

Approach to Nosocomial Infections

(See also *Harrison's Principles of Internal Medicine*, 17th Edition, Chapters 125 and e-1)

Definition

- Nosocomial infection is hospital-acquired infection that was neither present nor incubating at admission.
- Efforts to lower infection risks have been complicated by:
 - Growing numbers of immunocompromised patients
 - Antibiotic-resistant bacteria
 - Fungal and viral superinfections
 - Invasive devices and procedures

Epidemiology

- Incidence
 - Annually in U.S. hospitals, nosocomial infections:
 - Affect >2 million patients
 - Cost \$4.5 billion
 - Contribute to 88,000 deaths
 - Types of infections
 - Urinary tract infection (UTI): 40–45% of nosocomial infections
 - Pneumonia: 15–20% of nosocomial infections
 - Surgical wound infections: up to 20–30% of nosocomial infections
 - Vascular access/monitoring-related infections: cause up to 50% of nosocomial bacteremias
- Prevalence
 - Overall, 5–10% of hospitalized patients develop nosocomial infections.
 - Individual patient risk is related to duration of hospitalization, underlying illnesses, and other factors.
 - 25–50% of nosocomial infections are due to the combined effect of the patient's own flora and invasive devices.

Mechanism

General principles

- Nosocomial infections follow basic epidemiologic patterns that can help to direct prevention and control measures.
- Nosocomial pathogens
 - Have reservoirs and sources in:
 - Inanimate environments (e.g., tap water contaminated with *Legionella*)
 - Animate environments (e.g., infected or colonized health care workers, patients, and hospital visitors)

- Are transmitted by predictable routes
- Require susceptible hosts
- Mode of transmission
 - Cross-infection
 - For example, indirect spread of pathogens from patient to patient on inadequately cleaned hands of hospital personnel
 - Autoinoculation
 - For example, aspiration of oropharyngeal flora into the lungs along an endotracheal tube
 - Exposure via infectious droplets released by coughing or sneezing
 - For example, group A streptococci (GAS) and many respiratory viruses
 - Much less common modes with high epidemic risk
 - True airborne spread of droplet nuclei (e.g., nosocomial chickenpox)
 - Common-source spread by contaminated materials (e.g., iodophors contaminated with *Pseudomonas*)
- Increased host susceptibility from:
 - Underlying conditions
 - Medical-surgical interventions and procedures that bypass or compromise normal host defenses

Specific types of infection

- UTI
 - Almost all nosocomial UTIs are associated with preceding instrumentation or indwelling bladder catheterization.
 - 3–10% risk of infection each day
 - Caused by:
 - Ascent of pathogens up the periurethral space from the perineum or GI tract
 - Most common pathogenesis in women
 - Intraluminal contamination of urinary catheters
 - Usually due to cross-infection by caregivers irrigating catheters or emptying drainage bags
 - Inadequate disinfection of urologic equipment (occasionally)
 - Contaminated supplies (rarely; e.g., dilute aqueous benzalkonium chloride, an ineffective disinfectant)
- Bacterial hospital-acquired pneumonia
 - Almost all cases are caused by aspiration of endogenous or hospital-acquired oropharyngeal (and occasionally gastric) flora.
- Surgical wound infection
 - Usually caused by patient's endogenous or hospital-acquired skin and mucosal flora
 - Occasionally caused by airborne spread of skin squames shed into the wound from members of the operating-room team
 - True airborne spread of infection through droplet nuclei is rare in operating rooms unless there is a staff "disseminator" (e.g., of GAS or staphylococci).
 - Risk factors
 - Common
 - Deficits in surgeon's technical skill
 - Patient's underlying conditions (e.g., diabetes mellitus or obesity)
 - Inappropriate timing of antibiotic prophylaxis
 - Other
 - Presence of drains
 - Prolonged preoperative hospital stays
 - Shaving of the operative site the day before surgery

- Long duration of surgery
 - Infection at remote sites
 - Most common pathogens
 - Staphylococcus aureus
 - Coagulase-negative staphylococci
 - Enteric and anaerobic bacteria
 - In rapidly progressing postoperative infections (within 24–48 hours of a surgical procedure)
 - GAS
 - Clostridia
- Intravascular device–related infections
 - Derive largely from cutaneous microflora at the insertion site
 - Pathogens migrate extraluminally to the catheter tip.
 - Other mechanisms
 - Contamination of hubs of central vascular catheters
 - Intrinsic contamination of infusate (rare)

Epidemic and emerging problems

- Outbreaks and emerging pathogens probably account for <5% of nosocomial infections.
 - Chickenpox
 - Tuberculosis
 - GAS infection
 - Aspergillosis
 - Legionellosis
 - Others (e.g., pertussis)
- Antibiotic-resistant bacterial infection
 - Vancomycin-resistant enterococci (VRE)
 - Initially an intensive care unit problem; now on general wards
 - Particularly problematic because of:
 - Substantial "iceberg" effect: For each individual with clinical infection, many others are colonized.
 - GI and skin colonization: reflects fecal contamination on the skin of hospitalized patients
 - Propensity for organisms to contaminate the patient's environment, possibly increasing the risk of cross-infection
 - Spread of vancomycin resistance to *S. aureus* is a major concern.
 - Clinical infections with methicillin-resistant *S. aureus* (MRSA) strains exhibiting high-level vancomycin resistance due to VRE-derived plasmids have been reported with prolonged or repeated vancomycin treatment and/or VRE colonization.
 - MRSA
 - Epidemic in community-acquired as well as hospital-acquired infections
- Bioterrorism preparedness
 - See Tularemia, Smallpox, Anthrax, Plague.

Symptoms & Signs

- In general, signs and symptoms of nosocomial infection may range from the very subtle (e.g., poor appetite without localizing complaints) to the more obvious and severe (e.g., respiratory failure).

- UTI
 - 40–45% of nosocomial infections
 - Most associated with prior instrumentation or indwelling bladder catheterization
 - See Urinary Tract Infection for details.
- Hospital-acquired pneumonia
 - 15–20% of nosocomial infections
 - See Hospital-Acquired Pneumonia for details.
- Surgical wound infection
 - 20–30% of nosocomial infections
 - Average incubation period of 5–7 days
 - Often becomes evident after patients have left the hospital
 - Findings
 - Range from obvious cellulitis or abscess formation to subtle clues (e.g., a sternal "click" after open-heart surgery)
 - Additional findings
 - Erythema with a diameter >2 cm around the wound margin
 - Local pain and induration
 - Fluctuance, pus, or dehiscence of the wound
 - Diagnosis of deeper organ-space infections or subphrenic abscesses requires a high index of suspicion.
 - Diagnosis of infections of prosthetic devices (e.g., orthopedic implants) may be particularly difficult.
- Intravascular device-related infections
 - Account for up to 50% of nosocomial bacteremias
 - Central vascular catheters account for 80–90% of these infections.
 - See Intravascular Device-Related Infections for details.
- Miscellaneous infections
 - Antibiotic-associated *Clostridium difficile* diarrhea
 - Decubitus ulcers
 - See Infections of the Skin, Muscle, and Soft Tissues.
 - Sinusitis

Differential Diagnosis

- Depends on type of infection
- See:
 - Urinary Tract Infection
 - Hospital-Acquired Pneumonia
 - Intravascular Device-Related Infections

Diagnostic Approach

- Hospitalized patients should be monitored closely for signs of institutionally acquired infection.
- Patients at especially high risk include those:
 - With chronic indwelling devices
 - On respirators
 - With surgical site wounds
- Culture for common pathogens to confirm a suspected diagnosis.
- Examine patients carefully, looking for:
 - Erythema or drainage from such locations as wounds, line sites, decubitus ulcers
 - Fluctuance or other suggestions of deeper collections in wound sites

- Abdominal tenderness
- Lung crackles
- Rash
- Sinus tenderness
- Other changes from baseline values
- Patients with suspected nosocomial infection (e.g, fever and/or leukocytosis) but without specific localizing symptoms
 - Perform:
 - Urinalysis
 - Cultures of blood, urine, and sputum (along with sputum Gram staining)
 - Replace long-term indwelling bladder catheters in order to obtain a freshly voided specimen and avoid culturing catheter-biofilm flora that may not reflect the pathogen in a UTI.
 - Sputum samples that lack polymorphonuclear leukocytes or are heavily contaminated with epithelial cells are unlikely to represent deep secretions harboring the pathogens that cause a lower respiratory tract infection.
 - Chest radiography
 - Stool study for *C. difficile*, especially if there is diarrhea
 - Liver enzyme panel
 - Consider imaging of any areas with recent surgical sites (e.g, abdominal CT).

Laboratory Tests

- Nonspecific tests
 - Leukocytosis with bandemia
 - Fecal leukocytes
 - Sputum Gram's staining
 - Urinalysis
 - Liver enzyme panel
- Specific tests
 - Culture of urine, wound, sputum, or blood as appropriate, given the suspected diagnosis
 - Stool studies for *C. difficile*

Imaging

- Pneumonia
 - Chest radiography
 - Chest CT
 - May help in assessing for parapneumonic effusion
- Surgical site infection
 - CT or MRI
 - Used in diagnosis of deep organ-space infections or subphrenic abscesses
 - Interventional radiography
 - To diagnose infections of prosthetic devices (e.g., orthopedic implants)
 - To obtain periprosthetic specimens for culture

Diagnostic Procedures

- Biopsy for culture may be necessary to diagnose surgical wound infections.
- Bronchoscopy for culture may be necessary to diagnose pneumonia.

Treatment Approach

- Treatment is initiated on the basis of the suspected infection and pathogen and is refined according to culture results.
- Severely ill patients require empirical antibiotic treatment while culture results are awaited.
- Many patients who are not severely ill and whose infection source is not obvious can be observed without empirical treatment while the results of culture and other diagnostic workup procedures are awaited.
- Empirical treatment should be selected after review of the patient's prior culture data.
 - Chronic colonization with highly resistant flora (e.g., gram-negative organisms producing extended-spectrum β -lactamases) suggests that the patient is at risk for infection with such flora and may require empirical treatment with drugs that are effective against these organisms.

Specific Treatments

UTI

- General information
 - For more detail, see Urinary Tract Infection.
 - Base treatment on results of quantitative urine cultures.
 - Treatments listed below are for use pending information about the etiologic agent.
 - Therapy should be modified once the infecting agent has been identified.
 - All doses below are for adults with normal renal function.
- Complicated UTI in men and women
 - Mild to moderate illness, no nausea or vomiting: outpatient therapy
 - Oral quinolone for 10–14 days
 - Ciprofloxacin: 500 mg bid
 - Levofloxacin: 500–750 mg qd
 - Moxifloxacin: 400 mg qd
 - Severe illness or possible urosepsis: hospitalization required
 - Initial therapy choices (until defervescence)
 - Parenteral ampicillin (1–2 g IV every 4–6 h) and gentamicin (1 mg/kg every 8 h or 4–7 mg/kg IV every 24 h) **or**
 - Fluoroquinolone (ciprofloxacin, 400 mg every 12 h; ofloxacin, 400 mg every 12 h; or levofloxacin, 500–750 mg/d) **or**
 - Ceftriaxone (1–2 g/d) **or**
 - Aztreonam (1–2 g every 8–12 h) for β -lactam-allergic patients **or**
 - Ticarcillin/clavulanate (3.1 g every 4–6 h) **or**
 - Imipenem–cilastatin (250–500 mg every 6–8 h)
 - Subsequent therapy for 10–21 days, with duration depending on severity of infection and susceptibility of infecting strain
 - Oral quinolone (as listed above) **or**
 - Trimethoprim–sulfamethoxazole (double-strength tablet bid)

Surgical wound infection

- Drainage or surgical excision of infected or necrotic material and antibiotic therapy aimed at the most likely or laboratory-confirmed pathogens
- See *Staphylococcus aureus* Infections, Coagulase-Negative Staphylococcal Infections, and anaerobic bacterial infections.

Intravascular device–related infections

- See Intravascular Device–Related Infections.

Acute diarrhea

- Nosocomial diarrhea or diarrhea in outpatients taking antibiotics
 - *C. difficile* is the most common infectious cause.
 - Omit antiperistaltic agents.
 - Metronidazole (250 mg qid or 500 mg tid for 10 days)
 - Some authorities recommend vancomycin (125–500 mg PO qid) or metronidazole (500 mg IV tid) for patients with severe disease.
- See Pseudomembranous Colitis for details.

Decubitus ulcers

- May or may not be actively infected
 - When ulcers are infected, the flora is often polymicrobial (from stool contamination), requiring broad-spectrum coverage.
- See Infections of the Skin, Muscle, and Soft Tissues.

Nosocomial sinusitis

- Broad-spectrum antibiotic treatment to cover nosocomial flora (*S. aureus*, gram-negative bacteria)
- Tailor to results of culture and susceptibility testing.
- For more details, see Sinusitis.

Monitoring

- Hospitalized patients should be monitored closely for development of infection.
- Patients with indwelling catheters or devices are at high risk.

Complications

- Increased duration of hospital stay
 - Predisposes to further nosocomial infections
- Antibiotic resistance
- Impaired wound healing in nosocomially infected surgical wounds
- *C. difficile* colitis
 - Toxic megacolon
 - Bowel perforation
- Sepsis
- Death

Prognosis

- Depends on type of infection
 - UTIs contribute only 10–15% to prolongation of hospital stay and extra costs.

- Pneumonia accounts for 24% of extra hospital days and 39% of extra costs.
 - Associated with more deaths than are infections at any other body site
 - Ventilator-associated pneumonia: attributable mortality rate of 6–14%
- Surgical wound infections
 - Contribute up to 57% to extra hospital days and 42% to extra costs
- Vascular catheter infections
 - Attributable mortality rate of 12–25%

Prevention

- See Infection Control for general measures and for control plans for specific pathogens.
- Prevention of UTIs
 - Placement of catheters only when absolutely necessary (not solely for convenience of caregivers)
 - Use of aseptic technique for:
 - Catheter insertion
 - Urinary tract instrumentation
 - Manipulation and opening of drainage systems as infrequently as possible
 - Removal of catheters as soon as is feasible
 - Sealing of catheter/drainage tube junctions
 - Possible additional measures
 - Topical meatal antimicrobial agents
 - Drainage bag disinfectants
 - Anti-infective catheters
 - Systemic antimicrobial agents (given for other purposes) decrease the risk of infection during the first 4 days of catheterization.
 - Selective decontamination of the gut
 - Not performed routinely
- Prevention of nosocomial pneumonia
 - Remediation of risk factors in general patient care (e.g., minimizing aspiration-prone supine positioning)
 - Meticulous aseptic care of respirator equipment
 - Disinfection or sterilization of all in-line reusable components (e.g., nebulizers)
 - Replacement of tubing circuits at intervals >48 hours (rather than more frequently), to decrease number of breaks in system
 - Instruction in aseptic technique for suctioning
- Prevention of wound infections
 - Preoperative therapy for active infection
 - Antimicrobial prophylaxis at start of high-risk procedures
 - Attention to technical surgical issues and operating-room asepsis—e.g.:
 - Not shaving the operative site until surgery
 - Avoiding open or prophylactic drains
 - Use of supplemental oxygen
 - Maintenance of normothermia
 - Improved perioperative glucose control
 - New recommendations for decontamination of surgical instruments
 - Especially for operations on the central nervous system or in patients with dementing illness of unknown cause
- See Intravascular Device–Related Infections.

ICD-9-CM

- 136.9 Unspecified infectious and parasitic diseases (includes Infectious disease NOS)

See Also

- Coagulase-Negative Staphylococcal Infections
- Diarrhea, Acute
- Hospital-Acquired Pneumonia
- Intravascular Device-Related Infections
- Pseudomembranous Colitis
- Urinary Tract Infection

Internet Sites

- Professionals
 - Infection Control in Healthcare Settings
U.S. Centers for Disease Control and Prevention
 - Infection Control
MedlinePlus
 - Homepage
Association for Professionals in Infection Control and Epidemiology

General Bibliography

- Boyce JM et al: Guideline for Hand Hygiene in Health-Care Settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. *MMWR Recomm Rep* 51:1, 2002 [PMID:12418624]
- Dodek P et al: Evidence-based clinical practice guideline for the prevention of ventilator-associated pneumonia. *Ann Intern Med* 141:305, 2004 [PMID:15313747]
- Hubmayr RD et al: Statement of the 4th International Consensus Conference in Critical Care on ICU-Acquired Pneumonia--Chicago, Illinois, May 2002. *Intensive Care Med* 28:1521, 2002 [PMID:12583368]
- Jensen PA et al: Guidelines for preventing the transmission of Mycobacterium tuberculosis in health-care settings, 2005. *MMWR Recomm Rep* 54:1, 2005 [PMID:16382216]
- Maki DG, Weinstein RA: Nosocomial infection in the intensive care unit, in *Critical Care Medicine—Principles of Diagnosis and Management in the Adult*, 2d ed, JE Parillo, RP Dellinger (eds). Saunders, Philadelphia, 2001, pp 981–1046
- Mermel LA et al: Guidelines for the management of intravascular catheter-related infections. *Clin Infect Dis* 32:1249, 2001 [PMID:11303260]
- Neuhauser MM et al: Antibiotic resistance among gram-negative bacilli in US intensive care units: implications for fluoroquinolone use. *JAMA* 289:885, 2003 [PMID:12588273]
- O'Grady NP et al: Guidelines for the prevention of intravascular catheter-related infections. *Infect Control Hosp Epidemiol* 23:759, 2002 [PMID:12517020]
- Schwartz DS, Weinstein RA: Fever in hospitalized patients, in *Clinical Infectious Diseases: A Practical Approach*, R Root et al (eds). New York, Oxford University Press, 1999, pp 449–458
- Sehulster L et al: Guidelines for environmental infection control in health-care facilities. Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR Recomm Rep* 52:1, 2003 [PMID:12836624]

- Tablan OC et al: Guidelines for preventing health-care--associated pneumonia, 2003: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. *MMWR Recomm Rep* 53:1, 2004 [PMID:15048056]
- Weinstein RA, Bonten M (eds): *Infection Control in the ICU Environment*. Boston, Kluwer, 2002

PEARLS

- To decrease the risk of nosocomial infection, place invasive devices (e.g., urinary catheters, intravascular lines/monitors) only if clinically necessary (not for convenience), and remove them when no longer necessary.
- Avoid treating organisms isolated from cultures that do not suggest active infection—e.g.:
 - Yeast in urine from a patient with a negative urinalysis and no symptoms suggesting UTI
 - *S. aureus* in sputum that is obtained from a patient without signs or symptoms suggesting pneumonia and that shows no polymorphonuclear leukocytes on Gram staining
 - Highly resistant flora isolated from a postsurgical drain that has been in place for several days
- Narrow the spectrum of antibiotic therapy once a pathogen is isolated.
- Notify infection control practitioners of potential infection-control problems (e.g., surgical wound infections that manifest after a patient's discharge).