Microbiology, Infections, and Antibiotic Therapy

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Grand Rounds Presentation
March 22, 2000
Basic Bacteriology

Shape
Arrangement
Gram Staining
Cell Wall Characteristics

- **Gram Positive**
- **Gram Negative**

<table>
<thead>
<tr>
<th>Gram positive</th>
<th>Gram negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flagellum</td>
<td>Flagellum</td>
</tr>
<tr>
<td>Capsule</td>
<td>Capsule</td>
</tr>
<tr>
<td>Pilus</td>
<td>Pilus</td>
</tr>
<tr>
<td>Peptidoglycan</td>
<td>Peptidoglycan</td>
</tr>
<tr>
<td>Outer membrane</td>
<td>Outer membrane</td>
</tr>
<tr>
<td>Cytoplasmic membrane</td>
<td>Cytoplasmic membrane</td>
</tr>
<tr>
<td>Periplasmic space</td>
<td>Periplasmic space</td>
</tr>
</tbody>
</table>
Bacterial Growth

- Binary Fission = Exponential Growth
- Four Phases of Growth
## Normal Bacterial Flora

<table>
<thead>
<tr>
<th>Location</th>
<th>Important Organisms¹</th>
<th>Less Important Organisms²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td><em>Staphylococcus epidermidis</em></td>
<td><em>Staphylococcus aureus</em>, <em>Corynebacterium</em> (diptheroids), various streptococci, <em>Pseudomonas aeruginosa</em>, anaerobes (eg, <em>Peptococcus</em>), yeasts (eg, <em>Candida albicans</em>)</td>
</tr>
<tr>
<td>Nose</td>
<td><em>Staphylococcus aureus</em></td>
<td><em>S epidermidis</em>, <em>Corynebacterium</em> (diptheroids), various streptococci</td>
</tr>
<tr>
<td>Mouth</td>
<td>Viridans streptococci</td>
<td>Various streptococci</td>
</tr>
<tr>
<td>Dental plaque</td>
<td><em>Streptococcus mutans</em></td>
<td></td>
</tr>
<tr>
<td>Gingival crevices</td>
<td>Various anaerobes, eg, <em>Bacteroides</em>, <em>Fusobacterium</em>, streptococci, <em>Actinomyces</em></td>
<td>Various streptococci (including <em>Streptococcus pyogenes</em> and <em>S pneumoniae</em>), <em>Neisseria</em> species, <em>Haemophilus influenzae</em>, <em>S epidermidis</em></td>
</tr>
<tr>
<td>Throat</td>
<td>Viridans streptococci</td>
<td></td>
</tr>
<tr>
<td>Colon</td>
<td><em>Bacteroides fragilis</em>, <em>Escherichia coli</em></td>
<td><em>Bifidobacterium</em>, <em>Eubacterium</em>, <em>Fusobacterium</em>, <em>Lactobacillus</em>, various aerobic gram-negative rods, <em>Streptococcus faecalis</em> and other streptococci, <em>Clostridium</em></td>
</tr>
<tr>
<td>Vagina</td>
<td><em>Lactobacillus</em>, <em>E coli</em>,³ group B streptococci³</td>
<td>Various streptococci, various gram-negative rods, <em>B fragilis</em>, <em>Corynebacterium</em> (diptheroids), <em>C albicans</em></td>
</tr>
<tr>
<td>Urethra</td>
<td></td>
<td><em>S epidermidis</em>, <em>Corynebacterium</em> (diptheroids), various streptococci, various gram-negative rods</td>
</tr>
</tbody>
</table>
Host Defense Mechanisms

- **Nonspecific Immunity**
  - barriers
  - inflammatory response

- **Specific Immunity**
  - Passive
  - Active
    - humoral
    - cell-mediated

### Diagram

<table>
<thead>
<tr>
<th>NATIVE (INNATE) IMMUNITY</th>
<th>SPECIFIC (ACQUIRED) IMMUNITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteria + Phagocyte → Phagocytosis (inefficient)</td>
<td>B Lymphocyte + Antibody → Opsonization and Phagocytosis</td>
</tr>
<tr>
<td>Bacteria + Serum complement → Bacterial lysis</td>
<td>B Lymphocyte + Antibody → Enhanced complement activation</td>
</tr>
<tr>
<td>Bacteria + Phagocyte → Phagocytosis (inefficient)</td>
<td>T Lymphocyte + Activated Macrophage</td>
</tr>
</tbody>
</table>
Clinical Microbiology

- Gram Positive Cocci
- Gram Positive Bacilli
- Gram Negative Cocci
- Gram Negative Bacilli
- Anaerobes
- Spirochetes
- Mycobacteria
Gram Positive Cocci

- Staphylococcus
- Streptococcus
Staphylococcus

- S. aureus, S. epidermidis, S. saprophyticus
- S. aureus

**Enzymes**
- Coagulase
- Catalase
- Hyaluronidase
- Fibrinolysin
- Lipase
- Nuclease
- Penicillinase

**Toxins**
- Cytotoxins (alpha, beta, delta, gamma leukocidin)
- Exfoliative (epidermolytic) toxin
- Toxic shock syndrome
- Enterotoxin (A-F)

**Other**
- Slime production
- Capsule
- Cell wall
Streptococcus

*S. viridans*
- oral flora
- infective endocarditis
S. pyogenes

- Group A, beta hemolytic strep
- Pharyngitis, cellulitis
- Rheumatic fever
  - Fever
  - Migrating polyarthritis
  - Carditis
  - Immunologic cross reactivity
- Acute glomerulonephritis
  - Edema, hypertension, hematuria
  - Antigen-antibody complex deposition
S. pneumoniae
Gram Negative Cocci

- Neisseria
  - meningitidis
  - gonorrhea
- Moraxella catarrhalis
Gram Positive Bacilli

- Clostridium
- Bacillus
- Corynebacterium
- Listeria
- Actinomyces
- Nocardia
C. tetani
C. botulinum

- Descending weakness --> paralysis
- Diplopia, dysphagia --> respiratory failure

Table 18-4  *Clostridium botulinum* Disease

<table>
<thead>
<tr>
<th>Disease</th>
<th>Source of Toxin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical botulism</td>
<td>Ingestion of contaminated food</td>
</tr>
<tr>
<td>Infant botulism</td>
<td>In vivo production in colonized infant</td>
</tr>
<tr>
<td>Wound botulism</td>
<td>In vivo production in infected wound</td>
</tr>
</tbody>
</table>
C. perfringens
C. diphtheriae

- Fever, pharyngitis, cervical LAD
- Thick, gray, adherent membrane
- Sequelae→airway obstruction, myocarditis
- Colony morphology
L. monocytogenes

[Diagram showing natural reservoirs, common routes for human exposure, and population at greatest risk.

- **Natural reservoirs**: Mammals, Fish, Birds, Insects
- **Common routes for human exposure**: Food products from fish, fowl, beef, pork, etc., Direct contact.
- **Population at greatest risk**: Healthy children and adults (Asymptomatic carriage), Pregnant women (Asymptomatic carriage, Septicemia, Neonatal disease), Immunocompromised (e.g., cancer or transplant patients) (Asymptomatic carriage, Meningitis, Septicemia, Other infections).]
Actinomyces

- Part of normal oral cavity flora
- 50% of infections occur in face & neck
- Forms abscesses with sulfur granules
- Draining sinus tracts
Nocardia
Gram Negative Bacilli

- **Facultative Anaerobes**
  - Respiratory
    - Haemophilus
    - Bordetella
    - Legionella
  - Zoonotic
    - Yersinia
    - Francisella
    - Pastuerella
  - Enteric
    - Klebsiella
    - Serratia
    - Proteus
    - Enterobacter

- **Strict Aerobes**
  - Pseudomonas

- **Anaerobes**
  - Bacteroides
## Table 9-1 Family Enterobacteriaceae

<table>
<thead>
<tr>
<th>Tribe</th>
<th>Genus</th>
<th>(Number of Species)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichiae</td>
<td><em>Escherichia</em></td>
<td>(5)</td>
</tr>
<tr>
<td></td>
<td><em>Shigella</em></td>
<td>(4)</td>
</tr>
<tr>
<td>Edwardsielleae</td>
<td><em>Edwardsiella</em></td>
<td>(3)</td>
</tr>
<tr>
<td>Salmonelleae</td>
<td><em>Salmonella</em></td>
<td>(5)</td>
</tr>
<tr>
<td>Citrobactereae</td>
<td><em>Citrobacter</em></td>
<td>(3)</td>
</tr>
<tr>
<td>Klebsielleae</td>
<td><em>Klebsiella</em></td>
<td>(7)</td>
</tr>
<tr>
<td></td>
<td><em>Enterobacter</em></td>
<td>(10)</td>
</tr>
<tr>
<td></td>
<td><em>Hafnia</em></td>
<td>(3)</td>
</tr>
<tr>
<td>Proteae</td>
<td><em>Serratia</em></td>
<td>(9)</td>
</tr>
<tr>
<td></td>
<td><em>Proteus</em></td>
<td>(4)</td>
</tr>
<tr>
<td></td>
<td><em>Morganella</em></td>
<td>(1)</td>
</tr>
<tr>
<td>Yersiniae</td>
<td><em>Providencia</em></td>
<td>(4)</td>
</tr>
<tr>
<td>Erwmineae</td>
<td><em>Yersinia</em></td>
<td>(5)</td>
</tr>
<tr>
<td></td>
<td><em>Erwinia</em></td>
<td>(2)</td>
</tr>
</tbody>
</table>
K. rhinoscleromatis
K. rhinoscleromatis

- Catarrhal
  - purulent rhinorrhea
- Granulomatous
  - mucosal nodules
- Cicatricial
  - fibrosis
  - stenosis
### H. influenzae

<table>
<thead>
<tr>
<th>Meningitis</th>
<th>Unencapsulated</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF 50%-95% culture positive</td>
<td>Otitis media</td>
</tr>
<tr>
<td>Blood 50%-95% culture positive</td>
<td>Tympanocentesis</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>50%-70% culture positive</td>
</tr>
<tr>
<td>Eye 50%-75% culture positive</td>
<td>Sinusitis</td>
</tr>
<tr>
<td>Blood &lt; 10% culture positive</td>
<td>Sinus aspirate</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>50%-75% culture positive</td>
</tr>
<tr>
<td>Skin 75%-90% culture positive</td>
<td>Pneumonia, bronchitis</td>
</tr>
<tr>
<td>Blood 50%-75% culture positive</td>
<td>Sputum 25%-75% culture positive</td>
</tr>
<tr>
<td>Epiglottitis</td>
<td>Blood 10%-30% culture positive</td>
</tr>
<tr>
<td>Blood 90%-95% culture positive</td>
<td></td>
</tr>
<tr>
<td>Epiglottitis culture contraindicated</td>
<td></td>
</tr>
<tr>
<td>Arthritis</td>
<td></td>
</tr>
<tr>
<td>Synovial fluid</td>
<td></td>
</tr>
<tr>
<td>70%-90% culture positive</td>
<td></td>
</tr>
<tr>
<td>Blood 50%-80% culture positive</td>
<td></td>
</tr>
</tbody>
</table>
Legionella

- Community and Nosocomial pneumonia
- Contaminated water sources
B. pertussis

<table>
<thead>
<tr>
<th></th>
<th>Incubation</th>
<th>Catarrhal</th>
<th>Paroxysmal</th>
<th>Convalescent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration</strong></td>
<td>7-10 days</td>
<td>1-2 weeks</td>
<td>2-4 weeks</td>
<td>3-4 weeks (or longer)</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>None</td>
<td>Rhinorrhea, malaise, fever, sneezing, anorexia</td>
<td>Repetitive cough with whoops, vomiting, leukocytosis</td>
<td>Diminished paroxysmal cough, development of secondary complications (pneumonia, seizures, encephalopathy)</td>
</tr>
<tr>
<td><strong>Bacterial culture</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Zoonotic Gram Negative Rods

- **Yersinia**
  - plague

- **Franciscella**
  - tularemia

- **Pasturella**
  - dog/cat bites
Pseudomonas

**Box 10-1  Pseudomonas Aeruginosa Infections**

- Bacteremia
- Endocarditis
- Pulmonary infections
  - Tracheobronchitis
  - Necrotizing bronchopneumonia
- Ear infections
  - Chronic external otitis
  - Malignant external otitis
  - Chronic otitis media
- Burn wound infections
- Urinary tract infections
- Gastroenteritis
- Eye infections
- Musculoskeletal infections
Anaerobic Bacteria

- Bacteroides
- Fusobacterium
- Peptostreptococcus
- Actinomyces
- Prevotella
Spirochetes

- Treponema
- Borrelia
### Manifestations of Syphilis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Signs and symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubation period</td>
<td>Usually 3 wk, asymptomatic</td>
</tr>
<tr>
<td>Primary stage</td>
<td>Primary chancre at the site of initial inoculation, reactive lymphadenopathy</td>
</tr>
<tr>
<td>Secondary stage</td>
<td>2–12 weeks after contact, white macules or papules on the oral mucosa, loss of eyelashes, localized alopecia, acute rhinitis, laryngitis, otitis media, pharyngitis, eruptions of the external ear, regional adenopathy, constitutional symptoms, meningitis</td>
</tr>
<tr>
<td>Latent stage</td>
<td>Relatively asymptomatic, although mucocutaneous relapses may occur; one third go into complete remission, one third remain latent, and one third progress to the tertiary stage</td>
</tr>
<tr>
<td>Tertiary stage</td>
<td>Saddle deformity of the nose with nasoseptal or hard palate ulceration; granulomatous infiltration of the maxilla, mandible, tongue, larynx; osteomyelitis of the temporal bone; cranial nerve injury with vocal cord paralysis, dysphagia; sensorineural hearing loss, vertigo</td>
</tr>
<tr>
<td>Congenital syphilis</td>
<td>Frontal bossing, short maxilla, saddle nose, protruding mandible, high palatal arch, Hutchinson's incisors, mulberry molars, mental retardation, rhagades (radiating scars about the mouth), sensorineural hearing loss (same as with tertiary syphilis—sudden, bilateral, fluctuating, poor word discrimination), Tullio's and Hennebert's signs</td>
</tr>
</tbody>
</table>
Lyme Disease

- Cutaneous lesions
  - Erythema chronicum migrans

- Nonspecific symptoms
  - Malaise, fatigue, headache, fevers, chills, myalgias, arthralgias, lymphadenopathy

- Late manifestations
  - Neurologic
  - Cardiac
M. tuberculosis

- Pulmonary disease (82%)
- Extrapulmonary disease (18%)
ENT Manifestations of TB

- **Scrofula**
  - Matted lymphadenopathy: posterior triangle

- **Laryngeal TB**
  - Edema, ulcers, polypoid changes: arytenoids

- **Oral TB**
  - Painless ulcers: tongue

- **Aural TB**
  - Thickened TM → hyperemia → multiple perforations
  - Thin, watery otorrhea → thick, cheesy discharge
M. leprae
Antibiotic Therapy

- Identify infecting organism
- Evaluate drug sensitivity
- Target site of infection
- Drug safety/side effect profile
- Patient factors
- Cost
Classification of Antibiotics

- Bacteriostatic
- Bactericidal

Graph showing the effect of antibiotics on bacterial growth:
- Control (no drug)
- Bacteriostatic agent added (such as chloramphenicol)
- Bactericidal agent added (such as penicillin)
Classification of Antibiotics

- Chemical Structure
- Spectrum of Activity
- Mechanism of Action
Mechanism of Action

- Inhibitors of metabolism (Chapter 30)
  - Sulfonamides
  - Trimethoprim
  - β-Lactams
  - Vancomycin

- Inhibitors of cell wall synthesis (Chapter 29)

- Inhibitors of protein synthesis (Chapter 31)
  - Tetracyclines
  - Aminoglycosides
  - Macrolides
  - Clindamycin
  - Chloramphenicol

- Inhibitors of nucleic acid function or synthesis (Chapter 32)
  - Fluoroquinolones
  - Rifampin
Inhibitors of Cell Wall Synthesis

**β-LACTAM ANTIBIOTICS**
- Penicillin G
- Penicillin V
- Methicillin
- Nafcillin
- Oxacillin
- Cloxacillin
- Dicloxacillin
- Ampicillin
- Amoxicillin
- Carbenicillin
- Ticarcillin
- Piperacillin
- Mezlocillin
- Azlocillin

**OTHER ANTIBIOTICS**
- Vancomycin
- Bacitracin

**β-LACTAMASE INHIBITORS**
- Clavulanic acid
- Sulbactam
- Tazobactam

**PENICILLINS**

**CEPHALOSPORINS**

**CARBAPENEMS**
- Imipenem/Cilastatin

**MONOBACTAMS**
- Aztreonam

**1st GENERATION**
- Cefazolin
- Cefadroxil
- Cephalexin
- Cephalothin
- Cephapirin
- Cephradine

**2nd GENERATION**
- Cefaclor
- Cefamandole
- Cefonicid
- Cefmetazole
- Cefotetan
- Cefoxitin
- Cefuroxime

**3rd GENERATION**
- Cefixime
- Cefoperazone
- Cefotaxime
- Ceftazidime
- Ceftizoxime
- Ceftriaxone
- Moxalactam
Beta Lactam Antibiotics

- Penicillins
- Cephalosporins
- Carbapenems
- Monobactams

Nature of the R group determines the drug’s stability to enzymatic or acidic hydrolysis, and affects its antibacterial spectrum.

Site of cleavage by bacterial penicillinase or by acid.
Penicillins

- Derived from the fungus Penicillium
- Therapeutic concentration in most tissues
- Poor CSF penetration
- Renal excretion
- Side effects: hypersensitivity, nephritis, neurotoxicity, platelet dysfunction
Natural Penicillins

- Penicillin G, Penicillin V

**PNEUMOCOCCAL PNEUMONIA**
- Streptococcus pneumoniae is a major cause of bacterial pneumonia in all age groups.
- Infection often occurs in an institutional setting in individuals ill from other causes.

**LISTERIOSIS**
- Fever, CNS disturbances are common.
- Majority of infections occur in the newborn.
- Listeria can also cause endocarditis, urethritis, conjunctivitis and abortions
- Listeria monocytogenes is sensitive to penicillin, ampicillin and tetracyclines.

**SYPHILIS**
- A contagious venereal disease
- A progressive disease affecting many tissues

**Bacteria**
- Gram (+) cocci
- Gram (+) bacilli
- Gram (-) bacilli
- Neisseria gonorrhoeae Neisseria meningitidis
- Treponema pertenue (Yaws)
- Treponema pallidum (Syphilis)
- Spirochetes
- Leptotrichia buccalis
- Other Gram (-) bacilli (most are resistant)
- Staphylococcus aureus
- Streptococcus pneumoniae
- Streptococcus pyogenes
- Streptococcus viridans group
- Bacillus anthracis
- Clostridium perfringens
- Corynebacterium diphtheriae
- Listeria monocytogenes

**GONORRHEA**
- Silver nitrate drops in eyes prevents gonococcal ophthalmia in newborns
- Penicillinase-producing strains are treated with spectinomycin, ceftriaxone or cotrimoxazole.
Antistaphylococcal Penicillins

- Methicillin
- Nafcillin
- Oxacillin
- Dicloxacillin
Aminopenicillins

- Amoxicillin +/- clavulanate
- Ampicillin +/- sulbactam
Antipseudomonal Penicillins

- Carbenicillin
- Ticarcillin +/- clavulanate
- Piperacillin +/- tazobactam

B. Antimicrobial spectrum of carbenicillin, ticarcillin, and piperacillin

- Other Gram (-) bacilli
- Gram (-) enteric rods
- Haemophilus influenzae
- Pseudomonas aeruginosa
- Enterobacter species
- Escherichia coli
- Proteus mirabilis
- Proteus (indole positive)
Cephalosporins

- Structurally similar to penicillins
- Therapeutic concentration in many tissues, 3rd and 4th generation into CSF
- Renal Excretion
- Side Effects
  - allergy
  - disulfiram-like effect
  - anti-Vitamin K
Generations of Cephalosporins

Therapeutic disadvantages of selected cephalosporins

First Generation
- **Cefazolin**
- **Cefadroxil**
- **Cephalexin**
- **Cephalothin**
- **Cephradine**

- Associated with serum sickness.

This first-generation parenteral cephalosporin has a longer duration of action and a similar spectrum of action compared to other first-generation drugs. Good penetration into bone.

Prototype of first-generation oral cephalosporins. Oral administration twice daily is effective against pharyngitis.

Second Generation
- **Cefaclor**
- **Cefamandole**
- **Cefonicid**
- **Cefmetazole**
- **Cefotetan**
- **Cefoxitin**
- **Ceftroxime**
- **Cefuroxime axetil**

These cephalosporins contain the methylthiotetrazole side chain and can cause hypoprothrombinemia and bleeding problems as well as a disulfiram effect, that is, an intolerance to ingested ethanol.

Shows good activity against anaerobes, particularly *Bacteroides fragilis*. Useful in patients with intraabdominal sepsis, and against gynecologic sepsis including pelvic inflammatory disease.

This prototype second-generation parenteral cephalosporin has a longer half-life than similar agents. It crosses the blood-brain barrier and can be used for community-acquired bronchitis or pneumonia in the elderly and for patients who are immunocompromised.

Oral administration twice daily. Well absorbed. Active against ß-lactamase-producing organisms.

Third Generation
- **Cefixime**
- **Cefoperazone**
- **Cefotaxime**
- **Ceftazidime**
- **Ceftriaxone**

Oral dosing once daily.

Good penetration into CSF.

Active against *Pseudomonas aeruginosa*.

Longest half-life of any cephalosporin (6-8 hrs) permits once a day dosing. High levels of drug can be achieved in blood and CSF. Effective against genital, anal and pharyngeal penicillin-resistant *N. gonorrhoeae*. Drug excreted in bile and may be used in patients with renal insufficiency. Good penetration into bone.
Monobactams

- **Aztreonam**
  - Single beta lactam ring
  - Narrow spectrum: gram-negative aerobes
    - Enterobacteriacea
    - Pseudomonas
  - Given IV/IM
  - Renal excretion
  - Little cross-reactivity with other beta lactams
  - Side effects: phlebitis, rash, elevated LFT's
Carbapenems

- **Meropenem/Imipenem**
  - Broad spectrum
  - Active against MRSA
  - Given IV
  - Penetrates CSF
  - Renal metabolism and excretion
  - Addition of cilastin
  - Side effects: GI upset, eosinophilia, neutropenia, lowering of seizure threshold
Vancomycin

- Tricyclic glycopeptide
- Inhibits synthesis of phospholipids and cross-linking of peptidoglycans
- Activity against gram-positive organisms
- Useful for beta lactam resistant infections
- Widely distributed, penetrates CSF
- Renal elimination, follows creatinine cl.
- Side effects: phlebitis, red man syndrome, ototoxicity, nephrotoxicity
Protein Synthesis Inhibitors

- Human Ribosome
  - 80S
    - 40S
    - 60S

- Bacterial Ribosome
  - 70S
    - 30S
    - 50S
Tetracyclines

- Isolated from Streptomyces aureofaciens
- Reversibly bind 30S ribosomal subunit
- Penetrate sinus mucosa, saliva and tears
- Metabolized in liver --> excreted in bile --> reabsorbed --> eliminated in urine
- Side effects: GI upset, hepatotoxicity, photosensitivity, bony deposition
- Contraindicated in pregnant or breast feeding women, children under 8 y/o
**Tetracyclines**

**CHLAMYDIAL INFECTIONS**
- Lymphogranuloma venerum: an infectious venereal disease marked progressively by lymph node hypertrophy, lymphatic obstruction, and elephantiasis of external genitalia.
- Psittacosis: usually takes the form of pneumonia; other clinical forms include hepatitis, myocarditis, and coma.

**ROCKY MOUNTAIN SPOTTED FEVER**
- A rickettsial disease characterized by fever, chills, aches in bones and joints.
- Response to tetracyclines is prompt if drug is started early in disease process.

**MYCOPLASMA PNEUMONIA**
- Common cause of pneumonia in young adults and in people who live in close confines, as in military camps.
- Treatment leads to shorter duration of fever, cough, and malaise.
- Treatment with *erythromycin* also effective.

**LYME DISEASE**
- A spirochetal infection caused by *Borrelia burgdorferi*.
- Infection results in skin lesions, headache, fever, followed by meningoencephalitis and eventually arthritis.
- Disease transmitted by bite of infected ticks.

**CHOLERA**
- Cholera is caused by *Vibrio cholerae* ingested as part of fecally contaminated food or water.
- The organism multiplies in the gastrointestinal tract where it secretes an enterotoxin producing diarrhea.
- Treatment includes (1) *doxycycline*, which reduces the number of intestinal vibrios, and (2) fluid replacement.
Aminoglycosides

- Derived from Streptomyces and Micromonospora
- Irreversible binding to 30S subunit
- Actively transported into bacterial cells
- Variable tissue penetration, unreliable CSF levels
- Concentrate within perilymph
- Renal elimination
- Nephrotoxicity, ototoxicity, neurotoxicity
Aminoglycosides

INFECTIONS DUE TO PSEUDOMONAS AERUGINOSA

- *Pseudomonas aeruginosa* rarely attacks healthy individuals but can cause infections under special circumstances:
  1. When introduced into the lungs of debilitated patients through contaminated mechanical ventilators.
  2. When infection occurs in immunocompromised patients, *Pseudomonas* can cause septic arthritis.
  3. When burn victims are receiving antibiotic therapy *Pseudomonas* can cause infection because of its resistance to many antimicrobial agents.

- Treatment includes *tobramycin*, *gentamicin*, or *amikacin* alone or in combination with an antipseudomonal penicillin, such as *piperacillin* or *ticarcillin*.

CHRONIC URINARY TRACT INFECTIONS

- *Escherichia coli* is the most common cause of urinary tract infections.
- *Morganella* or *Enterobacter* are less common pathogens of the urinary tract.
- *Aminoglycosides* are NOT indicated for the treatment of uncomplicated urinary tract infections; these infections respond to less toxic antimicrobial agents, such as *trimethoprim-sulfamethoxazole*.

TULAREMIA

- *Streptomycin* is effective in treating this rare lymphoid disease.
- Tularemia is commonly acquired during rabbit-hunting season by hunters skinning infected animals.
- Pneumonic tularemia results from infection by the respiratory route, or by bacteremic seeding of lung.

PNEUMONIA

- An aminoglycoside plus *ampicillin* is sometimes used for pneumonia caused by sensitive strains of *Escherichia coli*.
- An aminoglycoside plus a cephalosporin, *mezlocillin*, or *piperacillin*, is effective against sensitive strains of *Klebsiella*. 
Macrolides

- Macrocyclic lactone structure
- Irreversible binding to 50S subunit
- Therapeutic concentrations in oropharyngeal and respiratory secretions
- No CSF penetration
- Metabolized in liver, excreted in feces and urine
- Side effects: GI upset, ototoxicity, hepatotoxicity
Erythromycin

**CHLAMYDIAL INFECTIONS**
- *Erythromycin* is an alternative to tetracycline in treating uncomplicated urethral, endocervical, rectal, or epididymal infections due to Chlamydia.
- *Erythromycin* is the drug of choice for urogenital infections due to Chlamydia occurring during pregnancy.

**UREAPLASMA**
- Causes urethritis in males; genital tract infections in females.
- Major cause of fetal death, miscarriage and low birth weight.

**MYCOPLASMAL PNEUMONIA**
- Called “atypical” pneumonia because causative mycoplasma escape isolation by standard bacteriological techniques.
- Tetracyclines are also effective.

**CORYNEBACTERIUM DIPHTHERIAE**
- *Erythromycin* or penicillin used to eliminate the carrier state.

**LEGIONNAIRES' DISEASE** (LEGIONELLOSIS)
- Legionellosis represents 0.5-2.0% of all pneumonia in the United States.
- Undiagnosed or asymptomatic infections are common.

**SYphilis**
- *Erythromycin* is used to treat syphilis in patients who are allergic to penicillin G.
Alternate Macrolides

**Clarithromycin**

Comparing *erythromycin*... with *clarithromycin*

Key:
- Increased activity compared to *erythromycin*

**Azithromycin**

Comparing *erythromycin*... with *azithromycin*

Key:
- Decreased activity compared to *erythromycin*
Chloramphenicol

- Isolated from Streptomyces
- Reversible binding to 50S subunit
- Broad spectrum of activity
- Indicated for severe anaerobic infections or unresponsive life-threatening infections
- Widely distributed, enters CSF
- Metabolized in liver (inhibits P-450), eliminated in urine
- Toxicities: reversible anemia, hemolytic anemia, aplastic anemia, gray baby syndrome
Clindamycin

- Semisynthetic derivative of Lincomycin
- Irreversible binding to 50S subunit
- Covers anaerobes and gram + aerobes
- Widely useful for head and neck infections
- Penetrates saliva, sputum, pleural fluid, and bone, but not CSF
- Metabolized in liver --> reabsorbed --> eliminated in urine
- Side effects: rash, neutropenia/thrombocytopenia, pseudomembranous colitis
Inhibitors of Metabolism

- Sulfonamides
- Trimethoprim

Interfere with the production of folic acid coenzymes that are required for purine and pyrimidine synthesis
Sulfonamides

- Derived from prontosil
- Competitive antagonist of PABA
- Wide distribution, penetrate CSF, cross placenta
- Metabolized in liver, eliminated in urine
- Side effects: rash, angioedema, Stevens-Johnson syndrome, kernicterus
- Avoid in pregnancy and infants
Sulfonamides

**Topical Use**
- Sulfacetamide, silver sulfadiazine, or mafenide are used in prevention of colonization of burns and wounds.

**Nocardiosis**
- Nocardia is an actinomycete that causes pneumonia and brain abscess, particularly in immunosuppressed or debilitated patients.
  - Treatment: sulfisoxazole or sulfadiazine or a tetracycline.
  - Advanced cases may require coadministration of ampicillin or erythromycin.

**Trachoma**
- Causative agent, Chlamydia trachoma grows in conjunctival cells causing chronic inflammation, scarring, and eventual blindness.
- Trachoma is the most common cause of preventable blindness worldwide.
- Treatment: Topical and systemic sulfacetamide or a tetracycline.

**Urinary Tract Infections**
- Previously untreated infections respond to sulfonamides, such as sulfisoxazole.
- Escherichia coli is the most common cause of cystitis.
- See Figure 29.7 for treatment of chronic UTI with co-trimoxazole.
Trimethoprim

- Inhibits dihydrofolate reductase
- 1000x higher affinity for bacterial enzyme than human enzyme
- Similar spectrum and pharmacokinetic profile as sulfas
- Side effects: folate deficiency anemia, leukopenia, granulocytopenia
Co-Trimoxazole (TMP/SMX)

✿ Combination gives synergistic antibacterial action
Co-Trimoxazole (TMP/SMX)

**PNEUMOCYSTIS CARINII PNEUMONIA (PCP)**
- *Pneumocystis carinii* is the fungus responsible for a mild respiratory infection common in infants.
- PCP is the most common opportunistic infection complicating AIDS.
- Mortality in immunocompromised patients, even with *co-trimoxazole* treatment, is over 50%.

**RESPIRATORY INFECTIONS**
- *Co-trimoxazole* is effective against *Haemophilus influenzae* and *Streptococcus pneumoniae*.
- *Co-trimoxazole* is an alternative treatment for *Legionella pneumophila*.

**GENITAL INFECTIONS**
- *Co-trimoxazole* is useful in the treatment of acute gonococcal urethritis in both men and women.
- Drug is effective as oral therapy of oropharyngeal gonorrhea caused by penicillinase-producing organisms.

**PROSTATE AND URINARY TRACT INFECTIONS**
- *Trimethoprim* concentrates in prostate and vaginal fluids making it effective in treating infections at these sites.
- Chronic and recurrent urinary tract infections respond to *co-trimoxazole*.

**GASTROINTESTINAL INFECTIONS**
- *Co-trimoxazole* is useful in the treatment of shigellosis and non-typhoid salmonellosis.
- Drug is also effective in the management of carriers of *Salmonella typhi*.
Inhibitors of Nucleic Acid Function/Synthesis

ลอย Fluoroquinolones

- Bind bacteria DNA gyrase (topoisomerase II)
- Concentrate in sinus and middle ear mucosa, penetrate cartilage and bone
- Partially metabolized in liver --> GI or renal excretion
- Side effects: nausea, dizziness, phototoxicity, nephrotoxicity
- Avoid in pregnant or nursing women
- ? Use in children -- possible effect on articular cartilage
**Fluoroquinolones**

**RESISTANT RESPIRATORY INFECTIONS**
- *Ciprofloxacin* is often effective in treating infections unresponsive to β-lactam antibiotics, such as ampicillin.
- *Ciprofloxacin* is not the drug of first choice for pneumonia or sinusitis since the fluoroquinolones have only weak activity against *Streptococcus pneumoniae*, a common causative agent.

**GONORRHEA**
- *Ciprofloxacin* is equally active in infections due to penicillinase-producing and non-penicillinase-producing strains.

**URINARY TRACT INFECTIONS**
- *Ciprofloxacin* and *norfloxacin* are effective in treating, uncomplicated and complicated urinary tract infections.
- Clinical and bacteriologic response is similar to that of *sulfamethoxazole-trimethoprim*.

**GASTROINTESTINAL TRACT INFECTIONS**
- *Ciprofloxacin* is highly efficacious in treating acute diarrheal illnesses due to enteric pathogens.
- Clinical resolution occurs in over 90% of patients.
Antimycobacterial Therapy

- Must address two distinct populations of tubercle bacilli
- First-line treatment: regimens of 3-4 drugs for 6 months to 2 years
- Second-line therapy: reserved for multidrug resistant organisms or unresponsive infection
First-Line Agents

- **Isoniazide**
  - Most potent drug
  - Inhibits formation of outer mycolic acid
  - Widely distributes and penetrates CSF
  - Metabolized in liver, excreted in urine, saliva, and sputum
  - Side effects: hypersensitivity, neuropathy, hepatotoxicity

- Rifampin
- Pyrazinamide
- Ethambutol
- Streptomycin
First-Line Agents

- Isoniazide
- Rifampin
- Pyrazinamide
- Ethambutol
- Streptomycin

**Rifampin**
- from Streptomyces
- antibacterial and anti-tubercule
- interferes with RNA transcription
- wide distribution, penetrates CSF
- metabolized in liver
- gives orange-red color to stool, urine and tears
- side effects: rash, GI upset, hepatotoxicity
First-Line Agents

- Isoniazide
- Rifampin
- Pyrazinamide
- Ethambutol
- Streptomycin

- Pyrazinamide
  - hydrolyzed to pyrazinoic acid
  - unclear mechanism
  - widely distributed, including CSF
  - side effects: GI upset, hepatotoxicity, hyperuricemia
First-Line Agents

- Isoniazide
- Rifampin
- Pyrazinamide
- Ethambutol
- Streptomycin

- Ethambutol
  - inhibits cell wall synthesis and maintenance
  - widely distributed, penetrates CSF
  - partially metabolized, excreted in urine
  - potential for optic neuritis
First-Line Agents

- Isoniazide
- Rifampin
- Pyrazinamide
- Ethambutol
- Streptomycin

**Streptomycin**

- aminoglycoside
- binds 30S subunit
- penetrates synovial, pleural, pericardial, and ascitic fluids but not CSF
- renal excretion
- side effects: hypersensitivity, paraesthesias, auditory or vestibular dysfunction, nephrotoxicity
Antimycobacterials for Leprosy

**Dapsone**
- structurally related to sulfonamides
- PABA antagonist
- activity against M. leprae
- also effective for pneumocystis and brown recluse spider bites
- wide distribution
- acetylated in liver, eliminated in urine
- side effects: erythema nodosum leprosum, peripheral neuropathy, methemoglobinemia

**Clofazimine**
- synthetic phenazine dye
- binds DNA and inhibits replication and transcription
- activity against M. leprae and MAI
- wide distribution, does not penetrate CSF
- partially metabolized, excreted in bile
- side effects: GI upset, red/purple discoloration of skin and body fluids
Antibiotic Prophylaxis

- Post-op wound infection is the second most common nosocomial infection.
- Cost of this complication approaches $5 billion annually.
- Prolongs hospital length of stay by 15 days.
- Costs nearly $22,000 more for one post-op wound infection that to use prophylactic clindamycin on 100 patients.
Classification of Wounds

Class I--Clean Wounds

- Strict sterile technique
- Surgery does not involve penetration of aerodigestive tract
- 1-5% infection rate
- Prophylactic antibiotics not cost-effective and not indicated
Classification of Wounds

Class II--Clean-contaminated Wounds

- The surgical procedure involves entrance into the aerodigestive or genitourinary tracts
- Contact with bacterial contaminated secretions
- 8-11% inherent infection rate
- Increased length or complexity of surgery may be associated with increased rates of infection--reports vary from 28-87%
Classification of Wounds

Class III -- Contaminated Wounds
- Traumatic wounds, surgical cases involving spillage from the GI tract
- Inherent infection rate 15-17%
Prophylactic Antibiotics

- Cover bacterial flora involved in the surgical field
- Administer within 2 hours before or 3 hours after surgery has begun
- Maintain therapeutic blood level during lengthy procedures
- Continue prophylaxis for the 24 hour period surrounding surgery
Effective Prophylactic Regimens

- Cefazolin +/- metronidazole
- Cefoperozone
- Clindamycin +/- gentamycin or amikacin
- Amoxicillin/clavulanate
- Ampicillin/sulbactam
- Ticarcillin/clavulanate
Topical Antibiotic Prophylaxis

- Clindamycin or Peridex oral rinses
- Significantly reduce bacterial counts in the oral cavity
- Both immediate effect and prolonged effect for approximately 4 hours
- Reduce post-op wound infections alone and in combination with parenteral antibiotic therapy
Indications for Antibiotic Prophylaxis in ENT Surgery

Prophylaxis Indicated

- Any Class II Head and Neck Procedure
- Tonsillectomy
- Neurotologic/Skull Base Procedures
- Open Mandible Fracture Repair

Prophylaxis NOT Indicated

- Basic Sinonasal Procedures
- Otologic Procedures
- Midface Fracture Repair
- Closed Mandible Fracture Repair