

Healthcare-acquired Infections

1. Introduction

Hospitals are perceived as potentially dangerous by the lay public as well as by elected officials. This has resulted in increased scrutiny of patient safety and several states have mandated public reporting of hospital-acquired infections. In NYS, we report central venous catheter bloodstream infection rates in ICU patients and post-operative wound infections following coronary artery bypass surgery and colon surgery. Some states are also mandating reporting MRSA infection rates.

2. Definition of Healthcare-acquired Infections

Over the past two decades the terminology has changed from nosocomial infections to hospital-acquired infections to the most recent term: healthcare-acquired infections. This latest term acknowledges recent changes in healthcare delivery whereby healthcare is delivered not only in hospitals, but in chronic care facilities, outpatient settings, and non-healthcare settings such as the home. The term healthcare-acquired also acknowledges the 'revolving door' that occurs between settings and the difficulties distinguishing site of acquisition of some infections..

In efforts to standardize surveillance for such infections, HAI are defined as infections that are acquired > 48 hours of admission without signs or symptoms of infection at the time of admission.

3. Epidemiology of hospital-acquired infections (HAI)

The burden of HAI in the USA is staggering. There are an estimated 1.7 million HAI in USA each year. Approximately 5% of hospitalized patients develop at least one HAI during their hospital stay resulting in 98,987 deaths. The cost of HAI is equally staggering; in 2000 dollars, HAI cost \$5 billion each year.

Several sources are used to obtain rates of HAI. The most commonly used source is the CDC's National Nosocomial Surveillance System (NNIS). Other sources include state data bases and databases from large healthcare systems such as Kaiser Permanente.

The most common HAI are device-related infections complicating the use of urinary tract catheters, central venous catheters, and ventilators as well as surgical site infections, most commonly wound infections. Infections of artificial joints, particularly hips, and of artificial valves, resulting in endocarditis, can also occur.

In the USA, approximately 30,000,000 urinary catheters are placed each year. These catheters are at very high risk of being associated with a urinary tract infection (UTI). The risk of infection increases with duration of use; there is a 5% risk of a UTI per

catheter-day. The estimated crude mortality rate of such infections is 5%. It is often difficult to tease out crude mortality (all deaths) from attributable mortality (death considered to be caused by the HAI). This is because it is often difficult to be certain that a given death is due to a specific infection given the frequency of severe comorbid conditions in patients developing HAI.

There are about 250,000 cases of ventilator-associated pneumonia (VAP) each year in the USA. In fact, about 25% of all pneumonias seen by physicians in hospitalized patients will be VAP. Such infections are associated with a 28-37% crude mortality rate.

It is estimated that 5,000,000 central catheters are placed each year and 3-8% will become infected. This represents about 10-15% of overall HAI infections. In case-control studies comparing patients with comparable comorbid conditions, catheter-related bloodstream infections were associated with 15% attributable mortality which represents 1% of deaths in USA.

Approximately 24,000,000 surgical procedures are performed annually, many of which are performed in out-patient settings. About 2.7% of procedures are complicated by infections which represents 486,000 cases per year with a 4.3% attributable mortality rate. Such infections are very costly as they lead to excess hospital-days and readmissions; annual costs are estimated to be \$3 billion.

4. Pathogenesis of Common Healthcare-associated Infections

Much work has been done to unravel the pathogenesis of HAI in efforts to lead to the development of preventive strategies.

Central venous catheter (CVC)-related bloodstream infections: There are 4 different ways that micro-organisms can colonize an intravascular device and subsequently disseminate into the bloodstream.

1. Skin flora can enter at the insertion site and track along outside of catheter and colonize the biofilm as described further below.

2. Organisms, generally from the hands of healthcare workers, can contaminate the catheter hub and track along inside of catheter and colonize the biofilm.

These two routes are most common and thus gram positive pathogens (coagulase negative staphylococci and *Staphylococcus aureus*) are the most common pathogens causing catheter-related bloodstream infections as will be described further below. Less common sources of potential pathogens are:

3. Hematogenous spread of micro-organisms from distal sites of infection such as UTIs or pneumonia.

4. Contaminated intravenous fluids can be administered. Such fluids may be contaminated at the time of manufacture (intrinsic contamination) or during preparation and administration in the hospital (extrinsic contamination).

Ventilator-associated pneumonia: A review of normal host defenses will help us understand how the use of a ventilator impairs these defenses putting patients at risk of developing pneumonia. These normal defenses include mechanisms that work in concert to remove particulate matter and microbes: the cough reflex, low gastric pH, mucociliary clearance, and components of the immune system-- macrophages and leukocytes that elaborate cytokines that activate cellular immune response and act as antigen presenting cells and immunoglobulins and complement that aid in opsonizing bacteria and facilitating phagocytosis.

Many of these normal host defenses are either impaired by the presence of an endotracheal tube (ETT) or by the comorbid conditions of patients requiring mechanical ventilation. For example, the immune system may be impaired by underlying cancer, transplantation, and/or immunosuppressive medications. The ETT thwarts the cough reflex, can compromise mucociliary clearance, and can serve as a conduit for organisms colonizing upper airway above the vocal cords to enter the lower respiratory tract (LRT).

Micro-organisms can gain access to the normally pathogen-free LRT by several potential routes:

1. Aspiration of microbe laden secretions from oropharynx or reflux from stomach to oropharynx to LRT. These microbes may be either a) endogenous flora from the patient or b) exogenous flora from another patient via staff hands, contaminated equipment, contaminated sinks, or contaminated environmental surfaces. Such micro-organisms differ from normal upper respiratory tract flora as described below.
2. Direct extension of pathogens from contiguous infection, e.g., the pleural space
3. Via inhalation of contaminated air or medical aerosols
4. Hematogenous spread to the lung from remote sites of infection such as the bloodstream or a UTI
5. A biofilm can develop on ETT and micro-organisms can be dislodged from the biofilm during suctioning.

A second component of the pathogenesis of ventilator-associated pneumonia is the changes that can occur in upper airway flora among hospitalized patients. To review, normal upper airway flora consists of viridans streptococci, *Haemophilus* spp., and anaerobes. In critically ill patients the upper airway becomes colonized with gram negative bacilli which are often antibiotic resistant and gram positive pathogens, including *S. aureus*. Furthermore, microbial adherence to the upper airway is facilitated due to reduced mucosal IgA, increased protease production, denuded mucous membranes with increased bacterial receptors.

Outbreaks of VAP: In addition, to endemic infections, outbreaks of VAP can occur from a variety of pathogens as shown in the following table.

Source	Example of Pathogen
• Contaminated respiratory therapy equipment	• Multidrug-resistant gram negative bacilli, e.g., <i>Acinetobacter</i> ,
• Contaminated bronchoscopes	• <i>P. aeruginosa</i> , non-tuberculous mycobacteria
• Medications	• <i>B. cepacia</i> , <i>P. aeruginosa</i>
• Contaminated hospital water supplies	• <i>Legionella</i> spp.
• Coincident with community outbreaks: Ill staff and visitors	• Viruses: RSV, influenza, SARS

Catheter-related Urinary Tract Infections: As described for ETT, urinary catheters also compromise host defenses by permitting increased access of potential pathogens to the bladder and by compromising complete voiding. Sources of organisms include extraluminal microbes colonizing the urethra and intraluminal microbes that ascend from contaminated tubing or the drainage bag.

Role of Biofilm in HAI: Biofilms are a complex 3-dimensional structure of host cells, bacteria, and extracellular matrix that serve as a common pathogenic pathway for device related infections. Several components are required for biofilm formation. These include:

1. Adherence of microorganisms to the surface of a device or to each other
2. Change in bacterial gene expression resulting in a non-planktonic mode of growth
3. Formation of an extracellular matrix that consists of both bacterial secreted polysaccharide matrix and host components.

Host components vary depending on the site of the device. For biofilms formed on central venous catheters, host components include fibrin, fibronectin, and platelets. For biofilms formed on urinary tract catheters, host components consist of proteins, electrolytes, and organic molecules.

Pathogenesis of Surgical Site Infections: Pathogens causing surgical site infections (SSI) can originate from several sources. These include:

1. Endogenous sources – most commonly, the patient’s own skin, mucous membranes or viscera
2. Exogenous sources – through contact of the wound with the contaminated environment, operating room personnel, contaminated air, or surgical instruments
3. Hematogenous or lymphatic sources of potential pathogens

The CDC has developed a classification schema for SSI reflecting the level of infection: superficial incisional infection of the skin or subcutaneous tissue, deep incisional infection of the muscle or fascia, versus organ space infection. Furthermore, the risk of infection is categorized by the type of surgery as shown in the following table:

- Clean (<2%)
- Clean contaminated (<10%)
- Contaminated (20%)
- Dirty (30-40%)
- Elective, primary closure, no transection of mucous membranes
- Urgent or emergent, controlled entry of the GI, respiratory, or biliary tract
- Acute, spill from organ, penetrating trauma, no purulence,
- Purulence, abscess, pre-operative perforation, penetrating trauma > 4 hours

5. Host Risk Factors for HAI:

There are numerous host risk factors for HAI. These have largely been derived from case-control studies. As described above, disruptions to host defenses by devices and other medical interventions such as nasogastric tubes which can occlude the sinuses leading to sinusitis are risk factors. Burn sites, with non-intact skin are at high risk of developing infections. Various medications including immunosuppressive medications, steroids, and chemotherapy lead to impairment of the immune system. Medications that alter the gastric pH such as antacids and proton pump inhibitors may increase the risk of VAP and catheter-related bloodstream infections. Patients at the extremes of age such as premature infants and the elderly have increased rates of infections. For example, the risk of bloodstream infections is inversely proportional to birthweight in preterm infants; the smallest infants have the greatest risk of infection. Finally, patients with a prolonged length of hospitalization are at increased risk of infection due to comorbid conditions and colonization with potentially virulent multidrug-resistant pathogens.

6. Antibiotic Resistance and HAI

Many HAI are caused by antibiotic resistant pathogens. As expected, antibiotic utilization increases selective pressure on flora leading to resistance. We are now encountering pathogens within the hospital that are resistant to all antibiotics. Patients with infections are hospitalized longer allowing them to serve as reservoirs for multidrug-resistant pathogens with potential transmission to other patients.

Micro-organisms within a biofilm are difficult to eradicate as they evade host defenses and the activity of antimicrobial agents. Biofilms may promote the development of antimicrobial-resistant infections by:

1. serving as a nidus for deposition and growth of resistant strains that cause infection,
2. bacteria imbedded in biofilm may be exposed to sub-inhibitory concentrations of drug which can promote the emergence of resistance, and
3. providing a matrix in which bacteria can exchange resistance factors.

7. Common Pathogens Causing HAI

The following table provides examples of common pathogens causing common hospital-acquired infections. Knowledge of the potential sources of organisms for different types of infections further clarify this table. For example, gram positive skin flora is the most common causes of bloodstream infections and wound infections. Gram negative GI tract organisms are most likely to colonize the external surface of urinary tract catheters leading to UTIs.

Pathogen	Types of Infection
<i>S. epidermidis</i>	Bloodstream infections
<i>S. aureus</i> (MRSA)	Wound infections
<i>E. coli</i>	Urinary tract infections
<i>P. aeruginosa, Acinetobacter</i> spp.	Pneumonia
RSV, influenza	Lower respiratory tract
<i>C. difficile</i>	Diarrhea
<i>Candida</i> spp.	Bloodstream infections Urinary tract infections
<i>M. tuberculosis, Legionella</i> spp., <i>Aspergillus</i> spp.	Pneumonia

8. Hospital Factors Contributing to HAI

In addition to the previous routes of acquisition of potential pathogens, additional hazards may be found within the hospital. Construction and renovation activities may generate dust which contains mold spores, most commonly *Aspergillus* spp. These spores may then be inhaled by vulnerable patients, most commonly transplant recipients, and cause cavitory pneumonia. Hospital water supplies may be contaminated by organisms that exist within the biofilm of water pipes. The most notorious of these pathogens are *Legionella* spp. which can grow at relatively high temperatures. Construction and renovation activities can disrupt these biofilms further. Vulnerable patients drinking or

showering in such water may aspirate *Legionella* and develop pneumonia. Finally, the inanimate environment can be heavily contaminated with potential pathogens, particularly those associated with GI tract colonization and infection due to the high burden of organisms. These include: vancomycin resistant *enterococci*, *C. difficile*, as well as multidrug-resistant gram negative bacilli.

In addition to hospital facility factors, other more insidious factors such as overcrowding, understaffing and / or inadequately trained staff may increase the risk of HAI.

9. Diagnosis of Device-related Infections

CVC-related Bloodstream Infection: The diagnosis of CVC-related bloodstream infections requires maintaining a high index of suspicion. This diagnosis requires ruling-out other sites of infection resulting in bacteremia such as urinary tract infections and pneumonia. The appropriate diagnosis includes obtaining at least 2 blood cultures at least one of which is drawn from a peripheral vein. Multiple positive cultures helps to distinguish true infection from colonization (e.g., blood culture from central venous catheter positive, but peripheral culture negative) vs. contamination (e.g., blood culture from central venous catheter negative, but peripheral culture positive). An adequate blood volume must be obtained (1 cc in a preterm infant, 10 cc per bottle in an adult) to maximize the yield. Both anaerobic and aerobic blood cultures should be sent.

VAP: The diagnosis of VAP is very complex and many of the signs and symptoms mimic other respiratory tract processes. Cultures of the upper respiratory tract do not reflect lower tract pathogens and cultures of the lower respiratory tract often involve bronchoscopy which is not always readily available and may be associated with complications, particularly in an unstable patient. Thus the current clinical case definition, developed by the CDC and used in many hospitals, is a combination of radiology signs, clinical signs, and microbiology criteria are optional, but highly desirable to promote targeted therapy as described below. The following table lists the criteria often used.

Radiology signs (≥ 1) noted on two or more serial chest x-rays	<ul style="list-style-type: none"> ✓ New or progressive or persistent infiltrate ✓ Consolidation ✓ Cavitation
Clinical signs (≥ 1)	<ul style="list-style-type: none"> ✓ Fever ✓ Leukopenia or leukocytosis ✓ Adults ≥ 70 years old altered mental status ✓ PLUS (≥ 2) <ul style="list-style-type: none"> ▪ New onset purulent sputum or change in sputum character or increased secretions ▪ New or worsening cough, dyspnea, tachypnea ▪ Rales or bronchial breath sounds

	<ul style="list-style-type: none"> ▪ Worsening gas exchange
Microbiologic criteria (optional, ≥ 1)	<ul style="list-style-type: none"> ✓ (+) blood culture unrelated to another source of infection ✓ (+) pleural fluid culture ✓ (+) quantitative culture from bronchoalveolar lavage ✓ (+) 5% cells with intracellular bacteria on gram stain ✓ Histopathologic evidence of pneumonia

10. Treatment of HAI

Initially, empiric therapy is used for suspected HAI based on common pathogens, local epidemiology and resistance patterns in the hospital, or more importantly in the particular unit in which the patient developed the infection.

Once cultures are available, therapy targeted at the specific pathogen is used. This may require changing or adding to the empiric therapy, discontinuing an agent, or ideally, using a narrower spectrum agent. This last is critically important to minimize antimicrobial resistance due to inappropriate use of broad spectrum agents. A further treatment consideration is to remove the device whenever possible.

11. Prevention Strategies for HAI

Healthcare systems spend most of their budgets on hospital care. Thus, interventions to reduce HAI are critically important. The CDC has developed a series of 12 Step Programs aimed at reducing hospital-acquired infections and antimicrobial resistance in high risk populations (<http://www.cdc.gov/drugresistance/healthcare/>). These interventions focus on preventing infections, diagnosing infections appropriately, treating infections appropriately, and preventing transmission.

The CDC and other professional organizations have promoted many Key Prevention Strategies. These include appropriate hand hygiene at every opportunity (Before and after every patient contact, after touching patient care equipment or environmental surfaces, before performing invasive procedures and after removing gloves), cleaning and disinfection of the healthcare environment and medical equipment, sterilization of medical devices, aseptic techniques for surgical procedures and device placement, appropriate antimicrobial use, surveillance for rates of hospital-acquired infections, and appropriate patient isolation to prevent transmission of potential pathogens to other patients. The known mechanisms of transmission of common pathogens are shown.

Transmission Route

Pathogens

Precautions

Contact with patient or their contaminated secretions or environmental surfaces or equipment contaminated with secretions	Multidrug-resistant pathogens <i>C. difficile</i> RSV	Single room Hand hygiene Staff wear gown and gloves
Droplets (relatively large) containing infectious particles that drop within 3-6 feet of coughing patient	Pertussis Influenza	Single room Staff wear mask (surgical) to prevent large droplets from being inhaled
Airborne infectious droplet nuclei or dust that waft large distances and remain suspended for hours	Tuberculosis Measles	Single room under negative pressure Staff wear mask (N-95) to prevent droplet nuclei from being inhaled

Era of Bundle Strategies – Preventing CVC Bloodstream Infections

As evident by the multiple strategies employed to reduce hospital-acquired infections, it is obvious that no single strategy is sufficient. Thus, prevention of specific types of infections employs a set of evidence-based interventions, so-called Bundle Strategies. To prevent CVC-related bloodstream infections the following strategies are indicated: education of staff about each of the strategies, use aseptic technique during catheter insertion which includes maintaining sterile barriers during insertion and using an appropriate antiseptic agent at insertion site. In addition, it is recommended that transparent dressings be placed over the insertion site to aid visualization of the site which should be inspected at least daily. It is important to minimize 'breaches' of the catheter and therefore minimize entries into catheter. To reduce rates of CVC-related bloodstream infections, many institutions use anti-infective coated catheters which can be coated on both the internal and external surfaces with antiseptic agents such as silver sulfadiazine-chlorhexidine or antibiotics such as minocycline- rifampin. In addition, chlorhexidine patches can be placed over insertion site to reduce entry of skin flora. Finally daily assessment to review the need for the catheter is recommended.

Prevention of SSI: Prevention of post-operative wound infections requires different strategies which include the following:

1. Patients shower with antiseptic agent before day of surgery to reduce bacterial burden on skin
2. Clip hair, don't shave to avoid micro-abrasions of skin caused by razor
3. Use antiseptic agent for skin prior to incision
4. Administer antibiotic prophylaxis 1 hr prior to incision and again intra-operatively if case is 6 hours or longer
5. Control patient's serum glucose

6. Maintain normothermia for patient

13. Conclusions - The Perfect Storm

In conclusion, the hospital environment is a 'perfect storm' for HAI. Within a confined space, pathogenic organisms, with a multitude of routes of transmission, reside close to vulnerable patients. Multiple prevention strategies are increasingly being used with a marked reduction in some HAIs.

Key Take Home Points

- Device related infections and surgical site infections are the most common HAIs.
- Both host factors and healthcare environment factors increase the risk of HAIs.
- Pathogens causing HAI can be either endogenous flora or transmitted from patient to patient by healthcare workers.
- Pathogens causing HAI are generally multidrug-resistant and biofilms may contribute to resistance.