followed by Gram-negative organisms: *P. aeruginosa* (16%), *Enterobacter* spp. (8%), *A. baumannii* (8%), *K. pneumoniae* (7%), and *E. coli* (5%) (14).

Various infection control measures can help modify the risk factors for pneumonia. Intubations and reintubations should be avoided if possible, and noninvasive modes of ventilation should be used whenever possible. Orotracheal intubations and orogastric tubes, semirecumbent position rather than supine position, continuous aspiration of subglottic secretions, adequate endotracheal cuff pressures to prevent leakage of bacterial pathogens into the lower respiratory tract, and passive humidifiers or heat-moisture exchangers can all help decrease the risk for VAP (47).

SURGICAL SITE INFECTIONS (SSIs)

SSIs are second only to UTIs in frequency, accounting for 22% of all HAIs (5). It is estimated that SSI develop in 2–5% of the 27 million patients undergoing surgical procedures each year (49, 50). Healthcare personnel and operating room environment have been implicated as common sources of pathogens for SSIs. Prolonged preoperative stay, preoperative shaving, length of surgery, and skill of surgeons are well-documented risk factors for SSIs (51). Intrinsic host-related risk factors include: severity of underlying illness (e.g., high American Society for Anesthesiology score, DM), obesity, advanced age, malnutrition, trauma, loss of skin integrity (e.g., psoriasis), and presence of remote infections at time of surgery (32).

Most common etiologic agents are: *S. aureus* (30%), coagulase-negative *Staphylococcus* (14%), *Enterococcus* spp. (11%), *E. coli* (10%), *P. aeruginosa* (6%), *Enterobacter* spp. (4%), *K. pneumoniae* (3%), and *Candida* spp. (2%) (14).

Various pre-, intra- and postoperative measures will help minimize the risk of SSI (51). Preoperative bathing with an antimicrobial has been advocated to reduce skin colonization (52). Removing hair from the site of surgery and preoperative skin preparation reduces contamination of the operative site (53). Clipping with clippers or using cream to remove hair results in fewer surgical site infections than shaving (54). Intraoperatively, appropriate barrier devices, good skills, adequate hemostasis to prevent hematomas and seromas, and adequate debridement of dead tissue are some ways to reduce transmission of microorganisms (55). Postoperatively, adequate wound care will help prevent infections.

BLOODSTREAM INFECTIONS (BSIs)

Bloodstream infections (BSIs) are the fourth common cause of HAIs (5). Both the incidence and prevalence of BSIs have increased over the past several decades. An estimated 350,000 nosocomial BSIs are reported in the United States every year (56). Differentiating a clinically significant BSI from a blood culture contaminant remains a constant challenge for physicians (57). Because many patients receive home healthcare, including intravenous infusions and chemotherapy that until the recent past would have been administered in inpatient settings, the distinction between nosocomial and community-acquired BSIs has been difficult. Friedman et al. (58) and Siegman-Igra et al. (59) described 37% and 39% BSIs, respectively, that occurred in settings traditionally classified as community acquired and could be more accurately classified as healthcare-associated. The term "nosohusial" has been proposed to describe infections occurring in homecare subjects (60).

Various automated blood cultures systems that are reasonably comparable to each other are being used by most laboratories. To ensure appropriate identification of the pathogen, all efforts should be made to avoid contamination of the sample. Skin preparation plays a major role. Various methods have been used for skin preparation. This includes cleaning venipuncture site with alcohol followed by an iodophor or iodine tincture and povidone iodine. More recently, Mimoz et al. (61) showed that alcoholic chlorhexidine may be more efficacious in preventing skin contamination compared to povidone iodine. Reliability of blood culture results also depends on various other factors including amount of blood volume sampled, timing of blood cultures, and site from where blood cultures are obtained (57).

Bloodstream infections (BSIs) are associated with various risk factors. In the past, 75% of healthcare-associated (nosocomial) BSIs were secondary to SSIs, UTIs, intra-abdominal

infections, pneumonia, or skin and soft tissue infections (62, 63). Over the years, the proportion of primary nosocomial BSIs has increased and most episodes without an obvious source are thought to be related to intravascular catheters (57, 64). Age (<1 year and >65 years) is a known predisposing factor for BSI (32, 57, 65–67). Patients with underlying malignancies and/or neutropenia are long known to be at risk for BSI (68–70). Notably, patients with hematologic malignancies are at higher risk than those with solid tumors. Other risk factors include patient with chronic liver disease (71), hemodialysis patients (72), burn patients (73), spinal cord injury patients (74, 75), transplant patients (76), and patients admitted to the ICU (77).

The pathogens differ in patients with various risk factors. Based on most recent studies, the common pathogens associated with central line associated BSI are coagulase-negative *Staphylococcus* (34%), *S. aureus* (15%), *Enterococcus* spp. (12%), *Candida* spp. (11%), *E. coli* (10%), *P. aeruginosa* (8%), *K. pneumoniae* (6%), *Enterobacter* spp. (5%), and *A. baumannii* (3%)(14).

Various recommendations have been made to prevent catheter-related BSI (78). Use of an all-inclusive catheter cart kit and barrier devices, chlorhexidine-based antiseptic for skin preparations, disinfecting catheter hubs, needleless connectors, and injection ports before accessing the catheter and appropriate surveillance are a few of the recommendations made by the Society for Healthcare Epidemiology of America/Infectious Disease Society of America (SHEA/IDSA).

Epidemiology of Infectious Disease and the Hospital and Ambulatory Care Environment

Epidemiology is defined as the study of the determinants and distribution of health and disease in populations. It is well recognized that health and disease occur due to the complex interactions between an agent, the host that is the target of agent actions, and the environment. In relation to HAIs, agent refers to the various healthcare-associated microorganisms, the host comprises the patients or/and the healthcare workers, and the environment would include different healthcare components such as acute care hospital, intensive care units, hemodialysis centers, ambulatory clinics, and so on.

Various models and equations have been used to describe these multifarious interactions. The simplest epidemiologic model described is the triangle model (79) (Figure 1.1). It signifies, in the most simplified manner, the complex yet close interaction between the agent, host and environment. The Seesaw model (Figure 1.2) is another way by which the interplay between the three components (agent, host, environment) has been described (80). By introducing the Seesaw model, Fox et al. (80) has illustrated the role that environment plays to keep an equilibrium between the agent and the host. Conversely, any disequilibrium results in adverse events. Therefore, the environment provides platform upon which the interaction between host and agent takes place. An "equation of infection" has been used to determine the probability of a microbial agent to cause infection in the host (81):

$$IP = \frac{D \times S \times T \times V}{Hd}$$

where *Ip* is the probability of infection, *D* is the dose (number of microorganisms) transmitted to the host, *S* is the receptive host site of contact with the agent, *T* is the time

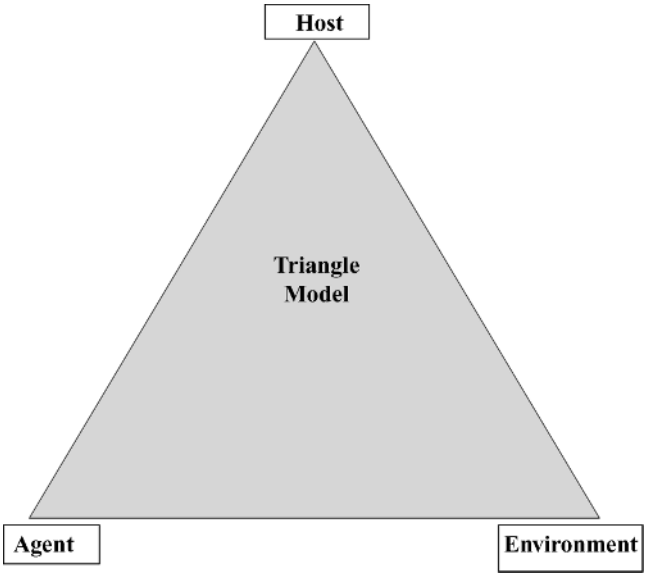


FIGURE 1.1 Triangle model for epidemiological relationships. The simplified model demonstrates the complex yet close interaction between the agent, host and environment.

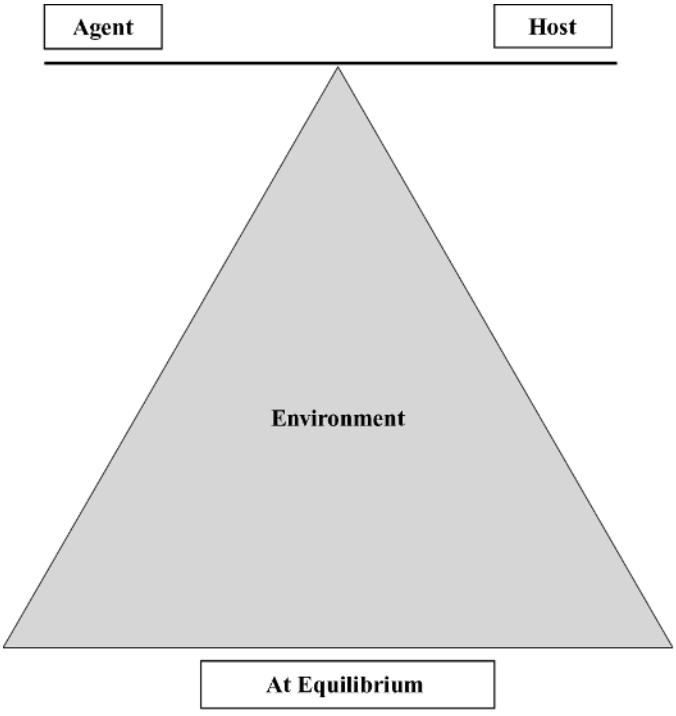


FIGURE 1.2 Seesaw model for epidemiological relationships. A second simple model to demonstrate the epidemiologic balance between the agent, host and environment.

of contact (sufficient for attachment and multiplication or not), *V* is the virulence (the intrinsic characteristics of the microorganism that allow it to infect), and *Hd* is the force of the combined host defenses attempting to prevent the infection. Thus, if there is any compromise in the host's defense system, as may happen in the case of an immunocompromised patient, there may be a propensity to cause infection with lesser quantity of the microorganisms. Similarly, the host site may be one that may have otherwise been an unlikely site. The time required for the agent to cause infection and the virulence of the agent may be variable as well. For example, in a patient with febrile neutropenia secondary to chemotherapy, an organism such as *Propionebacterium acnes* may be able to cause a BSI compared to an unlikely possibility of the same agent to cause an infection in a healthy host.

The Agent, Host, and the Environment

The healthcare environment provides the platform for the complex interactions between agent and host that eventually results in disease.

AGENT

Various bacteria, fungi, and viruses act as agents causing HAIs (32). These microorganisms are necessary, but by themselves they are not sufficient to cause an infection. The healthcare environment plays a pivotal role in aiding the disease process. The healthcare setting provides the required reservoir for these microorganisms to blossom. These reservoirs are numerous in the hospital environment. Humans are the most common reservoirs. These include healthcare workers (82–93), patients (94–102), the household members, and visitors of the patients (103–108). Healthcare workers are frequently colonized with MRSA (109). It is also known that clothing (including uniforms and lab coats) and personal protective equipment may get contaminated with potential pathogens after taking care of patients colonized with organisms including *A. baumannii* (29), MRSA, VRE, and *C. difficile* (110–113). Although these have not been implicated directly as sources of infections, there is definitely a potential for same that remains. Healthcare workers, patients, and visitors will transmit pathogens from their hands (114, 115). The bedrails, doors, and other objects in the patient's room are colonized with microorganisms; if appropriate hand hygiene is not followed, the organisms will get transmitted among patients. Commonly used patient care devices such as electronic thermometers, infusion sets, glucose monitoring devices, and blood pressure cuffs, if not cleansed properly, may transmit pathogens (116–119). *Legionella* spp. can survive in the air-conditioning humidification systems, *C. difficile* will remain in the rooms of patients treated for *C. difficile* for an extended time, and *Burkholderia* spp. and *P. aeruginosa* are known to be transmitted from patient to patient in adult and child clinics for patients with cystic fibrosis (120, 121).

HOST

As seen in the "equation of infection," the agent has a major role in disease occurrence. The virulence of organism, the number of organisms, and the duration of contact are all important; whether the disease will occur or not, as well as the severity of the disease, is greatly influenced by the host mechanisms. In all circumstances, the host's immune system

attempts to prevent occurrence of any infection. Any decrease in the host's immune response results in the host's increased susceptibility to infections. These host factors have been largely described as intrinsic factors and extrinsic factors. Intrinsic host factors mainly include extremes of age (32, 81, 122), various comorbidities of the host (DM (123, 124), HIV/AIDS (125, 126), malignancies, transplant history (127–129), chronic obstructive pulmonary disease (COPD) (32)), nutritional status (32, 130), gender (32), race, vaccination or immunization status, presence of distant infection (32), and the psychological state of the host (131). Similarly, various factors extrinsic to the host contribute to occurrence of disease. Indwelling devices are an increasing cause of infections. Indwelling urinary catheters (33), central venous and arterial catheters (57, 64, 132–134), endotracheal tubes, and mechanical ventilators (48) are common causes of HAIs. Any indwelling device will allow potential pathogens to bypass the local defense system of the body. This facilitates the formation of biofilms and allows microorganisms to not only adhere to these biofilms but also resist antimicrobial activity (135). Invasive surgical procedures will transmit pathogens causing infection (51). These agents can be derived from healthcare personnel or may be related to the endogenous colonization of the patient (136–140). Radiation therapy can affect skin integrity and contribute to decreased immunity. Use of antibiotics will alter normal microbial flora of the patient and increase risk of infections (81, 122). These are just a few examples of the numerous mechanisms and changes that occur in the healthcare setting.

To summarize, any factor—intrinsic or extrinsic—that has the propensity to diminish the host's immune response contributes to the complex pathogenicity and interaction with the host causing the disease. For this complex interaction, the various healthcare-related environments provide the appropriate base/platform.

ENVIRONMENT

The healthcare environment has widened in scope over a period of time. In the past, most infections were attributed to the hospital environment; but now, acute and nonacute healthcare settings contribute to spread of infections. Microorganisms are endemic in the healthcare environment and in any healthcare setting; the triad of agent, host, and environment will interact in various ways to cause HAIs.

Acute Healthcare Environment This refers to the hospital setting where acute care is provided to the patients. There are certain environmental factors that are common to all components of the hospital, and there are other unique features associated with specialized forms of healthcare settings.

Adult Care: General Patient Units, Telemetry Units, Step-Down Units, and Intensive Care Units (ICUs) Certain physical factors—heat, cold, humidity, air-conditioning, water reservoirs (water coolers, water tanks)—provide an optimal environment for the agents to replicate in any unit of the hospital. Biological factors include intermediary vectors that contribute to the spread of infections. Examples include insects or snail vectors. Social factors include: methods of food preparation or distribution, medical and surgical waste disposal; room size; and other healthcare amenities. Almost 30% HAIs occur in the ICU (pediatric and adult). Agent, host, and environmental factors play a major role. Patients in the ICU are sicker, with greater comorbidities and risk factors and more likely to be immunocompromised. Endemic microorganisms in the ICU environment such

as *P. aeruginosa* (84) and MRSA (95) are provided a greater opportunity to colonize and cause further infections by these host factors. Pediatric and adult ICUs are known to have outbreaks of bacterial, viral, and fungal pathogens secondary to various common sources and person–person contact, both of which are more frequent in the ICU (121, 141–146).

Pediatric Care Care of a pediatric patient poses various challenges different from the adult population. The host in this case has different risk factors for infection; this includes risk factors such as low birth weight and lack of immunization. Environmental factors are different as well. Pediatric populations are prone to contact with sibling visitors who may be responsible for outbreaks in the hospitals especially during seasonal epidemics (147–149). The child play areas provide opportunistic environment for infections. Not only is there more contact among children and person-to-person transmission, toys are known to be major culprits. It is well known that toys harbor pathogenic bacteria (150). A *P. aeruginosa* outbreak in a pediatric oncology unit was attributed to bath toys (151). Also, families and parents spending more time in the patient room—cuddling, feeding, playing, and changing soiled diapers—all provide multiple opportunities for spread of infection between child and family and even child and healthcare workers (122).

Burn Units Burn wound patients are susceptible hosts who are prone to colonization and infection by various nosocomial pathogens and increased morbidity and mortality (152–154). Hydrotherapy equipment is an environmental risk factor that is associated with increased BSI in burn patients with MRSA (155), *A. baumannii* (156), and *P. aeruginosa* (157). Burn wound infections caused by *Aspergillus* spp. and other molds have been implicated to environmental exposure during construction (158, 159).

Nonacute Healthcare Environment Healthcare is being increasingly provided in nonacute settings. Ambulatory care is the most common example. Furthermore, an increasing number of patients are now being managed in long-term care facilities, nursing homes, subacute rehabilitation centers, assisted-living facilities, and hospice. Healthcare is being provided in non-healthcare settings as well. Schools, prisons, military units, and shelters all provide unique environments for spread of infections. Ambulatory care includes outpatient clinics that may be hospital-based or out of the hospital in the form of private physician offices. Ambulatory care also includes urgent care centers, hemodialysis centers, infusion homes for chemotherapy and antibiotics, employee health clinics, public health clinics, and ambulatory surgical centers. Viral infections (hepatitis B, hepatitis C, and rarely HIV) have been reported in ambulatory care setting in association with use of multidose vials, intravenous solutions, and medical devices (160–165). Rubella has been transmitted in outpatient obstetric setting (166). Goodman et al. (167) described multiple cases of infections acquired in the healthcare setting. Cases of contaminated endoscope-related *Salmonella typhimurium* (168), *Mycobacterial* infections causing abscess from contaminated DTP vaccine (169), *S. marcescens*-related septic arthritis from contaminated antiseptic (170) have been documented in ambulatory care setting. Similarly, improper disinfection of ophthalmology equipment has been associated with Adenovirus type 8 epidemic kerato-conjunctivitis (171–175).

Healthcare is being increasingly provided at home in the forms of intravenous medication therapy and even in hospice care. Infectious homecare workers and contaminated equipments are risk factors for infections. In prisons and shelters, crowded

environment, poor ventilation, and economically disadvantaged individuals with chronic comorbidities such as alcoholism and intravenous drug use (IVDU) can provide a suitable environment for spread of infections including scabies, tuberculosis, hepatitis A virus, and norovirus (176, 177).

To summarize, the hospital and ambulatory care environment provides ample opportunities for pathogens to flourish and cause infections. Appropriate preventive measures and early diagnostic techniques are essential to prevent spread of infection and adverse outcomes in the population.

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