# Rational Antimicrobial Selection & Antimicrobial Prophylaxis

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# Rational Antimicrobial Selection

- **The initial selection of antimicrobial therapy may be empirical, prior to documentation and identification of the offending organism.**
- **A delay in antimicrobial therapy for some infections may result in serious morbidity and mortality.**

# Rational Antimicrobial Selection

**Empirical antimicrobial therapy selection should be based on:**

**1. The patient's history and physical examination.Results of Gram stains or other rapidly performed tests on specimens from the infected site.**

**2. Knowledge of the most likely offending organism for the infection in question.**

**3. Institution's local microbial susceptibility patterns.**

# Rational Antimicrobial Selection

- **Identification of the pathogen and its antimicrobial susceptibility are the most important factors in determining the choice of antimicrobial therapy.**

# Rational Antimicrobial Selection

**Infected materials must be sampled with starting antimicrobial therapy for two reasons:**

a) **A Gram stain might reveal bacteria, and an acid-fast stain might detect mycobacteria.**

b) **The premature use of antimicrobials can suppress the growth of pathogens which might result in false-negative cultures results.**

# Rational Antimicrobial Selection

- **Blood cultures should be performed in the acutely ill and febrile patient.**
- **Infected materials (blood, sputum, urine, stool, abscesses, wound or sinus drainage, spinal fluid, and joint fluid, …), from the suspected infection site must be obtained and tested.**

# Rational Antimicrobial Selection

- **When a pathogenic microorganism is identified:**

1. **antimicrobial susceptibility testing should be performed.**
2. **specific definitive antimicrobial therapy should be promptly administered.**

# Rational Antimicrobial Selection

**Selection of presumptive therapy:**

**A variety of factors must be considered:**

1) **The severity and acuity of the disease.**
2) **Local epidemiology and antibiogram.**
3) **Patient's history and host factors.**
4) **Factors related to the drug(s) to be used.**
5) **The necessity for using multiple agents.**

# Rational Antimicrobial Selection

- **In addition, there are generally accepted drugs of first choice for the treatment of most pathogens.**
- **Drugs of choice are compiled from a variety of sources and are intended as guidelines rather than as specific rules for antimicrobial use.**

# Rational Antimicrobial Selection

**Antibiograms (antibiotic susceptibilities):**

- **Local antimicrobial susceptibility data, NOT that from other institutions or national compilations.**
- **Susceptibility of bacteria can differ substantially among hospitals within a community.**

# Rational Antimicrobial Selection

**Patient History:**

- **As part of the medical history, the place where the infection was acquired should be determined: home (community acquired), nursing home environment, or hospital (nosocomial).**
- **Nursing home patients can be exposed to potentially more resistant organisms because they are often surrounded by ill patients who are receiving antibiotics.**

# Rational Antimicrobial Selection

## Host Factors:

## Allergy:

- **Allergy to an antimicrobial agent generally precludes its use.**
- **Cephalosporins should be avoided in patients allergic to penicillin for immediate or accelerated reactions (anaphylaxis, laryngospasm), but can be given under close supervision in patients with mild allergy such as skin rash.**

# Rational Antimicrobial Selection

**Age:**

- **Age is an important factor for identification of the likely etiologic agent and in the ability to eliminate the drug.**
- **In bacterial meningitis, the pathogens differ as the patient grows from the neonatal period through infancy and childhood into adulthood.**
- **For neonates, hepatic and liver functions are NOT well developed.**

# Rational Antimicrobial Selection

- **Neonates (especially when premature) can develop kernicterus when given sulfonamides, because of displacement of bilirubin from serum albumin.**
- **The major change in the elderly is decreased renal function, leading to increased adverse effects of antimicrobials eliminated by the kidney (aminoglycosides).**

# Rational Antimicrobial Selection

**Pregnancy:**

- **During pregnancy, the fetus is at risk of drug teratogenicity.**
- **The disposition of certain drugs by the mother may be altered.**
- **Penicillins, cephalosporins, and aminoglycosides are cleared more rapidly during pregnancy, because of increases in intravascular volume, glomerular filtration rate, and hepatic metabolic activities.**

# Rational Antimicrobial Selection

- **This results in a maternal serum antimicrobial concentrations ~ 50% lower than in the non-pregnant state.**
- **Thus, increased dosages of certain compounds might be necessary to achieve therapeutic levels during late pregnancy.**

# Rational Antimicrobial Selection

## Metabolic or Genetic Variation:

- **Patients with impaired blood flow may NOT absorb drugs given by intramuscular injection well.**
- **Inherited or acquired metabolic abnormalities will influence therapy of infectious diseases in a variety of ways.**
- **Patients who are slow acetylators of isoniazid are at greater risk for peripheral neuropathy.**

# Rational Antimicrobial Selection

- **Patients with severe deficiency of glucose-6-phosphate dehydrogenase can develop significant hemolysis when exposed to dapsone, sulfonamides, nitrofurantoin, nalidixic acid, and antimalarials.**
- **The antiretroviral drug abacavir is associated with severe hypersensitivity reaction (fever, rash, abdominal pain, and respiratory distress) in the presence of human leukocyte antigen allele HLA-B*5701.**

# Rational Antimicrobial Selection

## Organ Dysfunction:

- **Patients with diminished renal or hepatic function or both will need dosage adjustment to prevent drug accumulation and toxicity.**
- **Antibiotics that should be adjusted in severe liver disease: clindamycin, erythromycin, metronidazole, rifampin.**
- **Significant accumulation can occur when both liver and renal dysfunction are present for: nafcillin, sulfamethoxazole, cefotaxime, piperacillin.**

# Rational Antimicrobial Selection

**Concomitant Drugs:**

- **May influence the drug selection, dose, and monitoring.**
- **Administration of isoniazid with phenytoin can result in phenytoin toxicity due to inhibition of phenytoin metabolism by isoniazid.**
- **Drugs that possess similar adverse effect profiles can produce enhanced adverse effects (e. g: two drugs that cause nephrotoxicity or neutropenia).**

# Rational Antimicrobial Selection

## Major Drug Interactions with Antimicrobials:

1. **Aminoglycosides with:**

A. **Neuromuscular blocking agents: additive NMJ block.**

B. **Nephro- and Oto-toxins (Amphotericin, cisplatin, cyclosporine [N], furosemide [O], NSAIDs [N], radiocontrast media [N], vancomycin [N]) have additive toxicity.**

# Rational Antimicrobial Selection

2. Amphotericin B with nephrotoxins (aminoglycosides, cidofovir, cyclosporine, foscarnet, pentamidine): additive adverse effects.
3. Chloramphenicol decreases metabolism of phenytoin, tolbutamide, ethanol. (?!)
4. Foscarnet with pentamidine IV: increased risk of severe nephrotoxicity/hypocalcemia.

# Rational Antimicrobial Selection

5. **Isoniazid decreases metabolism of carbamazepine, phenytoin → nausea, vomiting, nystagmus, ataxia.**
6. **Macrolides/azalides with Digoxin: increased digoxin bioavailability.**
7. **Metronidazole with ethanol (drugs containing ethanol): disulfiram-like reaction.**

# Rational Antimicrobial Selection

**8. Penicillins and cephalosporins with probenecid, aspirin: blocked excretion of β-lactams.**

**9. Quinolones with:**

**A. Classes Ia and III antiarrhythmics: increased Q-T interval.**

**B. Multivalent cations (antacids, iron, sucralfate, zinc, vitamins, dairy products), citric acid, didanosine: decreased absorption of quinolones.**

# Rational Antimicrobial Selection

10. Rifampin increases metabolism of azoles, cyclosporine, methadone, propranolol, protease inhibitors, oral contraceptives, tacrolimus, warfarin..
11. Sulfonamides with sulfonylureas, phenytoin, warfarin: displacement from binding to albumin.
12. Tetracyclines with:

A. Antacids, iron, calcium, sucralfate: decreased absorption of tetracycline.

B. Digoxin: increased digoxin bioavailability (WHY?).

# Rational Antimicrobial Selection

## Drug Factors:

## Pharmacokinetic and Pharmacodynamic Considerations:

- **Important parameters to be considered are the minimal inhibitory concentration (MIC) and the time the concentration is above MIC.**

# Rational Antimicrobial Selection

- **Aminoglycosides exhibit concentration-dependent bactericidal effects, which allows a once-daily aminoglycosides administration.**
- **These drugs are given as a single large daily dose to maximize the peak/MIC ratio.**

# Rational Antimicrobial Selection

- **They also possess a postantibiotic effect (persistent suppression of organism growth after concentrations decrease below the MIC), which appears to contribute to the success of high-dose, once-daily administration.**
- **Fluoroquinolones also exhibit concentration-dependent killing activity, but optimal killing appears to be characterized by the AUC/MIC ratio.**

# Rational Antimicrobial Selection

- **β-Lactams display time-dependent bactericidal effects.**
- **Therefore, the important pharmacodynamic relationship for these antimicrobials is the duration that drug concentrations exceed the MIC.**
- **Frequent small doses, continuous infusion, or prolonged infusion of β-lactams appears to be correlated with positive outcomes.**

# Rational Antimicrobial Selection

## Tissue Penetration:

- **One important factors in treating an infection is the presence of the antimicrobial agent in an active form and at adequate concentration at the site of infection.**
- **Drugs that have low biliary fluid concentrations are NOT useful in the treatment of cholecystitis and cholangitis.**

# Rational Antimicrobial Selection

- **Some drugs have poor penetration to deep infections, such as abscesses, where various factors such as acidic pH, WBC products, and various enzymes can inactivate even high concentrations of certain drugs.**
- **Drugs that do NOT reach significant concentrations in the CSF should NOT be used in treatment of bacterial meningitis.**

# Rational Antimicrobial Selection

- **Body fluids where drug concentration data are clinically relevant include CSF, urine, synovial fluid, and peritoneal fluid.**
- **Parenteral therapy is indicated in: febrile neutropenia, meningitis, endocarditis, and osteomyelitis.**
- **Severe pneumonia often is treated initially with IV antibiotics then switched to oral therapy with clinical improvement.**

# Rational Antimicrobial Selection

- **Patients treated in the ambulatory setting for upper respiratory tract infections (pharyngitis, bronchitis, sinusitis, and otitis media), lower respiratory tract infections, skin and soft-tissue infections, uncomplicated urinary tract infections, and selected sexually transmitted diseases can usually receive oral therapy.**

# Rational Antimicrobial Selection

## Drug Toxicity:

- Toxic drugs should be avoided.
- Antibiotics associated with CNS toxicities, when not dose-adjusted for renal function, include penicillins, cephalosporins, quinolones, and imipenem.
- Reversible nephrotoxicity classically is associated with aminoglycosides and vancomycin.
- Irreversible ototoxicity can occur with aminoglycosides.

# Rational Antimicrobial Selection

- **Hematologic toxicities occur with prolonged use of nafcillin (neutropenia), piperacillin (platelet dysfunction), cefotetan (hypoprothrombinemia), chloramphenicol (bone marrow suppression, both idiosyncratic and dose-related toxicity), and trimethoprim (megaloblastic anemia).**

# Rational Antimicrobial Selection

- **In the outpatient setting, patients must be counseled regarding photosensitivity with azithromycin, quinolones, tetracyclines, pyrazinamide, sulfamethoxazole, and trimethoprim.**
- **Many antibiotics have been implicated in causing diarrhea and colitis secondary to *Clostridium difficile* superinfection. *************

# Rational Antimicrobial Selection

## Penicillins & Cephalosporins:

- **Hypersensitivity reactions (skin rash ….. anaphylaxis), drug fever, diarrhea, emesis, abdominal pain, hepatitis, interstitial nephritis, leukopenia, thrombocytopenia, Coomb's positive-hemolytic anemia, *C. difficile* colitis, electrolyte abnormalities, seizures.**

# Rational Antimicrobial Selection

## Carbapenems (imipenem):

- **Hypersensitivity reactions and rash, headache, nausea, diarrhea, seizures, drug fever, eosinophilia, thrombocytopenia, hepatitis, *C. difficile* colitis.**

## Monobactams (aztreonam):

- **Rash, diarrhea, nausea, hepatitis, thrombocytopenia, *C. difficile* colitis.**

# Rational Antimicrobial Selection

## Aminoglycosides:

- **Tubular necrosis and renal failure, vestibular and cochlear toxicity, neuromuscular blockade, vertigo, anemia, hypersensitivity.**

## Glycopeptides (vancomycin):

- **Red man syndrome (due to release of histamine independent on IgE), phlebitis, renal dysfunction, neutropenia, leukopenia, eosinophilia, thrombocytopenia, drug fever.**

# Rational Antimicrobial Selection

**Lipopeptides (daptomycin):**

- **Hepatotoxicity, CPK elevation with or without myopathy, diarrhea, eosinophilic pneumonia, *C. difficile* colitis.**

**Oxazolidinones (linezolid):**

- **Myelosuppression (thrombocytopenia, leukopenia, and anemia), peripheral neuropathy, optic neuropathy, blindness, lactic acidosis, diarrhea, nausea, serotonin syndrome, interstitial nephritis.**

# Rational Antimicrobial Selection

**Tetracyclines:**

- **GI upset, nausea, vomiting, diarrhea, hepatotoxicity, esophageal ulcerations, photosensitivity, azotemia, visual disturbances, vertigo, hyperpigmentation, deposition on teeth, hemolytic anemia, pseudotumor cerebri, pancreatitis, *C. difficile* colitis.**

**Chloramphenicol:**

- **Myelosuppression, aplastic anemia, "gray baby syndrome," optic neuritis, peripheral neuropathy, digital paresthesias, GI upset, *C. difficile* colitis, hypersensitivity.**

# Rational Antimicrobial Selection

## Rifamycines:

- **Discoloration of urine, tears, contact lenses, saliva, sweat; hepatotoxicity, GI upset, flu-like syndrome, hypersensitivity, thrombocytopenia, leukopenia, drug fever, interstitial nephritis, thrombocytopenia.**

## Macrolides/azalide:

- **GI intolerance, diarrhea, prolonged QTc, *torsade de pointes*, cholestatic hepatitis, reversible ototoxicity, rash, hypothermia, exacerbation of myasthenia gravis.**

# Rational Antimicrobial Selection

**Clindamycin:**

- **Diarrhea, *C. difficile* colitis, nausea, vomiting, generalized rash, hypersensitivity.**

**Fluoroquinolones:**

- **GI intolerance, headache, malaise, insomnia, dizziness, photosensitivity, QTc prolongation, tendon rupture, peripheral neuropathy, crystalluria, seizure, interstitial nephritis, Stevens-Johnson syndrome, allergic pneumonitis, *C. difficile* colitis.**

# Rational Antimicrobial Selection

**Sulfonamides and trimethoprim:**

- **GI intolerance, rash, hyperkalemia (by blocking amiloride-sensitive sodium channels in the cortical collecting duct), bone marrow suppression (anemia with folate deficiency, thrombocytopenia, and leukopenia), serum sickness, hepatitis, photosensitivity, crystalluria with azotemia, urolithiasis, methemoglobinemia, Stevens-Johnson syndrome, toxic epidermal necrolysis, aseptic meningitis, pancreatitis, interstitial nephritis, neurologic toxicity.**

# Rational Antimicrobial Selection

## Metronidazole:

- **GI intolerance, headache, metallic taste, dark urine, peripheral neuropathy, disulfiram-like reactions with alcohol, insomnia, stomatitis, aseptic meningitis, dysarthria.**

## Polymyxins (polymyxin B & colistin):

- **Nephrotoxicity, neurotoxicity (paresthesia, vertigo, ataxia, blurred vision, slurred speech), neuromuscular blockade, bronchospasm (administered via inhalation).**

# Rational Antimicrobial Selection

**Failure of antimicrobial therapy:**

- **Patients who fail to respond over 2 - 3 days require a thorough reevaluation.**

**Causes:**

a) **The disease is NOT infectious or is nonbacterial in origin.**

b) **There is an undetected pathogen in a polymicrobial infection.**

c) **Factors directly related to drug selection, the host, or the pathogen.**

d) **Laboratory error in identification, susceptibility testing, or both.**

# Rational Antimicrobial Selection

**Failures Caused by Drug Selection:**

1) **Inappropriate selection of drug, dosage, or route of administration.**
2) **Reduced absorption of a drug, resulting in subtherapeutic concentrations, because of:**

a. **GI disease (short-bowel syndrome).**

b. **Drug interaction (complexation of fluoroquinolones with multivalent cations).**

# Rational Antimicrobial Selection

3) Accelerated drug elimination (cystic fibrosis or during pregnancy), resulting in low concentrations.

4) Poor penetration into the site of infection (for sites such as the CNS, eye, and prostate gland).

5) Chemical inactivation of the drug at the site of infection.

# Rational Antimicrobial Selection

## Failures Caused by Host Factors:

a) **Patients who are immunosuppressed (granulocytopenia from immunosuppressants, chemotherapy or AIDS) may respond poorly because their defenses are inadequate to eradicate the infection despite seemingly adequate drug regimens.**

# Rational Antimicrobial Selection

a) **The need for surgical drainage of abscesses or removal of foreign bodies, necrotic tissue, or both. These infections will NOT be effectively treated without surgical procedures.**

# Rational Antimicrobial Selection

## Failures Related to Pathogens (Resistance):

- **Intrinsic resistance: when the antimicrobial agent never had activity against the bacterial species. (Gram-negative bacteria are naturally resistant to vancomycin because the drug cannot penetrate the outer membrane of gram negative bacteria).**
- **Bacteria that lack cell wall will not respond to β-lactam antibiotics.**

# Rational Antimicrobial Selection

- **Acquired resistance: occurs when the antimicrobial agent was originally active against the bacterial species but the genetic makeup of the bacteria has changed so the drug can NO longer be effective.**

# Rational Antimicrobial Selection

**Mechanisms of acquired bacterial resistance :**

a. **Alteration in the target site.**
b. **Change in membrane permeability.**
c. **Expression of an efflux pump.**
d. **Drug inactivation through either β-lactamases or aminoglycoside-modifying enzymes is the predominant mechanism of resistance.**

- **The expression of β-lactamases can be induced or constitutive.**

# Rational Antimicrobial Selection

**The increased resistance results from:**

1. **Continued overuse of antimicrobials in the community and in hospitals.**
2. **Long-term suppressive antimicrobials for the prevention of infections in immunosuppressed patients.**

# Rational Antimicrobial Selection

- **Enterococci with multiple resistance patterns have been isolated.**
- **They may be resistant to:**

1. **β-lactams (β-lactamase production, altered penicillin-binding proteins [PBPs], or both)**
2. **Vancomycin (alterations in peptidoglycan synthesis).**
3. **Aminoglycosides (high levels of AGs-degrading enzymes.**
4. ***Resistance to Tetracycline, Ciprofloxacin, Clindamycin, Erythromycin, quinupristin-dalfopristin has been demonstrated also.***

# Rational Antimicrobial Selection

- **Enterococci with multiple resistance patterns treatment:**

1. **Penicillin-Resistant Enterococci: Vancomycin + gentamicin or streptomycin.**
2. **Vancomycin-Resistant Enterococci (VRE): Linezolid, Daptomycin, tigecycline. Nitrofurantoin for UTI.**
3. ***Susceptiblity to: Imipenem, and Teicoplanin have been reported***

# Rational Antimicrobial Selection

- **Pneumococci resistant to penicillins, certain cephalosporins, and macrolides are increasingly common.**
- **These organisms generally are susceptible to vancomycin, the new fluoroquinolones (moxifloxacin and trovafloxacin), and cefotaxime or ceftriaxone.**

# Rational Antimicrobial Selection

- **Antimicrobial agents such as linezolid, daptomycin, telavancin (semi-synthetic derivative of vancomycin), and tigecycline (new tetracycline) have been used for resistant gram-positive bacteria.**

# Rational Antimicrobial Selection

- **Treatment of infections caused by *Enterobacter, Citrobacter, Serratia,* or *P. aeruginosa* with a third-generation cephalosporin or aztreonam may produce an initial clinical response by eradicating the susceptible bacteria.**
- **Within a few days, the highly resistant subpopulations can overgrow at the infection site to produce a relapse.**
- **These bacteria usually retain susceptibility to fluoroquinolones, aminoglycosides, carbapenems, but are resistant to all other β-lactams.**

# Rational Antimicrobial Selection

- **Host defenses are extremely important in this scenario.**
- **Debilitated patients with pulmonary infections, abscesses, or osteomyelitis are at high risk for drug failure.**
- **In these situations, a combination regimen to prevent the emergence of resistance or the use of carbapenem or a fluoroquinolone may be used for empiric therapy.**

# Rationale For Combination Antimicrobial Therapy

- **Most infections should be treated with a single antimicrobial agent.**
- **Although indications for combination therapy do exist, antimicrobial combinations are often overused in clinical practice.**
- **The unnecessary use of antimicrobial combinations increases toxicity and costs and may occasionally result in reduced efficacy due to antagonism of one drug by another.**

# Rationale For Combination Antimicrobial Therapy

- **Antimicrobial combinations should be selected for one or more of the following reasons:**

1. **To provide broad-spectrum empiric therapy in seriously ill patients.**
2. **To treat polymicrobial infections (intra-abdominal abscesses, which are due to a combination of anaerobic and aerobic gram-negative organisms, and enterococci).**

# Rationale For Combination Antimicrobial Therapy

- **The antimicrobial combination chosen should cover the most common known or suspected pathogens but not cover all possible pathogens.**

3. **To decrease the emergence of resistant strains – tuberculosis.**
4. **To obtain enhanced inhibition or killing.**

# Rationale For Combination Antimicrobial Therapy

5. **To decrease dose-related toxicity by using reduced doses of one or more components of the drug regimen.**

- **The use of flucytosine in combination with amphotericin B for the treatment of cryptococcal meningitis in non–HIV-infected patients allows for a reduction in amphotericin B dosage with decreased amphotericin B-induced nephrotoxicity.**

# Rationale For Combination Antimicrobial Therapy

## Broadening the Spectrum of Coverage:

- **Increasing the coverage of antimicrobial therapy generally is necessary in the following cases:**

1. **In mixed infections where multiple organisms are likely to be present (in intra-abdominal and female pelvic infections), in which a variety of aerobic and anaerobic bacteria can produce disease.**
- **A combination of a drug active against aerobic Gram-negative bacilli (aminoglycoside) and a drug active against anaerobic bacteria (metronidazole or clindamycin) are selected.**

# Rationale For Combination Antimicrobial Therapy

2. **For critically ill patients with health care-associated infections.**

- **These infections are frequently caused by multi-drug resistant pathogens.**
- **Combination therapy is used in this setting to ensure that at least one of the antimicrobials will be active against the pathogen(s).**

# Rationale For Combination Antimicrobial Therapy

**Synergism:**

- **This is necessary for infections caused by enteric Gram-negative bacilli in immunosuppressed patients.**
- **Traditionally, combinations of aminoglycosides and β-lactams have been used because these drugs together generally act synergistically against a wide variety of bacteria.**

# Rationale For Combination Antimicrobial Therapy

- **Synergistic combinations may produce better results in infections caused by *Pseudomonas aeruginosa* and *Enterococcus* species.**
- **The most obvious example of the use of synergy is the treatment of enterococcal endocarditis. The causative organism is usually only inhibited by penicillins, but it is killed rapidly by the addition of streptomycin or gentamicin to a penicillin.**

# Rationale For Combination Antimicrobial Therapy

**Preventing Resistance:**

- **The use of antimicrobial combinations to prevent the emergence of resistance has been demonstrated in the treatment of tuberculosis.**
- **Combinations of drugs with different mechanisms should be used in this case.**

# Disadvantages of Combination Therapy

1. **Increased cost.**
2. **Greater risk of drug toxicity (nephrotoxicity) with aminoglycosides, amphotericin, and vancomycin.**
3. **Superinfection with more resistant bacteria.**
4. **Antagonistic effects: when one drug induces β-lactamase production and the other is susceptible to β-lactamase.**

- **Cefoxitin and imipenem are capable of inducing β-lactamases and may result in more rapid inactivation of penicillins.**

# Antimicrobial Prophylaxis

- **Antimicrobial agents are effective in preventing infections in many settings.**
- **Antimicrobial prophylaxis should be used in circumstances in which efficacy has been demonstrated and benefits outweigh the risks of prophylaxis. (Evidence-Based Medicine).**

# Antimicrobial Prophylaxis

## Surgical Prophylaxis:

- **Surgical wound infections are a major category of nosocomial infections.**
- **Risk factors for postoperative wound infections:**

a) **operations on the abdomen.**

b) **operations lasting more than 2 hours.**

c) **contaminated or dirty wound.**

d) **at least three medical diagnoses.**

# Antimicrobial Prophylaxis

- **Surgical procedures that carry a significant risk of postoperative site infection and necessitate the use of antimicrobial prophylaxis include:**

a) **contaminated and clean-contaminated operations.**

b) **selected operations in which postoperative infection may be catastrophic such as open heart surgery.**

c) **clean procedures that involve placement of prosthetic materials.**

d) **any procedure in an immunocompromised host.**

# National Research Council (NRC) Wound Classification Criteria

**Clean:** Elective, primarily closed procedure; respiratory, gastrointestinal, biliary, genitourinary, or oropharyngeal tract not entered; no acute inflammation and no break in technique; expected infection rate ≤ 2%.

**Clean contaminated:** Urgent or emergency case that is otherwise clean; elective, controlled opening of respiratory, gastrointestinal, biliary, or oropharyngeal tract; minimal spillage or minor break in technique; expected infection rate ≤ 10%.

**Contaminated:** Acute nonpurulent inflammation; major technique break or major spill from hollow organ; penetrating trauma less than 4 hours old; chronic open wounds to be grafted or covered; expected infection rate about 20%.

**Dirty:** Purulence or abscess; preoperative perforation of respiratory, gastrointestinal, biliary, or oropharyngeal tract; penetrating trauma more than 4 hours old; expected infection rate about 40%.

# Antimicrobial Prophylaxis

- **General principles of antimicrobial surgical prophylaxis include the following:**

1. **The antibiotic should be active against common surgical wound pathogens; unnecessary broad coverage should be avoided.**
2. **The antibiotic should have proved efficacy in clinical trials.**
3. **The antibiotic must achieve concentrations greater than the MIC of the suspected pathogens, and these concentrations must be present at the time of incision.**

# Antimicrobial Prophylaxis

4. **The shortest possible course — ideally a single dose — of the most effective and least toxic antibiotic should be used.**
5. **The newer broad-spectrum antibiotics should be reserved for therapy of resistant infections.**
6. **If all other factors are equal, the least expensive agent should be used.**

## TABLE 51–7 Recommendations for surgical antimicrobial prophylaxis.

| Type of Operation | Common Pathogens | Drug of Choice |
|---|---|---|
| Cardiac (with median sternotomy) | Staphylococci, enteric gram-negative rods | Cefazolin |
| Noncardiac, thoracic | Staphylococci, streptococci, enteric gram-negative rods | Cefazolin |
| Vascular (abdominal and lower extremity) | Staphylococci, enteric gram-negative rods | Cefazolin |
| Neurosurgical (craniotomy) | Staphylococci | Cefazolin |
| Orthopedic (with hardware insertion) | Staphylococci | Cefazolin |
| Head and neck (with entry into the oropharynx) | *Staphylococcus aureus,* oral flora | Cefazolin + metronidazole |
| Gastroduodenal | *S aureus,* oral flora, enteric gram-negative rods | Cefazolin |
| Biliary tract | *S aureus,* enterococci, enteric gram-negative rods | Cefazolin |
| Colorectal (elective surgery) | Enteric gram-negative rods, anaerobes | Oral erythromycin + neomycin[1] |
| Colorectal (emergency surgery or obstruction) | Enteric gram-negative rods, anaerobes | Cefoxitin, cefotetan, ertapenem, or cefazolin + metronidazole |
| Appendectomy, nonperforated | Enteric gram-negative rods, anaerobes | Cefoxitin, cefotetan, or cefazolin + metronidazole |
| Hysterectomy | Enteric gram-negative rods, anaerobes, enterococci, group B streptococci | Cefazolin, cefotetan, or cefoxitin |
| Cesarean section | Enteric gram-negative rods, anaerobes, enterococci, group B streptococci | Cefazolin |

[1]In conjunction with mechanical bowel preparation.

# Antimicrobial Prophylaxis

- **The selection of vancomycin over cefazolin may be necessary in hospitals with high rates of methicillin-resistant *S. aureus or S. epidermidis infections.***
- **The antibiotic should be present in adequate concentrations at the operative site before incision and throughout the procedure.**

# Antimicrobial Prophylaxis

- **Parenteral agents should be administered during the interval beginning 60 minutes before incision up to the time of incision.**
- **In cesarean section, the antibiotic is administered after umbilical cord clamping.**
- **If short-acting agents such as cefoxitin are used, doses should be repeated if the procedure exceeds 3–4 hours in duration.**
- **Single-dose prophylaxis is effective for most procedures and results in decreased toxicity and decreased antimicrobial resistance.**

# Antimicrobial Prophylaxis

**Common errors in antibiotic prophylaxis include:**

a) Selection of the wrong antibiotic.

b) Administering the first dose too early or too late.

c) Failure to repeat doses during prolonged procedures.

d) Excessive duration of prophylaxis.

e) Inappropriate use of broad-spectrum antibiotics.

# Antimicrobial Prophylaxis

## Nonsurgical Prophylaxis:

- **Nonsurgical prophylaxis includes:**

a) **The administration of antimicrobials to prevent colonization and asymptomatic infection.**

b) **The administration of drugs following colonization by or inoculation of pathogens but before the development of disease.**

- **Nonsurgical prophylaxis is indicated in:**

a) **Individuals who are at high risk for selected virulent pathogens**

b) **Immunocompromised hosts.**

## TABLE 51–8 Recommendations for nonsurgical antimicrobial prophylaxis.

| Infection to Be Prevented | Indication(s) | Drug of Choice | Efficacy |
|---|---|---|---|
| Anthrax | Suspected exposure | Ciprofloxacin or doxycycline | Proposed effective |
| Cholera | Close contacts of a case | Tetracycline | Proposed effective |
| Diphtheria | Unimmunized contacts | Penicillin or erythromycin | Proposed effective |
| Endocarditis | Dental, oral, or upper respiratory tract procedures[1] in at-risk patients[2] | Amoxicillin or clindamycin | Proposed effective |
| Genital herpes simplex | Recurrent infection (≥ 4 episodes per year) | Acyclovir | Excellent |
| Perinatal herpes simplex type 2 infection | Mothers with primary HSV or frequent recurrent genital HSV | Acyclovir | Proposed effective |
| Group B streptococcal (GBS) infection | Mothers with cervical or vaginal GBS colonization and their newborns with one or more of the following: (a) onset of labor or membrane rupture before 37 weeks' gestation, (b) prolonged rupture of membranes (> 12 hours), (c) maternal intrapartum fever, (d) history of GBS bacteriuria during pregnancy, (e) mothers who have given birth to infants who had early GBS disease or with a history of streptococcal bacteriuria during pregnancy | Ampicillin or penicillin | Excellent |
| *Haemophilus influenzae* type B infection | Close contacts of a case in incompletely immunized children (> 48 months old) | Rifampin | Excellent |
| HIV infection | Health care workers exposed to blood after needle-stick injury | Tenofovir/emtricitabine and raltegravir | Good |
| | Pregnant HIV-infected women who are at ≥ 14 weeks of gestation; newborns of HIV-infected women for the first 6 weeks of life, beginning 8–12 hours after birth | HAART[3] | Excellent |
| Influenza A and B | Unvaccinated geriatric patients, immunocompromised hosts, and health care workers during outbreaks | Oseltamivir | Good |

| | | | |
|---|---|---|---|
| Malaria | Travelers to areas endemic for chloroquine-susceptible disease | Chloroquine | Excellent |
| | Travelers to areas endemic for chloroquine-resistant disease | Mefloquine, doxycycline, or atovaquone/proguanil | Excellent |
| Meningococcal infection | Close contacts of a case | Rifampin, ciprofloxacin, or ceftriaxone | Excellent |
| *Mycobacterium* avium complex | HIV-infected patients with CD4 count < 75/μL | Azithromycin, clarithromycin, or rifabutin | Excellent |
| Otitis media | Recurrent infection | Amoxicillin | Good |
| Pertussis | Close contacts of a case | Azithromycin | Excellent |
| Plague | Close contacts of a case | Tetracycline | Proposed effective |
| Pneumococcemia | Children with sickle cell disease or asplenia | Penicillin | Excellent |
| *Pneumocystis jiroveci* pneumonia (PCP) | High-risk patients (eg, AIDS, leukemia, transplant) | Trimethoprim-sulfamethoxazole, dapsone, or atovaquone | Excellent |
| Rheumatic fever | History of rheumatic fever or known rheumatic heart disease | Benzathine penicillin | Excellent |
| Toxoplasmosis | HIV-infected patients with IgG antibody to *Toxoplasma* and CD4 count < 100/μL | Trimethoprim-sulfamethoxazole | Good |
| Tuberculosis | Persons with positive tuberculin skin tests and one or more of the following: (a) HIV infection, (b) close contacts with newly diagnosed disease, (c) recent skin test conversion, (d) medical conditions that increase the risk of developing tuberculosis, (e) age < 35 y | Isoniazid or rifampin or isoniazid + rifapentine | Excellent |
| Urinary tract infections (UTI) | Recurrent infection | Trimethoprim-sulfamethoxazole | Excellent |

[1]Prophylaxis is recommended for the following: dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa, and invasive procedure of the respiratory tract that involves incision or biopsy of the respiratory mucosa, such as tonsillectomy and adenoidectomy.

[2]Prophylaxis should be targeted to those with the following risk factors: prosthetic heart valves, previous bacterial endocarditis, congenital cardiac malformations, cardiac transplantation patients who develop cardiac valvulopathy.

[3]Highly active antiretroviral therapy. See http://aidsinfo.nih.gov/ for updated guidelines.

**Tigecycline differs in spectrum:**

1. ***Staphylococcus aureus*** **including coagulase-negative, methicillin-resistant and vancomycin-resistant strains.**
2. **Streptococci including penicillin- resistant strains.**
3. **Enterococci including vancomycin- resistant strains.**
4. **Gram positive rods.**
5. **Enterobacteriaceae**
6. **Acinetobacter sp**
7. **Gram positive and gram negative anaerobes.**
8. **Atypical agents, rickettsiae, chlamydia and Legionella and rapidly growing Mycobacteria.**

**Adverse Effects:**

1. **Hypersensitivity reactions including drug fever and skin rash, and anaphylaxis.**
2. **GIT: nausea, vomiting and diarrhea.**
3. **Superinfections: *Pseudomonas, Proteus, Staphylococcus aureus*, Coliforms, Clostridia and Candida.**
4. **Bone & teeth:**

a) **Fetal teeth: fluorescence, discoloration, and enamel dysplasia.**

b) **Fetal bone: deformity or growth inhibition.**

c) **Similar changes occur in children below 8 years of age.**

5. **Liver toxicity: hepatic necrosis and impairment of hepatic function.**
6. **Pancreatitis.**
7. **Kidney toxicity: renal tubular acidosis and other renal injury.**
8. **Local tissue toxicity: Thrombophlebitis after IV administration, Local pain after IM administration.**
9. **Photosenstivity.**
10. **Vestibular reactions: dizziness, vertigo, nausea, vomiting.**