LESSON ASSIGNMENT

LESSON 3 Antibiotics and Sulfonamides.

TEXT ASSIGNMENT Paragraphs 3-1 through 3-17.

LESSON OBJECTIVES After completing this lesson, you should be able to:

3-1. Given the trade name of an antibiotic or sulfonamide agent and a list of generic names, select the generic name that corresponds to the trade name.

3-2. Given an antibiotic or sulfonamide agent and a list of side effects/toxicities, select the side effects/toxicities associated with that agent.

3-3. Given a generation of cephalosporins and a list of spectrums of activity, select the spectrum of activity associated with that generation of cephalosporins.

3-4. Given a caution/warning associated with antibiotics or sulfonamides and a list of antibiotics or sulfonamide agents, select the agent associated with that caution/warning.

3-5. Given a specific organism and a list of classifications of penicillins, select the penicillin that would be effective in treating an infection caused by that organism.

SUGGESTION After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
3-1. INTRODUCTION

a. Infection is the invasion of the body by a pathogenic organism, the tissue’s reaction to the organism, or the tissue’s reaction to a toxin produced by the organism. An infection occurs when the organism exerts its effect upon the cells or when host resistance is reduced. Resistance can be reduced if the normal immune process is compromised or changes occur in the normal makeup of organisms (flora) which give a harmful organism the opportunity to thrive.

b. The human body has numerous built-in barriers against infections. Mechanical barriers include the skin and mucous membranes. Acids in the stomach form a chemical barrier that kills bacteria found there. A third natural barrier is the normal flora existing in the body. There are normally many different types of organisms growing on the skin and in body cavities all competing with each other for nutrients and inhibiting the overgrowth of the other organisms. When something happens to disturb this natural balance (as when an antibiotic kills a large number of bacteria), the remaining organisms can then flourish and cause a problem. A good example of this is the overgrowth of yeast, which can occur in the presence of long-term antibiotic therapy. The final barrier is the body’s inflammatory process, which is initiated when there is tissue damage. Mast cells rupture and release histamine, while other mediators cause vasodilatation and increased capillary permeability. This allows better access to the inflamed area by infection-fighting cells.

3-2. ANTI-INFECTIVE AGENTS

An anti-infective or antimicrobial agent is a drug that is used in the treatment or prevention of infections. These agents are also sometimes referred to as chemotherapeutic agents, although this term is also commonly applied to drugs used to treat cancer and really applies to any chemical (drug) used for medical therapy. Antibiotics and sulfonamides are two examples of these agents. The group of organisms against which an agent is effective is called its spectrum. Broad-spectrum antibiotics are effective against a wide range of microorganisms, usually specific microorganisms in both gram positive and positive organisms only.

a. Bactericidal drugs are those drugs that kill pathogens. This can be accomplished by one of three methods.

(1) The drug disrupts cell wall synthesis of bacteria:

(2) The drug acts directly on cell membranes to increase permeability, leading to leakage of the bacteria’s intracellular contents.
(3) The drug affects the bacterial cell’s DNA, causing production of abnormal protein.

b. A drug or antibiotic that inhibits the reproduction of pathogens is called bacteriostatic. These drugs slow down the growth of an infection and give the natural defenses of the body a better opportunity to combat the infection on their own. They work in two ways. They may affect the function of the bacterial ribosomes, resulting in a reversible disruption of protein synthesis or they may block steps in the bacteria’s metabolic pathways that are essential to the life of the microorganisms.

3-3. BACTERIAL RESISTANCE TO ANTI-INFECTIVE AGENTS

Bacteria are constantly becoming resistant to anti-infective agents. This is one of the major reasons that new antibiotics are continually appearing on the market. As bacteria encounter a drug, they may begin forming new enzymes that destroy the drug more rapidly, making the drug ineffective. Such an enzyme is beta lactamase that deactivates such agents as penicillins and cephalosporins. Phosphorylating and acetylating enzymes, which change the structure of a drug, may render gram-negative bacteria resistant to certain antibiotics. Additionally, when an agent is used over an extended period, changes in the bacterial cell wall may make it less permeable to the drug. If the drug blocks one of the steps in the bacteria’s metabolic pathway, the bacteria may develop an alternate pathway which by-passes the block, just as a road detour can bypass an area where a road is blocked. There are also numerous other ways in which microorganisms can develop resistance to antibiotics. Over the past several decades, early abuse of antibiotics when they were not really needed and inappropriate therapy have contributed to the development of resistance. The prudent use of antibiotic therapy and the appropriate selection of agent and type of therapy can minimize the development of resistant strains of bacteria.

3-4. ANTIBIOTIC SELECTION

When selecting an anti-infective agent, it would seem that the easiest thing to do would be to use the antibiotic with the broadest spectrum. In fact, the best approach in therapy is to select the agent that is the most effective against the specific bacteria causing the infection. In order to do this microscopic examination, staining, or culturing in the laboratory can identify the organism. When an organism is cultured, it is also possible to determine its sensitivity to different antibiotics, as well as the antibiotic concentration required for effectiveness, the minimum inhibitory concentration (MIC). In this way, the most effective agent can be selected. Because a culture and sensitivity (C&S) takes several days to perform, the physician will usually evaluate several factors, such as patient condition, specific symptoms, and other similar cases which have been seen in making an initial antibiotic selection. When the C&S is available, the initial antibiotic may be changed to one that is more effective, or if the patient’s response has been satisfactory, the original selection may be continued.
3-5. **ANTIBIOTIC COMBINATION**

There are many instances when combining two or more antibiotics is necessary or desirable in treating an infection or disease. This may be the case when there is a mixed infection, in which there may be several organisms, or when there is a severe or life threatening infection of unknown origin. By combining several agents, they can sometimes be made more effective than either agent alone (synergy), thus allowing lower doses and reducing complications of therapy. With certain organisms, the use of combination therapy is necessary to prevent rapid resistance to the drug that is used.

3-6. **CHEMOPROPHYLAXIS**

Chemoprophylaxis is the use of antibiotics to prevent infection in a healthy individual or to prevent infection by other organisms (called superinfection) in an individual already being treated for an infection. This generally involves giving low doses of a drug on an infrequent schedule. For example, individuals who have had rheumatic fever as children may take a sulfonamide once a day (instead of the four times daily needed for treating an infection) to prevent the development of bacterial endocarditis, a life-threatening infection involving the heart.

3-7. **SUPERINFECTIONS**

Superinfections may occur during the use of anti-infective therapy. This is simply the overgrowth of nonsusceptible normal body flora. There is always an alteration of body flora, particularly that found in the G.I., urinary, and respiratory tract during antibiotic therapy. Usually, the organism that tends to overgrow is *Pseudomonas*, *Candida*, fungi, or beta lactamase producing staphylococci. Superinfection is most noticeable when broad-spectrum antibiotics have been administered over a period of 14 days or more.

3-8. **PENICILLIN GROUPS**

a. **Natural Penicillin.**

(1) Natural penicillins are derived from certain species of molds and other fungi. They produce their effects by inhibiting biosynthesis of cell wall mucopolypeptides. All classes of penicillin are bactericidal.

(2) Oral absorption of natural penicillin is incomplete and variable, except for the newer penicillin VK products. Oral absorption becomes more predictable if the penicillin is taken on an empty stomach, 1 hour before or 2 hours after meals. IV and IM routes produce transient, high-blood levels of the antibiotic. Penicillin is widely distributed to all tissues, especially soft tissues. However, it is not distributed to ocular, skeletal and cardiac muscle and to cerebrospinal fluid unless inflammation is present.
(3) Natural penicillins are not affected by the metabolic process and are excreted unchanged. Excretion is very rapid via the kidneys but can be retarded by the concurrent administration of probenecid. Combining penicillin G with procaine or benzathine may also retard excretion. This increases the amount of penicillin available in the body, prolonging the action and increasing the effectiveness.

(4) Dosage of the natural penicillins depends on the dosage form and the type and severity of the infection being treated. Parenteral doses are measured in units, with one unit equal to 0.6 mg of standard penicillin, USP.

(5) The natural penicillins are narrow spectrum antibiotics primarily effective against gram-positive and a few gram-negative bacteria. They are the first drugs of choice in the treatment of infection caused by gram-positive cocci and bacilli, gram-negative bacilli bacteroides, cocci, and spirochetes.

(6) The most common adverse reaction to these drugs is hypersensitivity. The degradation product, penicillenic acid, probably causes this. The most common manifestation is skin rash, with the most lethal reaction being anaphylactic shock. This reaction may vary from a mild fever, rash, or leukopenia to severe arthralgia or arthritis. Oral preparations may cause nausea and vomiting, epigastric distress, diarrhea, and black hairy tongue. Superinfections may occur but are rare.

(7) The use of natural penicillin is contraindicated in patients with penicillin allergy, which should be used with caution in patients with histories of other allergies. When administered, especially parenterally, steps should be taken to ensure that agents are available to manage hyper-sensitive reactions and to monitor the patient at least 30 minutes after he receives a parenteral injection. The usual course of therapy is 7-10 days, and the patient should be instructed to complete it.

(8) The natural penicillins are found in the following preparations.

(a) K+ or Na+ penicillin G (Penicillin G®)

(b) Procaine penicillin G (Wycillin®, Crysticillin®)

(c) Benzathine penicillin G (Bicillin LA®, Permapen®)

(d) Penicillin V potassium (V-Cillin®, Pen-Vee K®)

b. **Penicillinase Resistant Penicillins.**

(1) Penicillinase is an enzyme produced by certain bacteria, which converts penicillin to an inactive product and thus increases resistance to the drug. Drugs in this group are structurally resistant to beta-lactamase activity, interfere with transpeptidases of the cell, and are bactericidal.
(2) These penicillins are all excreted via the kidneys, with the exception of nafcillin, which is excreted via the biliary canal.

(3) This class is to be used when staphylococcal beta-lactamase infection is known or suspected. The organism in this case is *S. aureus*. Seventy percent of all community acquired staphylococcal infections are beta lactamase producing.

(4) Adverse reactions, cautions, and warnings for these drugs are the same as those for the natural penicillins. Some hepatotoxicity can be produced as noted by transient high levels of SGOT, SGPT, and LDH, especially with the use of oxacillin.

(5) These penicillins are available in the following preparations.

(a) Methicillin Na (Staphcillin®)
(b) Nafcillin Na (Unipen®)
(c) Oxacillin Na (Prostaphlin®)
(d) Cloxacillin Na (Tegopen®)
(e) Dicloxacillin Na (Dynapen®)

(c. Broad-Spectrum Penicillins.

(1) Drugs belonging to this class are natural penicillins that have been chemically modified. They are very similar to the natural penicillins in their method of action, metabolism and excretion, reaction, cautions, and warnings.

(2) These drugs are employed against the same microbes as the natural penicillins, but also have an increased chemical activity against *Proteus mirabilis*, *Haemophilus influenzae*, and *E. coli*.

(3) Resistance to these drugs is acquired by the gram-negative organisms. Additionally, the drugs are inactivated by beta-lactamase.

(4) These drugs are used for soft tissue infections, such as the respiratory, urinary, and gastrointestinal tract as well as otitis media infections. Some authorities consider them the drug of first choice in the treatment of uncomplicated gonorrhea.

(5) Broad-spectrum penicillins are ampicillin, which is indicated for both parenteral and oral use, and amoxicillin, which is for oral use only.
d. **Broad Spectrum Antipseudomonal Penicillins.**

(1) These drugs are widely distributed in most body fluids as with all penicillins. Carbenicillin is distributed into the non-inflamed CSF, (cerebrospinal fluid) which is not typical of most antibiotics.

(2) The spectrum of activity of these drugs has been increased to combat *Pseudomonas aeruginosa* and some strains of *Proteus* that are resistant to ampicillin.

(3) Patients taking large doses of these antibiotics must have their serum sodium levels closely monitored as these drugs contain excessive amounts of sodium. Resistance to these drugs is acquired very quickly if they are used alone. High serum levels potentiate neurotoxicity manifested by lethargy, neuromuscular irritability, and seizures.

(4) In this group of penicillins, the following preparations are found.

(a) Carbenicillin disodium (Geopen®, Pyopen®)

(b) Carbenicillin indanyl sodium (Geocillin®)

(c) Ticarcillin disodium (Ticar®)

(d) Azlocillin Sodium (Azlin®)

e. **Broad-Spectrum Antipseudomonal Penicillin With Activity Against Klebsiella.**

(1) This penicillin has properties similar to those of the natural penicillins. They possess the same bactericidal activity as carbenicillin; in addition, they are effective against *Klebsiella*. Some agents are more active against *Pseudomonas* than carbenicillin.

(2) These drugs can be found as mezlocillin (Mezlin®) or piperacillin (Pipracil®) which is the most active of all the penicillins against *Pseudomonas*.

3-9. **THE CEPHALOSPORINS**

a. These drugs have their origin in *Cephalosporium acremonium*, a fungus. This fungus contains three antibiotics of which cephalosporin C has the most promise for chemical modification. These modifications have proliferated to include three generations currently on the market and a fourth being prepared for marketing.

b. The action of the cephalosporins is similar to the penicillins, and they are bactericidal.
c. These agents are widely distributed to most body tissues and fluids with maximum concentrations in the liver and kidneys. Penetration of the CSF is accomplished only by moxalactam that penetrates with or without inflamed meninges. Therapeutic blood levels are reached in bone with the use of cephadine, cefamandole, and cefazolin. Cefazolin levels are even higher in inflamed bone tissue.

d. Metabolism does occur with some agents, but their metabolic byproducts show less antibacterial activity. The kidneys through glomerular filtration and tubular secretion excrete all of the cephalosporins.

e. Because of the many products available, it is best to check the appropriate literature for dosage information. Depending on the agent’s characteristics and route of administration, the dose may vary from 500mg to 12g per day.

f. First generation agents are discussed below.

(1) The prototype of first generation cephalosporins is cephalothin (Keflin®). These agents are effective against gram-positive and a large number of gram negative organisms. Gram-positive bacteria include Group A strep pyogenes, beta-lactamase producing and non-producing staph aureus, clostridium perfringens, and many other streptococcal infections. Examples of gram-negative include N. gonorrhea, Salmonella, most Shigella and Proteus, 75 percent of E. coli, 50 percent of H. influenzae, and all strains of Klebsiella.

(2) Hypersensitivity is the most common adverse reaction of these agents, especially in patients with demonstrated immediate allergic reaction to penicillin. A rash may develop after several days of therapy and may or may not be accompanied by fever or eosinophilia. High doses of first generation agents will cause a positive Coombs’ reaction but hemolysis seldom occurs. High doses may also cause nephrotoxicity, especially in elderly patients. Administering these agents intravenously can cause thrombophlebitis, and IM injections are painful.

(3) With first generation cephalosporin therapy, all patients should be monitored for superinfection, and elderly patients should have their renal functions monitored.

(4) The first generation cephalosporin preparations are:

(a) Cephalothin (Keflin®)
(b) Cephalexin (Keflex®)
(c) Cefadroxil (Duricef®)
(d) Cephradine (Velosef®, Anspor®)
(e) Cephapirin (Cefadyl®)

(f) Cefazolin (Ancef®, Kefzol®)

g. Second generation agents are discussed below.

(1) These agents are similar to first generation agents; in addition, they are active against *Haemophilus influenzae*, including ampicillin resistant strains. They are also beta-lactamase resistant. Some agents are more active against gram-negative bacilli, especially indole positive *Proteus* and anaerobes.

(2) Second generation cephalosporin agents cause adverse reactions similar to first generation agents and require the same cautions and warnings.

(3) Examples of these agents are:

(a) Cefaclor (Ceclor®)

(b) Cefamandole (Mandol®)

(c) Cefoxitin (Mefoxin®)

h. Third generation agents are discussed below.

(1) These agents are parenteral antipseudomonal cephalosporins with expanded activity against gram-negative organisms, but less activity against gram-positive organisms than the previous generation.

(2) Because of its good CSF penetration, moxalactam may be the initial drug to use when a gram-negative bacilli is stained from a meningeal infection. However, this agent is reported to cause hypoprothrombinemia and it should be administered concurrently with vitamin K.

(3) These agents cause similar adverse reactions and require the same cautions and warnings as previous generations.

(4) Some examples of third generation cephalosporin agents are:

(a) Cefoperazone (Cefobid®)

(b) Cefotaxime (Claforan®)

(c) Moxalactam (Moxam®)
3-10. ERYTHROMYCIN

a. Erythromycin is a product of the fungus Streptomyces erythreus, which was first found in a soil sample collected in the Philippine Islands. This agent inhibits protein synthesis to exert bacteriostatic activity.

b. Erythromycin is acid labile unless it is formulated in an enteric coated form or is combined with a salt such as stearate or ethylsuccinate. It is distributed to most body tissue and is prominent in prostatic fluid. There is minimal concentration of this agent in the CSF unless there is meningitis.

c. The clinical spectrum of this agent is similar to penicillin G, and it is the drug of choice in the treatment of mycoplasma pneumonia and Legionnaire’s disease. It is a useful substitute for penicillin in people who are hypersensitive to penicillin.

d. Adverse reactions to erythromycin are similar to the penicillins except that estolate salt has been known to cause cholestatic hepatitis. Therefore, it should not be used in patients with pre-existing liver disease. Large oral doses of erythromycin can cause epigastric distress.

e. As an antibiotic agent, erythromycin can be found in the following preparations: Erythromycin base (EMycin®), Erythromycin estolate (Ilosone®), Erythromycin stearate (Erythrocin®), and Erythromycin ethylsuccinate (E.E.S.*).

3-11. CLINDAMYCIN (CLEOCIN®)

a. Clindamycin is derived from the actinomycete Streptomyces lincolnensis. A bacteriostatic agent suppresses protein synthesis.

b. When taken orally, absorption of clindamycin is rapid and almost complete. It is widely distributed to body tissues with the exception of the CSF (cerebrospinal fluid).

c. Enzymes in the liver accomplish metabolism of the agent. The metabolites are excreted through the urine and bile.

d. Clindamycin is indicated in the treatment of serious infections caused by anaerobic bacteria. It is the drug of choice for use against Bacteroides fragilis.

e. Adverse reactions noted with the use of clindamycin include abdominal pain, esophagitis, nausea, vomiting, and diarrhea. Colitis, which can be fatal, is a serious reaction to this agent. Consequently, other less toxic agents, such as erythromycin or penicillin, should be used if possible. If significant diarrhea or colitis appears while the patient is using clindamycin, its use should be discontinued. This colitis can then be treated with the agent vancomycin.
3-12. THE AMINOGLYCOSIDES

a. These agents are a result of a systematic search to find an antibiotic that was effective against gram negative bacteria. During this research, a strain of actinomycetes, *Streptomyces griseus*, was isolated. It produced a potent antimicrobial leading to the discovery of streptomycin. These agents are bactericidal in nature; their MOA is to inhibit protein synthesis.

b. The body normally cannot absorb these agents when administered orally. They must be administered by either IM or IV routes. They are widely distributed in body fluids, except the CSF and the eye. They are found mainly in extracellular fluid.

c. The aminoglycosides are excreted unchanged by glomerular filtration. Elimination is dependent almost exclusively on renal function. The incidence of nephrotoxicity and ototoxicity is directly related to the concentration to which aminoglycosides accumulates in the serum.

d. The initial dose for these agents depends, of course, on the agent used. After the initial dose has been administered, it is best to use serum peak and trough levels to estimate subsequent doses. Consistent peak serum levels seem to make the patient more prone to ototoxicity. Elevated trough levels lead to nephrotoxicity.

e. Clinical uses are discussed in this paragraph. Streptomycin is occasionally used in combination with isoniazid in the treatment of tuberculosis. Neomycin and kanamycin are seldom used parenterally. When used in their oral form, they suppress the flora of the GI tract prior to surgery. Occasionally, kanamycin is used parenterally by pediatricians for gram negative bacteria; it is not effective against *Pseudomonas*. Gentamicin, tobramycin, and amikacin, in combination with carbenicillin, are used primarily in serious gram-negative infections, especially *Pseudomonas aeruginosa*. Amikacin is the most effective aminoglycoside against gentamicin resistant strains and is generally reserved for these cases.

f. Ototoxicity, which is some cases may be irreversible, occurs more frequently with the use of streptomycin, neomycin, and kanamycin. This reaction causes cochlear and vestibular damage leading to hearing loss, vertigo, ataxia, and loss of balance.

g. The incidence of nephrotoxicity, which is irreversible, occurs about 2-10 percent of the time and is more prevalent with the use of neomycin than any of the other agents. The factors that contribute to the incidence are: dose of the agent used, pre-existing renal damage, and contracted intravascular volume caused by the use of diuretics:

h. Prolonged high doses of any of the aminoglycosides may exert a curare-like effect on various body systems.
i. When any of the aminoglycosides are used, concomitant use with general anesthetics or neuromuscular blocking agents should be monitored because of recognized drug interactions. Additionally, the use of rapidly acting diuretics should be avoided, as ototoxicity and nephrotoxicity can be potentiated with their use. Renal functions should be monitored continuously when these agents are used.

j. Spectinomycin (Trobicin®) has an action similar to that of the aminoglycosides but without bactericidal action. It is used in the treatment of gonorrhea in patients that are hypersensitive to penicillin and cannot tolerate one of the tetracyclines. It is also used in the treatment of penicillinase producing Neisseria gonorrhoea (PPNG). Spectinomycin is usually given in a single IM dose, the strength of which is dependent on unknown resistance factors. There are very few adverse reactions of any significance associated with the use of this agent. However, it should not be used in the treatment of syphilis, and its safety in pregnant women has not been established.

3-13. TETRACYCLINES

a. These drugs originate from strains of Streptomyces containing broth that is fermented in deep tanks. Most of these agents are the result of chemical modifications of the broth by product. All of them are bacteriostatic. Their MOA is to inhibit protein synthesis in the microorganism.

b. If administered orally, absorption of these agents occurs primarily in the stomach and the upper portion of the small intestine. Administration intravenously results in wide distribution of the agent throughout the body, with penetration of the CSF.

c. Excretion of these agents occurs through either the urinary or the biliary tract, with the urinary tract as the primary route. Doxycycline is excreted almost exclusively through the feces. Minocycline appears to be the only agent that is metabolized, whereas the others are excreted unchanged.

d. The tetracyclines are true broad-spectrum antibiotics effective against gram positive and gram-negative bacteria. Agents in this group are the drugs of choice when treating Mycoplasma pneumoniae, chlamydia, cholera, and Rocky Mountain spotted fever. They are also used in the treatment of gonorrhea in patients hypersensitive to penicillin and in high doses in the treatment of syphilis in patients hypersensitive to penicillin.

e. Gastrointestinal reactions are common with the use of tetracyclines. Some of these conditions are epigastric distress, nausea, vomiting, diarrhea, and general abdominal discomfort. Hepatic and renal toxicity, photosensitivity, permanent discoloration of the teeth in pediatric patients or fetus, CNS vestibular disturbances, and other local irritations are additional adverse reactions associated with the use of these agents.
f. Tetracyclines should not be used in children during tooth development, which occurs in the last half of pregnancy, infancy, and through childhood up to 8 years of age. The tetracyclines can cross the placenta and have direct toxic effects on the bones of the developing fetus. They also appear in the milk of lactating mothers. Antacids, milk, dairy products, iron, or foods containing aluminum, calcium, or magnesium should be avoided when these agents are taken orally. The tetracyclines should never be used with the penicillins.

g. Tetracyclines appear in the following preparations:

(1) Tetracycline HCl (Achromycin®, Tetracycin®, Sumycin®)

(2) Doxycycline (Vibramycin®)

(3) Minocycline (Minocin®)

3-14. CHLORAMPHENICOL (CHLOROMYCETIN®).

a. This drug is produced by Streptomyces venezuelae, an organism first isolated in 1947 from a soil sample collected in Venezuela. It is bacteriostatic for most organisms and works by inhibiting protein synthesis.

b. Chloramphenicol is absorbed well by the body when it is administered orally. When it is administered IM, its absorption is questionable; therefore parenteral doses should be given IV. Distribution is generally good in all body fluids with concentration in the liver and kidneys. Therapeutic levels are achieved in the CSF without inflammation. Measurable levels can be detected in aqueous, vitreous humors, and bile.

c. During the metabolic process, most of the drug unites with glucuronic acid, and the free drug and metabolites are excreted through the urine.

d. Chloramphenicol is used in the treatment of serious infections such as meningitis and is the drug of choice in the treatment of typhoid fever.

e. Some of the adverse reactions associated with the use of this drug include aplastic anemia (which is irreversible and fatal if it occurs), gastrointestinal tract discomfort, and “gray baby syndrome” in infants. This is an absence or deficiency of certain enzymes during early neonatal life that prolongs the half-life of certain drugs and increases the half life of others, thus increasing the risk of toxicity. For example, immaturity of hepatic glucuronyl transferase activity in neonates diminishes conjugation (metabolism) of chloramphenicol to the inactive form, causing cardiovascular collapse and death.

f. To avoid these reactions, baseline blood studies prior to therapy and periodic checks every two days during therapy is recommended. The drug should not be used in pregnant patients.
3-15. METRONIDAZOLE

a. Metronidazole is a chemically synthesized drug with trichomonacidal properties selective for obligatory and facultative anaerobic organisms.

b. Oral absorption of the drug is good with both oral and IV administration resulting in wide distribution to all body tissues to include the CSF and saliva.

c. The bulk of the drug remains unchanged, but active metabolites are formed. Sixty to 80 percent of the drug is eliminated in the urine with a small portion excreted through the feces.

d. Adverse reactions associated with this agent are not usually severe and include nausea, anorexia, diarrhea, abdominal cramping, vertigo, and numbness of the extremities. Convulsive seizures have been reported with the use of this drug.

e. Patients using this drug should be monitored for candidiasis superinfection. It should not be used in the first trimester of pregnancy or in breast-feeding mothers because of its carcinogenic potential. Patients should avoid alcoholic beverages while taking the drug.

f. Examples of metronidazole preparations are:

   (1) Flagyl® IV
   (2) Flagyl® IV RTU
   (3) Flagyl® 250 mg

3-16. TOPICAL ANTI-INFECTIVES

a. These agents are used to help prevent or treat infection in minor cuts, burns, and abrasions. This use occasionally allows the overgrowth of nonsusceptible organisms, including fungi. Ideally, the topical application of these agents used systemically should be avoided due to sensitization. Systemic antibiotics are preferred in deeper, chronic infections.

b. Examples of these agents are:

   (1) Bacitracin ointment
   (2) Bacitracin-neomycin ointment
   (3) Povidone-Iodine (Betadine®) ointment
3-17. THE SULFONAMIDES

a. The compound p-aminobenzenesulfonamide, now known as sulfanilamide, was first synthesized in 1908, but it was not until many years later that its therapeutic value was known. In 1932, a red dye was prepared; it was later reported to have remarkable curative effects and was named Prontosil®. It was found that the bacterial property of the drug rested in the p-aminobenzenesulfonamide portion of the molecule. In 1937, sulfapyridine, which was the first sulfonamide used with great success in treating pneumonia, was synthesized. Since that time, over 3300 sulfonamides have been prepared, but only a few have been accepted for medical use.

b. The sulfonamides possess a wide antimicrobial spectrum, which include both gram-positive and gram-negative organisms. These agents compete with p-aminobenzoic acid and prevent its normal cellular utilization, particularly its incorporation into folic acid.

c. Most of the sulfonamides are absorbed from the gastrointestinal tract and distributed throughout the body. They should be taken with large amounts of water.

d. They are metabolized by enzymes in the liver, resulting in a product with no antimicrobial activity. Both the free drug and its metabolites are excreted through the kidneys.

e. Dosage of these agents is varied. Oral administration is preferred since parenteral forms are quite irritating to tissue. Short acting sulfonamides are usually given at 4 to 5 hour intervals and an initial loading dose is usually recommended. Longer acting agents are usually given every 8 to 12 hours.

f. There is a low incidence of adverse reactions with these agents. Some of the more common are large varieties of skin rashes, serum sickness, drug fever, acute disorders of the hematopoietic system, and disturbances of the urinary tract.

g. Sulfonamides should be used with caution in the presence of renal and hepatic dysfunction. Periodic complete blood counts should be done to monitor the patient for any possible blood disorders. They should be used cautiously in the presence of other highly protein binding drugs and in patients that are glucose-6-phosphate dehydrogenase (G-6-PD) deficient. Patients should maintain adequate fluid intake to prevent crystalluria in less soluble compounds.

h. Sulfonamide preparations.

(1) Sulfisoxazole (Gantrisin®)

(a) This is a short acting compound with good solubility and is the first drug of choice for urinary tract infections. The initial dose ranges from 2 to 4 grams, with maintenance dose ranging from 4 to 8g daily.
(b) Sulfisoxazole is indicated as a prophylactic for rheumatic fever in patients allergic to penicillin.

(c) Other sulfonamide preparations include:

1. Sulfamethizole (Thiosulfil Forte®)
2. Sulfadiazine (Microsulfan®)
3. Sulfamethoxazole (Gantanol®)

(2) Bactrim®, Septra®.

(a) These agents are derived from a combination of trimethoprim and sulfamethoxazole.

(b) There are many uses for this product. Its major use is in the treatment of chronic urinary tract infections. It is also indicated in the treatment of acute otitis media in children and the treatment of shigellosis and resulting enteritis if it is resistant to ampicillin and tetracycline.

(c) The dose for this drug depends on its strength and how it is to be utilized.

(3) Sodium sulfacetamide (Sulamyd®). This agent is an ophthalmic preparation used for external ocular infections. With the exception of burns, there are few, if any, adverse reactions; it is available in solution and ointment forms.

(4) Mafenide (Sulfamylon®).

(a) This is a topical agent used to prevent colonization of both gram positive and gram negative organisms in second and third degree burns.

(b) It causes intense pain at the application site, and carbonic anhydrase is inhibited causing metabolic acidosis.

(5) Silver Sulfadiazine (Silvadene®).

(a) This agent is used in the same manner as that described in (4) above. In addition, it is very effective against yeast organisms.

(b) Adverse reactions to this agent are infrequent and are limited to localized burning, rash, and itching.
(6) **Vaginal products.** These products are used in the treatment of vaginal infections caused by a variety of organisms. They are available either as suppositories or as creams. The most frequent adverse reaction to these products is localized vaginal itching. These products are available as AVC® or Sultrin®.

(7) **Urinary analgesics.**

(a) This class of drugs is not related to sulfonamides, but is often used in conjunction with them in the treatment of urinary tract infections. They reduce the pain caused upon urination and the itchy feeling associated with the infection.

(b) These compounds are azo dyes, and their use may discolor the urine or feces.

(c) The most commonly used urinary analgesic is phenazopyridine (Pyridium®).

Continue with Exercises

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EXERCISES, LESSON 3

INSTRUCTIONS: Answer the following items by marking the lettered response that best answers the item or best completes the incomplete statement.

After you have completed all of these items, turn to "Solutions to Exercises" at the end of the lesson and check your answers with the solutions. For each exercise answered incorrectly, reread the material referenced after the solution.

1. Antipseudomonal activity is first found in which generation of cephalosporins?
   a. First generation.
   b. Second generation.
   c. Third generation.

2. Beta lactamase resistant activity is found in which generation of cephalosporins?
   a. First generation.
   b. Second generation.
   c. Third generation.

For exercises 3 through 7, select the letter of the trade name on the right that corresponds to the generic name on the left.

3. ___ Spectinomycin  a. Geopen
4. ___ Cefazolin  b. Wycillin
5. ___ Cefoxitin  c. Trobicin
6. ___ Carbenicillin disodium  d. Vibramycin
7. ___ Procaine penicillin G  e. Mefoxin
     f. Geocillin
     g. Ancef
For exercises 8 through 10, select the letter of the side effect on the right that corresponds to the drug name or category on the left.

8. ___ Erythromycin
   a. Nephrotoxicity, ototoxicity

9. ___ Aminoglycosides
   b. Localized vaginal itching

10. ___ Sultrin®
    c. Photosensitivity
    d. Cholestatic hepatitis
    e. Discoloration of teeth

Check Your Answers on Next Page
SOLUTIONS TO EXERCISES, LESSON 3

1. c  (para 3-9h)
2. b  (para 3-9g)
3. c  (para 3-12j)
4. g  (para 3-9f(4))
5. e  (para 3-9g)
6. a  (para 3-8d(4))
7. b  (para 3-8a(8))
8. d  (para 3-10d)
9. a  (para 3-12c)
10. b  (para 3-17h(6))

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