Nosocomial infections are those that are acquired in hospitals. This is an ever increasing matter. Our goal in this lesson is to describe this challenging & significant problem.

This lesson provides 1.25 hours (0.125 CEUs) of credit, and is intended for pharmacists in all practice settings. The program ID # for this lesson is 707-000-12-007-H01-P. Pharmacists completing this lesson by July 31, 2015 may receive full credit.

To obtain continuing education credit for this lesson, you must answer the questions on the quiz (70% correct required), and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

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The objectives of this lesson are such that upon completion the participant will be able to:

1. Describe the impact of nosocomial infections.
2. Understand the pathophysiology & microbiology of nosocomial infections.
3. Discuss preventative measures to avoid nosocomial infections.

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BACKGROUND

Hospital-acquired Infections (HAIs), or nosocomial infections, are infectious complications that patients acquire from a hospital stay. They can be devastating and even fatal. The incidence of HAIs in U.S. hospitals in 2002 was approximately 1.7 million. This includes 52,328 HAIs among newborns in nurseries, 417,946 among adults and children in intensive-care units (ICUs) and 1,266,851 among adults and children outside of the ICUs. During this same time-period, it was approximated that over 98,000 patients died related to HAIs in U.S. hospitals.(1) The annual direct medical costs associated with HAIs range from 35 to 45 billion dollars.(2) Many of these infections are preventable and, therefore, are considered medical errors.

During the past decade, there has been increased awareness and efforts of understanding and preventing infections in the hospital environment. Transmission within a healthcare setting requires the interplay of three elements:

1. Source of the infectious agent,
2. Susceptible host with a portal entry receptive to the organisms, and
3. Mode of transmission for the infectious agent.

The Center for Disease Control and Prevention (CDC) and the Healthcare Infection Control Practices Advisory Committee (HICPAC) have published guidelines to promote the prevention of transmitting infectious agents in the healthcare setting to patients.(3) These guidelines are the standard of care for all institutions including hospitals, long-term facilities, ambulatory settings and home care. The hospital environment is filled with pathogenic organisms. These organisms can be found on the hands of healthcare providers, on doorknobs, keyboards, or even on medical equipment. The human reservoirs include patients, healthcare providers and household members and visitors. The source individuals may have an active infection, or may be colonized (either transiently or chronically) with pathogenic organisms. Infection with pathogenic organisms is a complex interplay between the host and the infectious agent. Some hosts are susceptible to symptomatic disease from exposure to pathogenic organisms; whereas, some hosts remain asymptomatic. The immune status of the patient at the time of the exposure to an infectious agent, interaction between pathogen and the virulence factors are important predictors of an individual’s outcome. Underlying patient factors such age, co-morbid conditions, immune status, malignancy and transplants can increase the susceptibility to infection. Medications that alter endogenous gastrointestinal flora (i.e. antimicrobial agents, gastric acid suppressors, corticosteroids, immunosuppressive drugs, and chemotherapeutic agents) can also increase a patient’s risk to develop an infection. The skin is also an important defense to prevent infections. Surgical procedures and radiation therapy may impair this defense. Indwelling devices such as urinary catheters, endotracheal tubes, central venous and arterial catheters and synthetic implants allow the development of nosocomial infections by allowing the organisms to bypass the natural defenses. The foreign devices provide surfaces that facilitate the development of biofilms. Biofilms provide a surface that allows the adherence of microorganisms and protection from antimicrobial activity. Infections associated with an invasive procedure or device is a result of either the patient's endogenous flora or transmission from within the healthcare facility. The infections related to transmitted organisms in the hospital environment are considered to be preventable and often are no longer reimbursable by the Center for Medicare and Medicaid Services (CMS).

INFECTION CONTROL IN THE HOSPITAL SETTING

The hospital environment plays a crucial role in exposing patients to various microorganisms. Because pathogens can be found on the hands of healthcare workers and in the hospital surroundings, multiple measures have been studied to reduce this burden and, subsequently, to lower the rates of nosocomial infections. (3)
HAND HYGIENE

Adherence to appropriate infection control practices decreases transmission of pathogens. One key measure of infection control is proper hand hygiene. It is an essential part of “Standard Precautions.” The details of Standard Precautions can be found in the CDC and HICPAC guidelines. Hand hygiene includes both hand washing with soap, plain or antiseptic, and use of alcohol-based products that do not use water. Alcohol-based products used for hand disinfection are preferred over soap and water because of their superior antimicrobial activity, reduced drying of the skin and convenience. (3) Adherence to hand hygiene practices has been associated with decreased incidence of resistant organisms, including methicillin-resistant S.aureus (MRSA) and Vancomycin-Resistant Enterococcus (VRE). (4) In addition to hand hygiene, isolating patients that are colonized with resistant organisms and thorough environmental cleaning are essential to preventing avoidable transmission of nosocomial infections.

The Center for Medicare and Medicaid Services (CMS) will no longer reimburse additional payments for four HAIs which include:

1. Catheter-related bloodstream infections (CrBSI),
2. Ventilator-associated pneumonia (VAP),
3. Surgical site infections (SSIs), and

This has provided motivation for the healthcare administrators to include additional resources for guidelines and preventive measures.

VENTILATOR-ASSOCIATED PNEUMONIA (VAP)

EPIDEMIOLOGY

VAP contributes to a high morbidity and mortality in U.S. hospitals. It is estimated that VAP affects 52,000 patients per year in the U.S. with the mortality rate ranging from 30-70%. (5,6) VAP is associated with increasing hospital stays by 7 to 9 days per patient and increases costs to over $40,000 per patient (6).

DEFINITION

Ventilator-associated pneumonia (VAP) is pneumonia in a patient that is mechanically ventilated. Definitions of VAP vary amongst organizations. The CDC and NHSN (National Healthcare Safety Network) definitions are complex, but they tend to follow clinical guidelines. In general, the signs and symptoms for VAP include fever, chills, malaise, purulent respiratory secretions, rhonchi (course rattling sound usually caused by secretions in bronchial airways), leukocytosis, an infiltrate on a chest X-ray and impaired oxygenation and ventilation. Blood cultures may be positive but have a low sensitivity (25%) because the organisms may originate from another source. The diagnosis of VAP is made from respiratory tract culture obtained from the upper or lower airways. A sterile culture from the lower tract (i.e. bronchoscopy, bronchoalveolar lavage or protected brush specimen sample) is often preferred because tracheal colonization can contaminate sputum cultures. (5,6)

PATHOGENESIS, MICROBIOLOGY AND TREATMENT

The majority of VAP cases are caused by aerobic gram-negative bacilli, specifically Acinetobacter species, Pseudomonas aeruginosa, E.coli, Klebsiella species and others. The remaining cause of VAP is Staphylococcus aureus. Empiric treatment is guided by local patterns of microbial susceptibility and risk factors for multi-drug resistant (MDR) organisms. Risk factors for MDR organisms include antimicrobial therapy in preceding 90 days, current hospitalization of 5 days or more, high frequency of antibiotic resistance in the community or specific hospital location, or immunosuppressive disease and/or therapy. A regimen recommended by the ATS (American Thoracic Society) guidelines includes an anti-pseudomonal antibiotic (e.g. ceftazidime, cefepime, ciprofloxacin, piperacillin-tazobactam, meropenem or imipenem) in combination with an antibiotic effective against MRSA (e.g. linezolid or vancomycin). (6) Once definitive cultures return, antibiotic therapy should be tailored to the narrowest possible spectrum. The optimal duration of VAP in adult patients is 8 days. Chastre et al, compared 8 days of therapy versus 15 days for VAP in a prospective, randomized, dou-
ble-blind trial. (7) Excess mortality, length of ICU stay, and recurrent infections were not different between the groups, excluding patients with pseudomonal infections. Patients with pseudomonal infections receiving 8 days of therapy had higher recurrence rate compared to those patients receiving 15 days of therapy. Based on this trial, the standard of care is 8 days of antibiotics for VAP except for pseudomonal infection which requires 15 days.

The pathogenesis of VAP is a fine balance between host defenses and microbial colonization and invasion. (5,6) The microorganisms must persist and invade the lower respiratory tract in order to cause VAP. Healthcare devices or the environment including air, water and other fomites (inanimate objects capable of carrying infectious organisms) can serve as the source of the infections. The transfer of microorganisms between staff and patients can also serve as a source for infections. The entry of microorganisms into the lower respiratory tract can occur when a patient aspirates oropharyngeal pathogens or bacteria around the endotracheal cuff, resulting in leaks into the trachea. (6)

PREVENTION
Preventive measures are targeted towards the pathogenesis of VAP. First and foremost, intubation and mechanical ventilation should be avoided whenever possible and non-invasive ventilation should be used when clinically appropriate. (6,8) If patients are intubated, the duration of ventilation should be minimized. Assessments for readiness to wean ventilation should be performed daily. Many institutions have weaning protocols and guidelines that focus on minimizing sedation administration. These measures shorten exposure to the endotracheal tube and aspiration of contaminated secretions. Maintaining patients in a semirecumbent position (30-45° elevation of the head of the bed) reduces the risk of aspiration. In a multivariate analysis for risk factors for VAP, patients who maintained semirecumbency during the first 24 hours of mechanical ventilation reduced their risk for VAP by 67%. (8)

The progression of the oropharyngeal colonization to tracheobronchitis to pneumonia is a dynamic process. Oropharyngeal colonization is an independent risk factor for the development of VAP. Several strategies have been tested to reduce colonization such as the administration of prophylactic antibiotics, routine use of oral chlorhexidine, gastric acid suppression for stress ulcer prophylaxis, and selective decontamination of the digestive tract. Acid suppressive therapy may increase colonization with potential pathogenic organisms. Several randomized trials have provided controversial results on the benefits of routine stress ulcer prophylaxis with either sucralfate or H2-antagonists to prevent VAP. (6,8) The American Thoracic Society recommends either sucralfate or H2-antagonists for those patients at risk for stress bleeding. (6) Routine oral care with chlorhexidine to reduce the oropharyngeal colonization is recommended by the Infectious Disease Society of America (IDSA). (8) Routine systemic antibiotics and selective decontamination of the digestive tract strategies to prevent VAP are not recommended by IDSA or ATS guidelines. Lastly, the Center for Disease Control recommends infection control strategies that include proper hand-hygiene to eliminate contamination from healthcare workers to patients. Institutions are recommended to monitor and adhere to these national guidelines in order to minimize the incidence of VAP.

CATHETER-ASSOCIATED URINARY TRACT INFECTIONS (CA-UTIs)

EPIDEMIOLOGY
Urinary tract infections (UTIs) are a common nosocomial infection, accounting for greater than 30% of the total. They are estimated to cause 449,334 infections each year in the U. S. (5) A majority of the UTIs are caused by instrumentation. CA-UTIs are associated with increased morbidity, mortality and costs. (9) Attributed costs associated add $800 per patient case, and overall contribute annually nationally to $450 million in hospital costs in the U.S. (5)

DEFINITION
An indwelling catheter is a drainage tube that is inserted into the urinary bladder through the urethra and is connected to a closed collection system. (10) This is also known as a foley catheter. Alternative methods can be employed such as intermittent catheters, or external catheters or a surgically inserted suprapubic catheter. CA-UTIs that are reported to the National Healthcare Safety Network (NHSN) only refer to the indwelling catheters. UTIs can be classified into 3 categories: symptomatic, asymptomatic and others. Asymptomatic bacteriuria (ASB) is a condition in which a
patient with or without an indwelling catheter has no signs or symptoms of infection (i.e. no fever, urinary urgency, dysuria, suprapubic tenderness or costovertebral angle pain), but there are positive urinary cultures with no more than two uropathogens. Uropathogens include gram-negative bacilli, *Staphylococcus* spp, yeasts, *beta-hemolytic Streptococcus* spp, *Enterococcus* spp, *G. vaginalis*, *Aerococcus urinae* and *Corynebacterium* (urease positive). (9,10) Treatment of ASB has not shown to be beneficial and contributes to the selection of antimicrobial-resistant organisms. Often ASB can be treated with removing the catheter without systemic antibiotics.

CA-UTI is defined by the CDC as a patient with an indwelling urinary catheter at the time of specimen collection and at least one sign or symptom without another recognized cause (fever, suprapubic tenderness, or costovertebral angle pain or tenderness and a positive urine culture (>10^5 colony-forming units/ml) with no more than 2 species of microorganisms). (9,10) A patient can have a CA-UTI after the foley catheter has been removed; therefore, the CDC provides an alternate definition for those patients—those who had a foley catheter removed within 48 hours prior to specimen collection and at least one of the following signs or symptoms without another recognized cause (fever, urgency, frequency, dysuria, suprapubic tenderness, or costovertebral angle pain or tenderness and a positive urine culture (>10^5 colony-forming units/ml) with no more than 2 species of microorganisms).

**PATHOGENESIS, MICROBIOLOGY AND TREATMENT**

CA-UTIs can be caused by microorganisms from meatal, rectal or vaginal colonization. (9,10) They can also be caused by an exogenous source such as contaminated hands of healthcare providers or equipment. The bacteria can enter the urinary tract by the extraluminal route by migrating along the outside of the catheter. The bacteria can also move along the internal lumen of the catheter from the contaminated collection bag. The pathogens that most frequently cause CA-UTIs include *E.coli*, *Candida* spp, *Enterococcus* spp, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Enterobacter* spp. The bacteria can form a biofilm (matrix of sessile microorganisms and host proteins) on the surface of the catheter and drainage system which universally occurs with prolonged duration of catheterization. The bacterial biofilm is resistant to antimicrobials and host defenses; they are impossible to eradicate unless the catheter is removed. (10) Therefore, the mainstay of treatment for CA-UTIs is catheter removal and appropriate targeted antimicrobial therapy. (5) Antimicrobial irrigation is not recommended for treatment of CA-UTIs, but may be used in select patients for fungal CA-UTIs.

**PREVENTION**

The key to preventing CA-UTIs is judicious use. It is estimated that 1 in 5 hospitalized patients have a catheter placed. (5) Indwelling catheters should only be used for selected indications. These include: patients with acute urinary retention or bladder outlet obstruction, critically ill patients who require assessment of urinary output, patients who had selected surgical procedures (e.g. urology procedures, prolonged duration of surgery, etc), patients who require assistance with healing of open sacral or perineal wounds in incontinent patients, or patients whom require prolonged immobilization. (10) The CDC guidelines emphasize that indwelling catheters should not be used as a substitute for nursing care as a means of obtaining urine for culture or other diagnostic tests when a patient can voluntarily void, or for prolonged postoperative duration without appropriate duration. Patients with an indication for an indwelling catheter should have it removed as soon as possible, preferably within 24 hours, if clinically appropriate. In addition, educational guidelines should emphasize sterile insertion technique, maintenance practices that keep the collection bag below the bladder to avoid reflux and preventing breaks in the collection system. A recent study conducted at the Minneapolis VA demonstrated that a multi-faceted approach including education, system redesign, rewards, feedback and involvement of a dedicated foley catheter nurse significantly reduced inappropriate catheter use. (11)

**SURGICAL SITE INFECTION**

**EPIDEMIOLOGY**

Surgical site infections (SSIs) contribute to 17% of all HAIs, second to CA-UTIs. It is estimated that SSIs occur in 2-5% of patients undergoing inpatient clean (extra-abdominal) surgeries and up to 20% of patients undergoing abdominal...
surgeries. (12, 13) Patients with SSIs have increased morbidity and mortality; they have up to 11 times higher risk of death. Surgical site infections cost an additional $3,000 to $29,000 per case depending on the procedure and pathogen. The costs attributed to SSIs are up to $10 billion annually in the U.S. (5, 13)

**DEFINITION**

Surgical site infections are classified by the infected site. They are superficial incisional (involving the skin or subcutaneous tissue), deep incisional (involving the fascia and/or muscular layers or the organ space). Surgical site infections often have positive bacterial culture from the infected site (i.e. tissue or fluid) and often have purulent drainage. In general, the majority of SSIs are found within 48 hours of the surgical procedure. (12, 13)

**PATHOGENESIS, MICROBIOLOGY AND TREATMENT**

Many SSIs are a result of the invasion of microorganisms into the surgical site at the time of the operation. The pathogens may come from the patient’s own flora, seeding from a distant focus of infection, or other exogenous sources, such as surgical personnel, the operating room environment and ventilation or tools and equipment. (5, 11) The risk for SSIs is a complex interplay between the microbe, patient, and surgical characteristics. Certain patient characteristics increase risk for postoperative infections such as advanced age, presence of diabetes mellitus, smoking status, nutritional status, body mass index, immunosuppression, and other co-morbid conditions (renal and hepatic failure). In addition, the characteristics of the surgery (i.e. the type of surgery, introduction of foreign material and amount of tissue damage) can affect the risk for SSIs. (12)

*Staphylococcus aureus* remains to be the most common microorganism isolated from SSIs after clean procedures. Other endogenous organisms may be involved in SSIs that may be present at the surgical site or resected organ (i.e. gastrointestinal, gynecological, respiratory tract). (5, 14)

**TREATMENT**

The mainstay of the treatment of SSIs is drainage of the infected wound, supplemented by wound care. (5). Systemic antimicrobial therapy should be administered and should be targeted to the isolated organism. Wound sponges with suction (vacuum-assisted closure (VAC)) have been used to assist with wound closure and maintenance.

**PREVENTION**

Many preventative measures have been reported to reduce the rate of complications associated with SSIs. (5, 12) Many organizations (CMS and Surgical Infection Prevention Collaborative) joined together to improve adherence to the best practices for avoiding SSIs. Three performance measures for quality improvement strategies related to antimicrobial therapy have been instituted:

1. Delivery of intravenous antimicrobial prophylaxis within 1 hour before incision (2 hours before incision for vancomycin and fluoroquinolones),
2. The use of antimicrobial prophylactic agents consistent with published guidelines, and
3. Discontinuation of the use of the prophylactic agent within 24 hours after the surgery.

In addition to these pharmacological interventions, the Surgical Infection Prevention Collaborative recommended three additional process measures to prevent SSI. These include:

1. Proper hair removal (avoid razors for hair removal),
2. Controlling blood glucose level during immediate postoperative period, and
3. Maintenance of perioperative normothermia. (5, 12, 13)

**CATHETER-RELATED BLOODSTREAM INFECTION (CrBSIs)**

**EPIDEMIOLOGY**

Intravenous catheter use in the nosocomial setting is common. It is estimated that central venous catheter use exceeds 15 million catheter-days each year in the U.S. (5) CrBSIs are the majority of the infections in this group, with
approximately 92,000 cases per year. The costs related to CrBSIs are estimated to be $25,000 to $45,000 per case. As with other nosocomial infections, CrBSIs are associated with increased length of hospital stay and costs, but have not been associated with increased mortality. (5, 15)

**DEFINITION**

CrBSIs are defined when microbiologic and clinical symptoms suggest the catheter as the source of the infection. Some signs and symptoms include both local (e.g. erythema, induration, purulence and tenderness at catheter site) and systemic (e.g. fever and leukocytosis). Some patients may only have the systemic signs and symptoms. Central-line associated bloodstream infections may be considered in a patient who has had a catheter placed within 48 hours prior to the development of the BSI and unrelated to another source of infection. (5, 15)

**PATHOGENESIS, MICROBIOLOGY AND TREATMENT**

CrBSIs are caused by translocation of skin flora along the surface of the catheter. Bacteria can also be introduced by direct contamination of the catheter or catheter hub by contact with hands or contaminated fluids or devices. (15) Less often, the catheters may become hematogenously seeded from another focus of infection or, rarely, contaminated infusate might lead to CrBSIs. Often the bacteria develop a biofilm which is often impermeable to antibiotics and evades the immune system. The most common causative microorganisms remain to be coagulase-negative *Staphylococci*, *Staphylococcus aureus*, *Enterococci* and *Candida spp*. Gram-negative organisms also cause CrBSIs. As with other nosocomial infections, antimicrobial resistance is a continued problem limiting the treatment options. (15)

The mainstay of CrBSI treatment is removal of the catheter, except for those caused by coagulase-negative *Staphylococcus* due to its rapid clearance. CrBSIs caused by fungi, *S. aureus* or gram-negative bacilli should be treated with systemic antimicrobials and removal of the catheter. Antibiotic therapy should be narrowed to the isolated organism. The duration of therapy can range from seven to ten days up to 4-8 weeks, if there is a complicated infection (i.e. infected thrombus, endocarditis, or osteomyelitis). (5)

**PREVENTION**

CrBSIs can be reduced by improving education and training, appropriate staffing and use of process checklists. The appropriate site selection (i.e. avoiding the femoral site), hand hygiene, aseptic technique and use of antiseptic skin preparations are essential for avoiding CrBSIs. In addition, careful and appropriate catheter site care is essential to avoid CrBSIs. (15)

**SUMMARY**

Nosocomial infections are common and are a tremendous burden to patients and the healthcare system. The social, economic and personal costs related to nosocomial infections are overwhelming for many institutions, but many researchers have demonstrated various interventions that decrease infection rates. A multi-faceted approach that includes staff education, minimizing patient risk factors and easy to understand institutional guidelines is needed to prevent these infections. This is an active area of research with advancements to patient care published frequently.

**ADDITIONAL RESOURCES**

Center for Disease Control and Prevention: [www.cdc.gov/hai/](http://www.cdc.gov/hai/)
Infectious Disease Society of America: [www.idsociety.org](http://www.idsociety.org)

**REFERENCES**

2. Scott DR. Division of Healthcare Quality Promotion National Center for Preparedness, Detection, and Control of Infectious Dieases Coordinating Center for Infectious Dieases. Center for Disease Control and Prevention. March 2009


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LESSON EVALUATION
Please fill out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1. Does the program meet the learning objectives?
   - Describe the impact of nosocomial infections
   - Understand the pathophysiology & microbiology of nosocomial infections
   - Discuss the preventative measures to avoid nosocomial infections
   YES NO

2. Was the program independent & non-commercial
   YES NO

3. Relevance of topic
   Poor 2 3 4 5 6 7

4. What did you like most about this lesson?
   ____________________________________________________________________________________

5. What did you like least about this lesson?
   ____________________________________________________________________________________

Please Select the Most Correct Answer(s)

1. Hospital associated infections are considered preventable & are considered medical errors.
   A. True          B. False

2. HAIs are associated with increased healthcare expenditures in the U.S.
   A. True is associated with:
   B. False A. Selection of resistant bacteria
   C. An environment with an infectious agent within 1 hour before surgical incision
   D. All of these

3. Transmission of HAIs can occur via the following pathway:
   A. Susceptible host with indwelling device
   B. A healthcare provider with colonization with an infectious agent
   C. An environment with an infectious agent
   D. All of these

4. Pathogenic organisms can be found in healthcare facilities (nursing homes, home care settings & hospitals) on:
   A. Healthcare providers
   B. Doorknobs, keyboards, medical eqpt
   C. Patients
   D. All of these

5. What are the key principles of infection control?
   A. Hand hygiene
   B. Environmental cleaning
   C. Isolating patients colonized with resistant organisms
   D. All of these

6. VAP can be prevented by:
   A. Minimizing days on the ventilator
   B. Maintaining a prone ventilation position
   C. Routine systemic antibiotics
   D. Bowel decontamination

7. Treatment of asymptomatic bacteriuria is associated with:
   A. Selection of resistant bacteria
   B. Improved clinical outcomes
   C. Reduced costs
   D. All of these

8. SSIs can be prevented by:
   A. Delivery of antimicrobial prophylaxis within 1 hour before surgical incision
   B. Use of appropriate antibiotic recommended by national guidelines
   C. Discontinuation of prophylactic antibiotics within 24 hours of a procedure
   D. All of these

9. SSIs are best treated with:
   A. Appropriate drainage of infected wound
   B. Wound care
   C. Antibiotics targeted toward the infecting organism
   D. All of these

10. In CrBSIs, the catheter is placed within 24 hours of signs/symptoms of infection
    A. True
    B. False
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