CHAPTER 37
Antibiotics

NDEG 26 A – Pharmacology I
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Antibiotics: Definition

• Medications used to treat bacterial infections
• Ideally, before beginning antibiotic therapy, the suspected areas of infection should be cultured to identify the causative organism and potential antibiotic susceptibilities

Antibiotics: Classes

• Sulfonamides
• Penicillins
• Cephalosporins
• Tetracyclines
• Macrolides
• Aminoglycosides
• Quinolones

Gram-negative bacterial infections are harder to treat because drug molecules have a harder time penetrating the more complex gram-negative cell wall.

Signs and symptoms of infection

• Fever
• Chills
• Sweat
• Redness
• Pain and swelling
• Fatigue
• Weight loss
• ↑ WBC (normal = 4300-10,800 or 5-10K)
• Pus
Antibiotic Therapy

• Empiric therapy: treatment of an infection before specific culture information has been reported or obtained
• Prophylactic therapy: treatment with antibiotics to prevent an infection, as in intraabdominal surgery

Antibiotic Therapy (cont'd)

Four common mechanisms of action
• Interference with cell wall synthesis
• Interference with protein synthesis
• Interference with DNA replication
• Acting as a metabolite to disrupt critical metabolic reactions inside the bacterial cell

Actions of Antibiotics

• Bactericidal: kill bacteria
• Bacteriostatic: inhibit growth of susceptible bacteria, rather than killing them immediately; will eventually lead to bacterial death

Antibiotics: Sulfonamides

One of the first groups of antibiotics
• sulfadiazine
• sulfamethoxazole
• sulfinosazole

Sulfonamides: Mechanism of Action

• Bacteriostatic action
• Prevent synthesis of folic acid required for synthesis of purines and nucleic acid—FOLATE ANTAGONIST ANTIMETABOLITE
• Do not affect human cells or certain bacteria—they can use preformed folic acid
Sulfonamides: Distribution and Route

Drug crosses blood-brain barrier

IV

Topical

Unchanged drug and acetylated metabolites appear in the urine

Sulfonamides

Sulfonamides: Indications

Figure 20.3
Typical therapeutic applications of sulfonamides. UTI = urinary tract infection.

Sulfonamides: Combination Products

- trimethoprim/sulfamethoxazole (Bactrim, Septra)
  - Used to treat UTIs, PCP, otitis media, other conditions
- erythromycin/sulfisoxazole (Pedialzole)
  - Used to treat otitis media
- sulfisoxazole (Gantrisin)
  - Used to treat otitis media, UTIs, other conditions

Sulfonamides: Side Effects

<table>
<thead>
<tr>
<th>Body System</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>Hemolytic and aplastic anemia, thrombocytopenia</td>
</tr>
<tr>
<td>Integumentary</td>
<td>Photosensitivity, exfoliative dermatitis, Stevens-Johnson syndrome, epidermal necrolysis</td>
</tr>
</tbody>
</table>

Sulfonamides: Side Effects (cont’d)

<table>
<thead>
<tr>
<th>Body System</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI</td>
<td>Nausea, vomiting, diarrhea, pancreatitis</td>
</tr>
<tr>
<td>Other</td>
<td>Convulsions, crystalluria, toxic nephrosis, headache, peripheral neuritis, urticaria</td>
</tr>
</tbody>
</table>
Penicillins

- Bacteria produce enzymes capable of destroying penicillins
- These enzymes are known as beta-lactamases
- As a result, the medication is not effective

Penicillins (cont'd)

- Chemicals have been developed to inhibit these enzymes:
  - Clavulanic acid
  - Tazobactam
  - Sulbactam
- These chemicals bind with beta-lactamase and prevent the enzyme from breaking down the penicillin
Penicillins: Adverse Effects

- Allergic reactions occur in 0.7% to 8% of cases
  - Urticaria, pruritus, angioedema
- 10% of allergic reactions are life threatening
  - 10% of these are fatal

Penicillins: Side Effects

- Common side effects
  - Nausea, vomiting, diarrhea, abdominal pain
- Other side effects are less common

Cephalosporins

- Semisynthetic derivatives from a fungus
- Structurally and pharmacologically related to penicillins
- Bactericidal action
- Broad spectrum
- Divided into groups according to their antimicrobial activity

Cephalosporins: First Generation (cont’d)

- Used for surgical prophylaxis, URIs, otitis media
  - cefazoline (Ancef and Kefzol): IV or PO
  - cephalaxin (Keflex): PO
Cephalosporins

Second Generation

• Good gram-positive coverage
• Better gram-negative coverage than first generation

Cephalosporins: Second Generation (cont'd)

• Cefoxitin (Mefoxin): IV and IM
  – Used prophylactically for abdominal or colorectal surgeries
  – Also kills anaerobes
• Cefuroxime (Kefurox and Ceftin): PO
  – Surgical prophylaxis
  – Does not kill anaerobes

Cephalosporins: Third Generation (cont'd)

• Cefixime (Suprax)
  – Only oral third-generation agent
  – Best of available oral cephalosporins against gram-negative
  – Tablet and suspension
• Ceftriaxone (Rocephin)
  – IV and IM, long half-life, once-a-day dosing
  – Easily passes meninges and diffused into CSF to treat CNS infections

Cephalosporins: Fourth Generation

• Cefepime (Maxipime)
  – Newest cephalosporin agents
  – Broader spectrum of antibacterial activity than third generation, especially against gram-positive bacteria
• Cefdinir
• Cefditoren pivoxil
Cephalosporins: Side Effects
Similar to penicillins

Carbapenems
- Very broad-spectrum antibacterial action
- Reserved for complicated body cavity and connective tissue infections
- May cause drug-induced seizure activity
- Imipenem-cilastatin (Primaxin)
- Used for treatment of bone, joint, skin, and soft tissue infections; many other uses

Monobactams
- Aztreonam (Azactam)
  - Synthetic
  - Primarily active against aerobic gram-negative bacteria (E. coli, Klebsiella, Pseudomonas)
- Bactericidal
- Used for severe systemic infections and UTIs

Macrolides
- Erythromycin (E-mycin, E.E.S, others)
- Azithromycin (Zithromax)
- Clarithromycin (Biaxin)
- Macrolides: Mechanism of Action
  - Prevent protein synthesis within bacterial cells
  - Bacteria will eventually die
Macrolides: Indications

- Strep infections
  - *Streptococcus pyogenes* (group A beta-hemolytic streptococci)
- Mild to moderate URI
  - *Haemophilus influenzae*
- Spirochetal infections
  - Syphilis and Lyme disease
- Gonorrhea, *Chlamydia, Mycoplasma*

Macrolides: Side Effects

GI effects, primarily with erythromycin
- Nausea, vomiting, diarrhea, hepatotoxicity, flatulence, jaundice, anorexia
- Newer agents, azithromycin and clarithromycin: fewer side effects, longer duration of action, better efficacy, better tissue penetration

Tetracyclines

- Broad-spectrum
- Obtained from cultures of *Streptomyces*
- Bacteriostatic—inhibit bacterial growth
- Protein synthesis inhibitor
- Stop many essential functions of the bacteria

Tetracyclines (cont'd)

- Bind to Ca²⁺ and Mg²⁺ and Al³⁺ ions to form insoluble complexes
- Thus, dairy products, antacids, and iron salts reduce absorption of tetracyclines

Tetracyclines

- demeclocycline (Declomycin)
- oxytetracycline
- tetracycline
- doxycycline (Doryx, Vibramycin)
- minocycline

Tetracyclines: Indications

- Wide spectrum
  - Gram-negative, gram-positive, protozoa, *Mycoplasma, Rickettsia, Chlamydia*, syphilis, Lyme disease
- Demeclocycline is also used to treat SIADH, and pleural and pericardial effusions
Tetracyclines: Side Effects

Strong affinity for calcium
• Discoloration of permanent teeth and tooth enamel in fetuses and children
• May retard fetal skeletal development if taken during pregnancy

(continuation)

Alteration in intestinal flora may result in:
• Superinfection (overgrowth of nonsusceptible organisms such as Candida)
• Diarrhea
• Pseudomembranous colitis

May also cause:
• Vaginal moniliasis
• Gastric upset
• Enterocolitis
• Maculopapular rash

Aminoglycosides

• gentamicin (Garamycin)
• kanamycin
• neomycin
• streptomycin
• tobramycin
• amikacin (Amikin)
• netilmicin
Aminoglycosides

- Natural and semisynthetic
- Produced from *Streptomyces*
- Poor oral absorption; no PO forms
- Very potent antibiotics with serious toxicities
- Bactericidal; prevents protein synthesis
- Kill mostly gram-negative; some gram-positive also

Aminoglycosides: Indications

- Used to kill gram-negative bacteria such as *Pseudomonas* spp., *E. coli*, *Proteus* spp., *Klebsiella* spp., *Serratia* spp.
- Often used in combination with other antibiotics for synergistic effect

Aminoglycosides: Indications (cont'd)

- All aminoglycosides are poorly absorbed through the GI tract, and given parenterally
- Exception: neomycin
  - Given orally to decontaminate the GI tract before surgical procedures
  - Also used as an enema for this purpose

Aminoglycosides: Agents

- Three most common (systemic): gentamicin, tobramycin, amikacin
- Cause serious toxicities
  - Nephrotoxicity (renal failure)
  - Ototoxicity (auditory impairment and vestibular [eighth cranial nerve])
- Must monitor drug levels to prevent toxicities

Aminoglycosides: Side Effects

- Ototoxicity and nephrotoxicity are the most significant
  - Headache
  - Paresthesia
  - Neuromuscular blockade
  - Dizziness
  - Vertigo
  - Skin rash
  - Fever
  - Superinfections
Quinolones

- ciprofloxacin (Cipro)
- lomefloxacin (Maxaquin)
- norfloxacin (Noroxin)
- ofloxacin (Floxin)
- levofloxacin (Levaquin)
- gatifloxacin (Tequin)

Quinolones

- Excellent oral absorption
- Absorption reduced by antacids
- First oral antibiotics effective against gram-negative bacteria

Quinolones: Mechanism of Action

- Bactericidal
- Effective against gram-negative organisms and some gram-positive organisms
- Alter DNA of bacteria, causing death
- Do not affect human DNA

Quinolones: Indications

- Lower respiratory tract infections
- Bone and joint infections
- Infectious diarrhea
- Urinary tract infections
- Skin infections
- Sexually transmitted diseases
- Anthrax

Quinolones: Side Effects

<table>
<thead>
<tr>
<th>Body System</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>Headache, dizziness, fatigue, depression, restlessness</td>
</tr>
<tr>
<td>GI</td>
<td>Nausea, vomiting, diarrhea, constipation, thrush, increased liver function studies</td>
</tr>
</tbody>
</table>

Quinolones: Side Effects (cont'd)

<table>
<thead>
<tr>
<th>Body System</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integumentary</td>
<td>Rash, pruritus, urticaria, flushing, photosensitivity (with lomefloxacin)</td>
</tr>
<tr>
<td>Other</td>
<td>Fever, chills, blurred vision, tinnitus</td>
</tr>
</tbody>
</table>
Other Antibiotics

- clindamycin (Cleocin)
- dapsone
- linezolid (Zyvox)
- metronidazole (Flagyl)
- nitrofurantoin (Macrodantin)
- quinupristin and dalfopristin (Synercid)

Other Antibiotics (cont'd)

- vancomycin
  - Natural, bactericidal antibiotic
  - Destroys cell wall
  - Treatment of choice for MRSA, and other gram-positive infections
  - Must monitor blood levels to ensure therapeutic levels and prevent toxicity
  - May cause ototoxicity and nephrotoxicity

Other Antibiotics

- vancomycin (cont'd)
  - Should be infused over 60 minutes
  - Monitor IV site closely
  - Redman’s syndrome may occur
    - Decreased BP, flushing of neck and face
    - Antihistamine may be ordered to reduce these effects
  - Ensure adequate hydration (2 L fluids/24 hr) if not contraindicated to prevent nephrotoxicity

Antibiotics: Nursing Implications

- Before beginning therapy, assess drug allergies; hepatic, liver, and cardiac function; and other lab studies
- Be sure to obtain thorough patient health history, including immune status
- Assess for conditions that may be contraindications to antibiotic use or that may indicate cautious use
- Assess for potential drug interactions

Nursing Implications

It is ESSENTIAL to obtain cultures from appropriate sites BEFORE beginning antibiotic therapy

Nursing Implications

- Patients should be instructed to take antibiotics exactly as prescribed and for the length of time prescribed; they should not stop taking the medication early when they feel better
- Assess for signs and symptoms of superinfection: fever, perineal itching, cough, lethargy, or any unusual discharge
Nursing Implications

For safety reasons, check the name of the medication carefully because there are many agents that sound alike or have similar spellings.

Nursing Implications

- Each class of antibiotics has specific side effects and drug interactions that must be carefully assessed and monitored.
- The most common side effects of antibiotics are nausea, vomiting, and diarrhea.
- All oral antibiotics are absorbed better if taken with at least 6 to 8 ounces of water.

Nursing Implications

Sulfonamides

- Should be taken with at least 2000 mL of fluid per day, unless contraindicated.
- Due to photosensitivity, avoid sunlight and tanning beds.
- These agents reduce the effectiveness of oral contraceptives.
- Oral forms should be taken with food or milk to reduce GI upset.

Nursing Implications

Penicillins

- Any patient taking a penicillin should be carefully monitored for an allergic reaction for at least 30 minutes after its administration.
- The effectiveness of oral penicillins is decreased when taken with caffeine, citrus fruit, cola beverages, fruit juices, or tomato juice.

Nursing Implications

Cephalosporins

- Orally administered forms should be given with food to decrease GI upset, even though this will delay absorption.
- Some of these agents may cause a disulfiram (Antabuse)-like reaction when taken with alcohol.

Nursing Implications

Macrolides

- These agents are highly protein-bound and will cause severe interactions with other protein-bound drugs.
- The absorption of oral erythromycin is enhanced when taken on an empty stomach, but because of the high incidence of GI upset, many agents are taken after a meal or snack.
Nursing Implications

Tetracyclines
- Milk products, iron preparations, antacids, and other dairy products should be avoided because of the chelation and drug-binding that occurs
- All medications should be taken with 6 to 8 ounces of fluid, preferably water
- Due to photosensitivity, avoid sunlight and tanning beds

Nursing Implications

Aminoglycosides
- Monitor peak and trough blood levels of these agents to prevent nephrotoxicity and ototoxicity
- Symptoms of ototoxicity include dizziness, tinnitus, and hearing loss
- Symptoms of nephrotoxicity include urinary casts, proteinuria, and increased BUN and serum creatinine levels

Nursing Implications

Quinolones
- Should be taken with at least 3 L of fluid per day, unless otherwise specified
- Intake of alkaline foods and drugs, such as antacids, dairy products, peanuts, and sodium bicarbonate should be limited

Nursing Implications

Monitor for therapeutic effects
- Improvement of signs and symptoms of infection
- Return to normal vital signs
- Negative culture and sensitivity tests
- Disappearance of fever, lethargy, drainage, and redness

Monitor for adverse reactions