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Pharmacy Journeyman

**Volume 5. Miscellaneous Drug
Therapy, Medical Aids, Poisonings**



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UNIT 1 discusses antibiotics. We take a look at some of the history behind the antibiotic, general theories of antimicrobial therapy and the specifics behind the antibiotics that we all see day in and day out.

Unit 2 covers miscellaneous drugs. These may be drugs that you don't dispense too often, or maybe not at all. We look into antimalarials, anthelmintics, and antivirals. After those, we'll examine an entirely new topic, never before covered in our career development course, herbal medications. We'll cover some of the most commonly used herbals and look at how they may interact with prescription medications.

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This volume is valued at 9 hours and 3 points.

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NOTE:

In this volume, the subject matter is divided into self-contained units. A unit menu begins each unit, identifying the lesson headings and numbers. After reading the unit menu page and unit introduction, study the section, answer the self-test questions, and compare your answers with those given at the end of the unit. Then do the unit review exercises.

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Unit 1. Antimicrobials, Miscellaneous Drug Therapy, and Herbal Medications

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ANTIMICROBIAL drugs are chemical substances that either kill microorganisms or prevent their growth. These drugs are commonly referred to as antibiotics. Due to the large number of these drugs, they are broken down into different categories. This unit discusses several different types of antibiotics before moving on to some miscellaneous therapies that didn't quite fit into the specific systems that we covered. Along with this, we'll dive into the new area of herbal medications. All drugs are presented with their Federal Drug Administration (FDA) approved indications, drug interactions, contraindications, and patient information. Of course, I'll be trying to break down the mechanism of action into terms that we all can understand. Now, on to the antibiotics! But before diving into them, we need to have a background on antimicrobial therapy.

1-1. Antibiotic Drugs

Antibiotics are chemical compounds produced as a result of the metabolic activities of living cells, and which inhibit, in very low concentrations, the growth of microorganisms. Today, most of these compounds are either partially or entirely prepared synthetically. Antibiotics differ markedly in physical, chemical, and pharmacological properties; antibacterial spectra; and mechanisms of action.

This unit will cover the penicillins, cephalosporins, macrolides, tetracyclines, sulfonamides, fluoroquinolones, aminoglycosides, and urinary anti-infectives. To make our discussion of the separate antibiotic classifications more understandable, we'll start the unit off with a brief discussion of antimicrobial therapy.

800. Antimicrobial action

The goal of antimicrobial therapy is to destroy or suppress the growth of infecting microorganisms so that the body's normal defense mechanisms can gain control of the infection, resulting in a cure. In order to exert their effects, antimicrobial agents must first gain access to certain sites of action or "target" sites. Usually, this is accomplished by drug absorption into and distribution via the circulatory system. Sometimes, as in the case of infections of the skin and eyes, local application to the infected area may be necessary. An antimicrobial drug's effect depends upon its mechanism of action. Once an antimicrobial agent reaches its target, it can have bacteriostatic or bactericidal effects, depending on that mechanism of action.

Bacteriostatic and bactericidal agents

Bacteriostatic agents inhibit bacterial growth, allowing the host (body) defense mechanisms additional time to remove the invading microorganisms. Bactericidal agents, on the other hand, cause bacterial cell death. This categorization, however, is not always valid. In some cases, an antimicrobial agent may have either effect, depending on the dose administered and the concentration achieved at

its site of action. Tetracycline, for example, is generally bacteriostatic but may be bactericidal in high concentrations.

Normally, antimicrobial agents may exert their bacteriostatic or bactericidal effects in one of four ways:

1. Inhibition of bacterial cell wall synthesis.
2. Disruption or alteration of bacterial membrane permeability.
3. Inhibition of protein synthesis.
4. Inhibition of synthesis of essential metabolites.

Antimicrobial activity

Another classification method is based on the characteristics of the bacteria. Bacteria are divided into two distinct groups, gram-positive and gram-negative. This classification refers to how the bacteria react when a staining dye is applied to it. If the bacteria have a defined cell wall, it becomes dyed and is clearly visible under microscopic examination, gram-positive. If the cell doesn't have a defined wall, there is no visible pattern in the dye, gram-negative. Certain groups of antibiotics are primarily effective against "gram-positive" bacteria while other drugs are primarily effective against "gram-negative" bacterial types. If an antibiotic is effective only against one type, gram-positive or gram-negative, it is said to have a relatively "narrow spectrum" of activity. Still others may be considered "broad-spectrum" drugs that effect both gram-positive and gram-negative bacteria. As always, there are exceptions to the rules for these drugs. Still they do help in remembering the antimicrobial spectrum of each drug.

Pharmacokinetic and host factors

Although the knowledge that an antibiotic is active against the infecting microorganism is critical, it is not the only factor to be considered. Successful antimicrobial therapy depends upon achieving inhibitory or bactericidal activity at the site of infection without significant toxicity to the host (patient). To accomplish this, several pharmacokinetic and host factors must be considered. These factors include infection location, drug penetration, and elimination rate. The location of the infection may, to a large extent, dictate the choice of drug and route of administration. Penetration of drugs into infected areas almost always depends on passive infusion. The rate of penetration is proportional to the concentration of free drug in the plasma or extracellular fluid. Drugs that are extensively bound to protein do not penetrate to the extent as those that are lesser bound. Knowledge of the drug's route of elimination is also essential. This is especially true when excessive plasma or tissue concentration of the drug may cause toxicity.

In addition to the pharmacokinetic factors, certain host factors must also be considered before initiating antimicrobial therapy. Host factors that alter the response of the infection and therapy include:

1. The patient's age.
2. Other diseases.
3. Organ impairment/insufficiency.
4. Pregnancy.
5. Allergies.
6. Other concomitant drug therapy.

While there is much, much more additional material pertaining to antimicrobial therapy, this information should give you a decent background for the rest of this unit. So, with that said, let's begin our discussion of antibiotics. We'll start with the penicillins, since they are the historical prototype, and cephalosporins, since they are closely related to the penicillins.

801. Penicillins and cephalosporins

Penicillins

Penicillin was the first antibiotic to be produced commercially and still assumes a position of major importance among antibiotics. Penicillins were the first true antibiotic agents isolated and used by mankind against bacteria. Discovered in 1928 and introduced into clinical practice in 1941, the penicillins constitute a large group of antimicrobial agents that remain among the most effective and least toxic of all available antimicrobials.

Penicillins can be divided into four groups based principally on their spectra of activity:

1. Natural penicillins.
2. Penicillinase-resistant penicillins.
3. Aminopenicillins.
4. Extended spectrum penicillins.

Penicillins work pretty well, however the bacteria try to fight back. A vital part of the penicillin molecule is its "beta-lactam ring." Some bacteria produce the enzyme beta-lactamase that breaks the beta-lactam ring of the penicillin, rendering it useless. Penicillins have then needed to be augmented. Several penicillins are available in combination with agents that inactivate the beta-lactamase enzymes and extend the antibiotic spectrum to include many bacteria normally resistant to the antibiotic. The available combinations include:

1. Ampicillin/sulbactam.
2. Amoxicillin/ potassium clavulanate.
3. Ticarcillin/potassium clavulanate.
4. Piperacillin/tazobactam.

The mechanism of action of penicillins is the interference with bacterial cell wall formation. They are bactericidal for a wide variety of gram-positive and some gram-negative organisms, requiring actively growing cells to be effective. If penicillins are used concomitantly with bacteriostatic antibiotics, the effectiveness of the penicillin is decreased or destroyed.

Penicillin's oral absorption is unpredictable. It's altered by foods and is limited by gastric acidity. Penicillin is excreted by the kidneys fairly rapidly. Concomitant probenecid administration blocks the tubular transport of penicillin resulting in higher and prolonged blood levels. Despite their unquestioned value, the penicillins do have some distinct disadvantages:

1. They are readily destroyed by gastric acid, making absorption unpredictable.
2. They are characterized by a relatively high incidence of allergic reactions.
3. They have a somewhat limited antibacterial spectrum, especially in gram-negative infections.

The second point from above warrants a little more coverage. Allergic reactions to penicillin are a significant problem. In fact, these reactions are probably the most common type of drug allergy. Acute anaphylactic reactions constitute the most important immediate danger associated with the use of penicillin. Among all of the antimicrobial drugs, the penicillins are most often responsible for anaphylaxis. Although the most common manifestation of this allergic response is skin rash, it is estimated that several hundred people die each year in the United States from penicillin-induced anaphylaxis.

The following table lists the available penicillins, their route of administration and the effects of food intake on the drug. Dosages are not listed because each disease state may require different and numerous dosages to clear the infection.

Drug	Route of Administration	Penicillinase Resistant	May be taken with meals
<i>Natural Penicillins</i>			
Penicillin G	IM and IV	no	NA
Penicillin V	Oral	no	yes
<i>Penicillinase Resistant</i>			
Cloxacillin	Oral	yes	no
Dicloxacillin	Oral	yes	no
Nafcillin	IM, IV, and Oral	yes	no
Oxacillin	IM, IV, and Oral	Yes	no
<i>Aminopenicillins</i>			
Amoxicillin	Oral	no	yes
Amoxicillin with potassium clavulanate	Oral	yes	yes
Ampicillin	IM, IV, and Oral	no	no
Ampicillin with sulbactam	IM and IV	yes	NA
Bacampicillin	Oral	no	yes
<i>Extended Spectrum</i>			
Carbenicillin	Oral	no	no
Mezlocillin	IM and IV	no	NA
Piperacillin	IM and IV	no	NA
Piperacillin with tazobactam sodium	IV	yes	NA
Ticarcillin	IM and IV	no	NA
Ticarcillin with potassium clavulanate	IV	yes	NA

Indications

Oral penicillins are generally indicated in the treatment of mildly to moderately severe infections caused by penicillin-sensitive microorganisms.

Parenteral penicillins are indicated in patients with severe infection or when there is nausea, vomiting, gastric dilatation, cardiospasm or intestinal hypermotility. Parenteral aqueous penicillin G (e.g., potassium, sodium) is the dosage form of choice in severe infections caused by penicillin-sensitive microorganisms when rapid and high penicillin serum levels are required.

Contraindications

Penicillins are contraindicated in patients with a history of hypersensitivity to penicillins, cephalosporins, or other beta lactamase inhibitors.

Warnings

Serious and occasionally fatal immediate hypersensitivity reactions have occurred. The incidence of anaphylactic shock is between 0.015 percent and 0.04 percent. Anaphylactic shock resulting in death has occurred in approximately 0.002 percent of the patients treated. Although anaphylaxis is more frequent following parenteral therapy, it may occur with oral use. Accelerated reactions (including urticaria and laryngeal edema) and delayed reactions (e.g., serum sickness-like reactions) may also occur. These reactions are likely to be immediate and severe in penicillin-sensitive individuals with a history of atopic conditions.

Individuals with a history of penicillin hypersensitivity have experienced severe reactions when treated with a cephalosporin. The incidence of cross-allergenicity between penicillins and cephalosporins is estimated to range from 5 percent to 16 percent.

Pregnancy

Penicillins cross the placenta. There are no adequate studies in pregnant women though. Penicillin is therefore in pregnancy category B.

Lactation

Penicillins are excreted in breast milk in low concentrations. Their use may cause diarrhea, candidiasis, or allergic response in the nursing infant. Ampicillin use by nursing mothers may lead to sensitization of infants; therefore make a decision to discontinue nursing or to discontinue ampicillin, taking into account the importance of the drug to the mother.

Drug interactions

The following table lists the drug interactions with penicillins. When a specific penicillin is affected it will be put into parenthesis.

Drug	Interaction
Anticoagulants	Large IV doses of penicillins can increase bleeding risks of anticoagulants by prolonging bleeding time.
Oral contraceptives	The efficacy of oral contraceptives may be reduced and increased breakthrough bleeding may occur. Although infrequently reported, contraceptive failure is possible; the use of an additional form of contraception during penicillin therapy is advisable.
Allopurinol (Ampicillin)	The rate of ampicillin-induced skin rash appears much higher when coadministered with allopurinol than with either drug by itself.
Tetracyclines	The bacteriostatic action of tetracycline derivatives may impair the bactericidal effects of penicillins.
Aspirin Sulfonamides Indomethacin Thiazide diuretics (Penicillin G)	These drugs may compete with penicillin G for renal tubular secretion and thus prolong the serum half-life of penicillin.

Patient information

1. Complete full course of therapy.
2. Take on an empty stomach one hour before or two hours after meals. Absorption of penicillin V, amoxicillin, bacampicillin tablets and amoxicillin/potassium clavulanate is not significantly affected by food.
3. Take each oral cloxacillin dose with a full glass of water. Do not take with fruit juice or a carbonated beverage.

4. Take at even intervals, preferably around the clock.
5. Notify physician if skin rash, itching, hives, severe diarrhea, shortness of breath, wheezing, black tongue, sore throat, nausea, vomiting, fever, swollen joints or any unusual bleeding or bruising occurs.
6. Discard any liquid forms of penicillin after seven days if stored at room temperature or after 14 days if refrigerated.

Cephalosporins

Cephalosporins are structurally and pharmacologically related to the penicillins. They are semisynthetic antibiotic derivatives of cephalosporin C, produced from the fungus *cephalosporium acremonium*. This fungus was first collected from a sewer outlet on the island of Sardinia in the 1940s. The cephalosporins are usually bactericidal in action. Their antibacterial activity results from interference with bacterial cell wall synthesis in a manner similar to that of penicillin. The cephalosporins are divided into groups called generations, which are primarily based on their spectrum of antimicrobial activity. Currently there are first, second, third, and fourth generation cephalosporins.

Generation	Description
First	Generally have good activity against gram-positive bacteria and moderate activity against some gram-negative organisms.
Second	Are usually active against the same bacteria covered by first generation, but they also show improved activity against gram-negative bacteria and even some anaerobic bacteria.
Third	Are generally less active against staphylococci than first generation cephalosporins, however, they have an expanded spectrum of activity against gram-negative bacteria than first or second-generation drugs. In addition, third-generation cephalosporins generally have some activity against pseudomonas and penetrate into the cerebro-spinal fluid. There is currently only one fourth-generation cephalosporin.
Fourth	Is actually an extended spectrum third-generation because the gram-negative coverage is the same with the gram-positive coverage being improved.

Like penicillins, some of these drugs are not absorbed well orally. The following table lists the cephalosporins by generation and their routes of administration. Dosages are not given because each infection may require a different strength.

Drug		Route	Indications					
			Upper Resp	Lower Resp	Urinary Tract	Skin	Otitis Media	STD
First Generation	Cefadroxil	Oral			X	X		
	Cefazolin	IM , IV	X	X		X		
	Cephalexin	Oral	X			X	X	
	Cephapirin	IM , IV	X	X	X	X		
	Cephradine	Oral, IM, IV	X		X	X	X	
Second Generation	Cefaclor	Oral	X	X	X	X	X	
	Cefmetazole	IM , IV		X	X	X		
	Cefonicid	IM , IV		X	X	X		
	Cefotetan	IM , IV		X	X	X		
	Cefoxitin	IV		X	X			
	Cefprozil	Oral				X	X	
	Cefuroxime	Oral, IM, IV		X	X	X	X	X
	Loracarbef	Oral	X	X	X	X	X	
Third Generation	Cefdinir	Oral	X	X		X	X	
	Cefepime	IM , IV		X	X	X		
	Cefixime	Oral			X		X	X
	Cefoperazone	IM , IV	X	X	X	X		
	Cefotaxime	IM , IV		X	X	X		
	Ceftazidime	IM , IV		X	X	X		
	Ceftibuten	Oral		X			X	
	Ceftizoxime	IM , IV		X	X	X		X
	Ceftriaxone	IM , IV		X	X	X		X
Fourth Generation	Cefpodoxime	Oral	X	X	X	X	X	X

Contraindications

Cephalosporins are contraindicated in patients with a hypersensitivity to cephalosporins or related antibiotics, especially penicillins. These drugs should be administered with caution to patients who are sensitive to penicillins. There is evidence of cross-sensitivity in approximately 5–16 percent of patients.

Warnings

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced.

Pregnancy

Cephalosporins are in pregnancy category B. Safety for use during pregnancy is not established. Use only when potential benefits outweigh potential hazards to the fetus. Cephalosporins appear safe for pregnant patients, but relatively few controlled studies exist. In addition, the pharmacokinetic parameters of these drugs appear to change in the pregnant woman; tendencies are toward shorter half-lives, lower serum levels, larger volumes of distribution, and increased clearance.

Lactation

Most of these agents are excreted in breast milk in small quantities. Levels range from 0.16 to 4 mcg/ml, or a breast-milk maternal serum ratio of 0.01 to 0.5 following 0.5- to 2-g doses. Modification/alteration of bowel flora, pharmacological effects, and interference with interpretation

of culture results in fever/infection workups may occur in breastfed infants whose mothers take cephalosporins.

Drug interactions

The next table lists the drug interactions with cephalosporins.

Drug	Interaction
Ethanol	Alcoholic beverages consumed concurrently with or \leq 72 hours after cefoperazone, cefazolin, cefmetazole, or cefotetan may produce acute alcohol intolerance (disulfiram-like reaction). The reaction begins within 30 minutes after alcohol ingestion and may subside 30 minutes to several hours afterwards. The reaction may occur \leq three days after the last dose of the antibiotic.
Anticoagulants	Hypoprothrombinemic effects of anticoagulants may be increased by cephalosporins.
Probenecid	Probenecid may increase and prolong cephalosporin plasma levels by competitively inhibiting renal tubular secretion.
Antacids	Plasma concentrations of some cephalosporins may be reduced by coadministration of antacids.
H ₂ antagonists	Plasma concentrations of some cephalosporins may be reduced by coadministration of H ₂ antagonists.
Iron supplements	Iron supplements and foods fortified with iron reduce the absorption of some cephalosporins. Cephalosporins should be taken two hours before or after the iron.
Loop diuretics	The risk of nephrotoxicity is increased with coadministration of these drugs.

Patient information

1. You must complete the entire course of therapy.
2. These drugs may cause GI upset; you may take them with food or milk.
3. Antacids containing magnesium or aluminum interfere with the absorption of some cephalosporins. Take the cephalosporin two hours before or after the antacid.

802. Macrolides and Tetracyclines

Although they are completely different, these two classes of drugs have many of the same uses. Another thing that they have in common for us is the fact that we'll cover them in the same lesson.

Macrolides

The terms *erythromycins* and *macrolides* are often used interchangeably. Erythromycin, the first and still most widely used macrolide antibiotic, has been used clinically as an antibiotic since 1952. Until recently, erythromycin and an infrequently used macrolide, troleandomycin, were the only members of this group. In 1991, azithromycin and clarithromycin were made available. These new agents appear to possess distinct advantages over erythromycin, but at a greater cost.

Macrolide antibiotics include azithromycin, clarithromycin, dirithromycin, erythromycin, and troleandomycin inhibit RNA-dependent protein synthesis. They are bacteriostatic at lower concentrations and become bactericidal at higher drug concentrations.

Indications

The following table lists some of the important information about the macrolides.

Macrolide	Route	Indications								
		Pharyngitis	Resp. Tract	Bronchitis	Skin	UTI	Pertussis	Diphtheria	Pneumonia	COPD
Azithromycin	Oral, IV	X			X					X
Clarithromycin	Oral	X		X	X				X	
Dirithromycin	Oral	X		X	X					
Erythromycin	Oral, IV		X		X	X	X	X		
Troleandomycin	Oral		X						X	

Contraindications

Contraindications to macrolides include hypersensitivity to any of the macrolide antibiotics. Macrolides are also contraindicated in any patient taking astemizole or cisapride and in any patient with a preexisting liver disease.

Warnings

Pseudomembranous colitis may occur in patients being treated with these medications. Treatment with these antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of antibiotic-associated colitis.

Pregnancy

Azithromycin and erythromycin are in pregnancy category B, while clarithromycin, dirithromycin, and troleandomycin are in category C. Clarithromycin has adverse effects on pregnancy outcome or embryo-fetal development in monkeys, rats, mice, and rabbits. Animal studies with dirithromycin demonstrated that fetal weight was significantly depressed at eight times the maximum recommended human dose with an increased occurrence of incomplete ossification. Erythromycin crosses the placental barrier but fetal levels are low. There are no adequate and well-controlled studies in pregnant women. Do not use clarithromycin in pregnant women except in clinical circumstances when no alternative therapy is appropriate. If pregnancy occurs while taking this drug, apprise the patient of the hazard to the fetus. Use clarithromycin and dirithromycin during pregnancy only if the potential benefit justifies the potential risk to the fetus. Use azithromycin and erythromycin only when clearly needed.

Lactation

Erythromycin is excreted in breast milk and may concentrate to a milk: plasma ratio of 0.5. Although no infant adverse effects are reported, potential problems for the nursing infant include modification of bowel flora, pharmacological effects, and interference with fever work-ups. According to the American Academy of Pediatrics, erythromycin is considered compatible with breastfeeding. It is not known whether clarithromycin, dirithromycin, or azithromycin is excreted in breast milk. Exercise caution when administering these drugs to a nursing woman.

Drug interactions

The following table lists the drug interactions for the macrolide class.

Drug	Interaction
Antacids	Aluminum- and magnesium-containing antacids reduce peak serum levels but not the extent of azithromycin absorption. When given immediately following antacids, dirithromycin absorption is slightly enhanced. When given immediately prior to antacids, the elimination rate constant of erythromycin may be slightly decreased.
Fluconazole	Coadministration may increase levels of macrolides.
H2 antagonists	When given immediately after H2 antagonists, macrolide absorption may be slightly enhanced.
Anticoagulants	Anticoagulant effect may be potentiated.
Astemizole	Coadministration of these drugs is contraindicated. Increased astemizole concentrations have occurred. Cardiovascular side effects, including death, cardiac arrest, and other ventricular arrhythmias have occurred.
Benzodiazepines	The plasma levels of certain benzodiazepines may be elevated, increasing and prolonging the CNS depressant effects.
Bromocriptine	Bromocriptine serum levels may be elevated, resulting in an increase in the pharmacologic and adverse effects.
Buspirone	Plasma buspirone concentrations may be elevated, increasing the pharmacologic and adverse effects.
Carbamazepine	Increased concentrations of carbamazepine may occur.
Cyclosporine	Elevated cyclosporine concentrations with increased risk of toxicity (nephrotoxicity, neurotoxicity) may occur.
Digoxin	Serum digoxin concentrations may be elevated because of the effect of the antibiotic on gut flora that metabolizes digoxin.
Methylprednisolone	The clearance of methylprednisolone is greatly reduced, resulting in increased blood levels.
Omeprazole	Coadministration may result in increased plasma levels of omeprazole.
Theophylline	Concurrent use may be associated with increased serum theophylline levels and plasma erythromycin levels may be decreased.

Patient information

1. Clarithromycin may be given without regard to meals and may be taken with milk.
2. Caution patients to take azithromycin suspension \geq one hour prior to a meal or \geq two hours after a meal. Azithromycin tablets can be taken with or without food.
3. Take dirithromycin with food or within one hour of eating.
4. Take erythromycin on an empty stomach (\geq one hour before or two hours after meals); if GI upset occurs, take with food. Erythromycin estolate, ethylsuccinate, and certain brands of erythromycin base enteric-coated tablets may be taken without regard to meals; consult the current package literature. Take each erythromycin dose with an adequate amount of water (180 to 240 ml).
5. Take erythromycin and troleandomycin at evenly spaced intervals during the day, preferably around the clock. Complete full course of therapy; take until gone.
6. Caution patients not to take aluminum- and magnesium-containing antacids and oral azithromycin simultaneously.
7. Patients should discontinue the drug immediately and contact a physician if any signs of an allergic reaction occur.
8. Do not cut, chew, or crush the tablets.

9. Notify physician if nausea, vomiting, diarrhea or stomach cramps, severe abdominal pain, yellow discoloration of the skin or eyes, darkened urine, pale stools, or unusual tiredness occurs with erythromycin.
10. Shake the suspension well before each use. Do not refrigerate.

Tetracyclines

The tetracyclines, introduced in 1948, were the first truly "broad spectrum" antibiotics. These drugs are usually bacteriostatic, but may be bactericidal in high concentrations. Tetracyclines interfere with the protein synthesis of the infectious organism halting its growth and reproduction. These drugs are readily, yet incompletely absorbed from the gastrointestinal tract. Absorption occurs mainly from the stomach and upper small intestine. Food and/or milk reduce GI absorption of most oral tetracyclines by 50 percent or more. The tetracycline class includes doxycycline, demeclocycline, minocycline, oxytetracycline, and tetracycline.

Indications

Tetracyclines have a wide spectrum of activity against many gram-negative and gram-positive organisms but are inactive against viruses and fungi. Although tetracyclines are effective against many gram-positive and gram-negative organisms, they should not be routinely used for gram-positive bacteria because many of these organisms exhibit resistance. Despite their relatively broad spectrum, tetracyclines have limited use. Clinical applications for tetracycline antibiotics include treatment of infections due to Rickettsia, mycoplasma pneumonia, and chlamydia. Tetracyclines are also used to treat Lyme disease, brucellosis, syphilis, and gonorrhea with patients who cannot take penicillin.

Contraindications

Hypersensitivity to any of the tetracyclines is a contraindication to their use.

Warnings

Photosensitivity, manifested by an exaggerated sunburn reaction, has been observed in some individuals taking tetracyclines.

Pregnancy

The tetracyclines are in pregnancy category D. Tetracyclines should not be used during pregnancy. They readily cross the placenta; concentrations of oxytetracycline in cord blood are approximately 50 percent of those of the mother. Tetracyclines are found in fetal tissues and can have toxic effects on the developing fetus (retardation of skeletal development). Evidence of embryotoxicity has also been noted in animals treated early in pregnancy.

Lactation

Tetracyclines are excreted in breast milk. A dosage of 2 g/day for three days has achieved a milk: plasma ratio of 0.6 to 0.8. Because of the potential for serious adverse reactions decide whether to discontinue nursing or discontinue the drug.

Use in children

A special warning about tetracycline use involves children. Tetracyclines should not generally be used in children under eight years of age, unless other drugs are not likely to be effective, or are contraindicated.

Teeth

The use of tetracyclines during the period of tooth development (from the last half of pregnancy through the eighth year of life) may cause permanent discoloration (yellow-gray-brown) of deciduous and permanent teeth. This adverse reaction is more common during long-term use of the drugs, but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported.

Bone

Tetracycline forms a stable calcium complex in any bone-forming tissue. Decreased fibula growth rate occurred in infants given oral tetracycline. This was reversible when drug was discontinued.

Drug interactions

The following table lists the interactions associated with tetracycline use.

Drug	Interaction
Antacids	Antacids containing aluminum, calcium, zinc or magnesium and bismuth salts impair absorption of tetracyclines due to formation of a poorly soluble chelate, possibly decreasing the antimicrobial efficacy.
Anticoagulants, oral	Tetracyclines may increase the hypoprothrombinemic effects of concurrent anticoagulants.
Cimetidine	Cimetidine may decrease the GI absorption of tetracyclines due to a pH-dependent inhibition of dissolution; antimicrobial effectiveness may be decreased.
Digoxin	Tetracyclines may increase the serum levels of digoxin leading to digoxin toxicity. These effects may last for months after tetracycline administration is discontinued.
Insulin	Tetracyclines may reduce insulin requirements.
Iron products	Iron may decrease the GI absorption of tetracyclines due to formation of poorly soluble chelate; antimicrobial effectiveness may be decreased. Give iron salts in non-enteric coated, non-sustained release form at least three hours before or two hours after tetracyclines.
Oral contraceptives	Coadministration of tetracyclines may decrease the pharmacologic effects of oral contraceptives; breakthrough bleeding or pregnancy may occur.
Penicillins	Bacteriostatic drugs such as tetracycline may interfere with the bactericidal action of penicillins; avoid concomitant administration

Patient information

1. Finish the entire course of therapy. Do not save any of these medications. Taking expired tetracyclines may be hazardous to your health.
2. Take tetracyclines on an empty stomach, at least one hour before or two hours after meals (doxycycline and minocycline may be taken with food or milk).
3. Take tetracyclines with full glass of water (240 ml).
4. Avoid simultaneous use of dairy products (milk, cheese), antacids, laxatives or iron-containing products. If an antacid must be taken, take at least two hours before or after tetracycline.
5. Avoid prolonged exposure to sunlight or sunlamps; may cause photosensitivity (especially demeclocycline).

803. Sulfonamides, flouroquinolones, aminoglycosides, and urinary tract anti-infectives

This lesson sounds like it may have a lot of information. However, there isn't a whole lot to say about these medications without asking you to just memorize the drug monographs. These drugs are important enough so that you should know some of the basic information about them and be able to give informed advise to the medical staff and properly counsel your patient when they receive one of these antibiotics. Let's jump right in to this last section of antibiotic therapy with a discussion of sulfonamides.

Sulfonamides

Sulfonamides have a broad antibacterial spectrum that includes both gram-positive and gram-negative organisms. Sulfonamides exert their bacteriostatic action by competitive antagonism of para-aminobenzoic acid (PABA), an essential component in folic acid synthesis. Microorganisms that require exogenous folic acid and do not synthesize folic acid are not susceptible to the action of sulfonamides. Sulfonamides differ only in their pharmacokinetics and, as such, are often classified according to their

duration of action or half-life. Short-acting sulfonamides include sulfacytine, sulfisoxazole, and sulfamethizole. Intermediate-acting agents include sulfadiazine and sulfamethoxazole.

The development of resistance in previously susceptible organisms and the discovery of more effective antibiotic agents have greatly diminished the usefulness of the sulfonamides. However, the combination of sulfamethoxazole with trimethoprim, marketed in 1973, has been shown to be effective in the treatment of specific bacterial infections and has increased the clinical use of sulfamethoxazole. And that's where we're going to go with sulfonamides, combination therapy. We're going to cover the sulfonamides as combination drugs. In this lesson we discuss two sulfonamide drugs: the combination drug products sulfamethoxazole/trimethoprim and erythromycin/sulfisoxazole. These drugs will be covered separately.

Sulfamethoxazole/trimethoprim (SMZ-TMP)

Sulfamethoxazole (SMZ) inhibits bacterial synthesis of dihydrofolic acid by competing with para-aminobenzoic acid. Trimethoprim (TMP) blocks the production of tetrahydrofolic acid by inhibiting the enzyme dihydrofolate reductase. Thus, this combination block two consecutive steps in the bacterial biosynthesis of essential nucleic acids and proteins.

Sulfamethoxazole/trimethoprim is available as oral tablets, a suspension, or a solution for injection.

Indications and dosage

Sulfamethoxazole/trimethoprim is indicated in the treatment of the following conditions:

- Bronchitis.
- Cholera.
- Enterocolitis.
- Nocardiosis.
- Pneumocystis carinii pneumonia (PCP) prophylaxis.
- Salmonella infection.
- Sinusitis.
- Urinary tract infection.
- Chancroid.
- Cystitis.
- Isosporiasis.
- Otitis media.
- Pertussis.
- Shigellosis.
- Traveler's diarrhea.
- Wegener's granulomatosis.

Dosages are individualized to the patient and to the disease.

Contraindications

Sulfamethoxazole/trimethoprim is contraindicated in patients with either sulfonamide or trimethoprim hypersensitivity. Death can follow.

Warnings

Sulfonamide-associated deaths, although rare, have occurred from hypersensitivity of the respiratory tract, Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias. Both TMP and SMZ can interfere with hematopoiesis.

Sulfonamides have a high incidence of allergic reactions. Most of these are manifested as a skin rash.

Instance	Warning
Pregnancy	Sulfonamides are in pregnancy category C. They readily cross the placenta with fetal levels reaching about 70–90 percent of maternal levels. Toxicities observed in the neonate include jaundice, hemolytic anemia, and kernicterus. Trimethoprim crosses the placenta, producing similar levels in fetal and maternal serum.
Lactation	TMP-SMZ is not recommended in the nursing period because sulfonamides are excreted in breast milk and may cause kernicterus.

Drug interactions

There aren't too many interactions, so I'll cover them in the old fashioned way, one at a time.

Drugs	Interaction
Antidiabetic agents, phenytoin, and warfarin	Sulfonamides such as sulfamethoxazole can displace oral antidiabetic agents, phenytoin, and oral anticoagulants (such as warfarin) from their protein-binding sites and also can inhibit the metabolism of these medications. These actions may increase the therapeutic or adverse effects of these medications. Dosage adjustments may be necessary during therapy with sulfamethoxazole/trimethoprim.
Digoxin	Trimethoprim can increase digoxin serum concentrations by reducing the tubular secretion of digoxin. Although digoxin concentrations increase only slightly, clinicians should be alert to signs and symptoms of digoxin toxicity in patients receiving sulfamethoxazole/trimethoprim.

Patient information

1. Complete the full course of therapy.
2. Take each oral dose with a full glass of water.
3. Maintain adequate fluid intake.
4. Notify physician immediately if sore throat, fever, chills, pale skin, yellowing of skin or eyes, rash, or unusual bleeding or bruising occurs.

Erythromycin/sulfisoxazole

Erythromycin and sulfisoxazole are used together in an oral preparation to treat otitis media. Erythromycin is a macrolide antibiotic, and sulfisoxazole is a sulfonamide antibiotic. They have different spectrums of antimicrobial activity, and the combination is effective against susceptible strains of *Hemophilus influenzae*. Erythromycin/sulfisoxazole is available in an oral suspension.

Indications

Erythromycin/sulfisoxazole is indicated in the treatment of otitis media.

Drug interactions

Refer back to lesson 802 for drug interactions with erythromycin. Additional interactions are discussed in the following table:

Drug	Interaction
Warfarin	Sulfisoxazole can potentiate the anticoagulant effects of warfarin. This is believed to result from sulfisoxazole inhibiting the hepatic metabolism of warfarin. A protein-binding interaction also may be possible, since warfarin is 96 to 98 percent protein-bound, and sulfonamides are well known to displace bilirubin from protein-binding sites. Limited data exist regarding this interaction, however. Most of the reported cases involved warfarin and sulfamethoxazole/trimethoprim. Due to the potential severity of excessive anticoagulation, sulfonamides should not be administered to patients already stabilized on warfarin. Although warfarin can be added to sulfonamide therapy, warfarin doses may need to be adjusted when sulfonamide therapy is discontinued.
Phenytoin	Different sulfonamides have produced variable effects on the hepatic metabolism of phenytoin. In addition, sulfisoxazole has been shown to displace phenytoin from protein-binding sites. Patients receiving phenytoin should be monitored for phenytoin toxicity if sulfisoxazole is added.
Penicillins and cephalosporins	Many medical textbooks caution against the concomitant use of bacteriostatic and bacteriocidal antibiotics, despite the absence of data that clearly demonstrate antagonism in this setting. Although sulfonamides should be avoided in patients receiving bacteriocidal antibiotics such as penicillins or cephalosporins, concomitant use is acceptable if both antibiotics are essential. Patients should be monitored for antibiotic antagonism, however.

Contraindications

Refer back to lesson 802 for contraindications of erythromycin. Additional contraindications are:

Drug/Condition	Description
Bone marrow depression, blood dyscrasias, megaloblastic anemia, and G6PD deficiency	<p>Sulfisoxazole is relatively contraindicated in patients with preexisting bone marrow depression, blood dyscrasias, or megaloblastic anemia secondary to folate deficiency because sulfonamides can aggravate these conditions. Sulfisoxazole is contraindicated in patients with glucose-phosphate dehydrogenase deficiency (G6PD deficiency) because the drug can cause hemolysis in these patients.</p> <p>G6PD—this may be a good time to briefly discuss this disorder (you'll see it a few more times). Glucose-6-phosphate dehydrogenase is an enzyme that processes glucose-6-phosphate in the metabolism of glucose. Many White males with Mediterranean background and about 10% of African-American males are deficient in this enzyme. The deficiency causes a change in cell shape similar to sickle-cell disease and when certain drugs are administered results in hemolytic anemia.</p>
Thiazide, sulfonyleurea, carbonic anhydrase inhibitor, furosemide, or sulfonamide hypersensitivity	<p>Because of structural similarity, sulfonamides should be used cautiously in patients with known allergic reactions to thiazide diuretics, oral sulfonyleureas, loop diuretics, or carbonic anhydrase inhibitors. However, despite the chemical similarities and the logical conclusion that cross-sensitivity would occur, a thorough review of the published literature and direct communication with the manufacturer revealed no data supporting the conclusion that patients with sensitivity to sulfonamides also develop sensitivity to furosemide. Less is known regarding the cross-sensitivity between sulfonamides and the other agents, although some clinicians doubt that significant risk exists.</p> <p>Nevertheless, sulfisoxazole should be avoided in patients with hypersensitivity to furosemide, thiazide, sulfonyleurea, or carbonic anhydrase inhibitor. Without question, sulfisoxazole should be avoided in patients with sulfonamide hypersensitivity.</p>

Warnings

Refer to lesson 802 for the warnings for erythromycin.

Deaths associated with the administration of sulfonamides have been reported from hypersensitivity reactions, hepatocellular necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias. Sore throat, fever, pallor, purpura, or jaundice may be early indications of serious blood disorders. Perform complete blood counts.

Condition	Description
Pregnancy	Sulfonamides are in pregnancy category C. Safety of use during pregnancy is not established. Sulfonamides cross the placenta; fetal levels average 70% to 90% of maternal serum levels. Significant levels may persist in the neonate if these drugs are given near term; jaundice, hemolytic anemia, and kernicterus may occur.
Lactation	Sulfonamides are excreted in breast milk in low concentrations. In the milk, plasma ratios for sulfonamides are as low as 0.5 to 0.6. According to the American Academy of Pediatrics, breastfeeding and sulfonamide use are compatible because sulfonamide excretion into breast milk does not pose a significant risk to the healthy full-term neonate.

Drug interactions

Refer to lesson 802 for the erythromycin interactions. Also, the drug interactions for sulfisoxazole are the same as those listed for sulfamethoxazole.

Patient information

1. Complete full course of therapy.
2. Take with a full glass of water.
3. Avoid prolonged exposure to sunlight; photosensitivity may occur. If outside, wear protective clothing and apply sunscreen to exposed areas.
4. Notify physician if any of the following occurs: Blood in urine, rash, ringing in ears, difficulty in breathing, fever, sore throat, or chills.

Fluoroquinolones

The fluoroquinolones are synthetic, broad-spectrum antibacterial agents. The fluoroquinolones were developed from older medications, quinolones. The addition of a fluorine molecule provides an increased potency against gram-negative organisms and broadens the spectrum to include gram-positive organisms. The fluoroquinolones have relatively few side effects, and microbial resistance does not develop as rapidly as it does to the older quinolone drugs. The first of these agents, norfloxacin, was marketed in 1986, followed by several others shortly thereafter. Currently, there are 10 fluoroquinolones available for systemic use, several of which are also approved for ophthalmic or otic use. Fluoroquinolones exhibit a prolonged post-antibiotic effect (PAE). Organisms may not resume growth for two to six hours after exposure to a fluoroquinolone, despite undetectable drug levels. In addition, fluoroquinolones are concentrated within human neutrophils. In general, the fluoroquinolones are best used in the treatment of infections due to aerobic gram-negative bacteria. Here we'll discuss ciprofloxacin and levofloxacin.

Indications

The next table lists our fluoroquinolones, their indications, available dosage forms, and dosing intervals. Exact dosages are not given because they vary greatly with each disease state and individual.

Drug	Indications	Dosage form	Dosage interval
Ciprofloxacin	Bone/joint, bronchitis, gonorrhea, infectious diarrhea, pneumonia, skin, typhoid fever, urinary tract infections	tablets, oral suspension, injection, otic, ophthalmic	Every 12 hours
Levofloxacin	Bronchitis, pneumonia, pyelonephritis, sinusitis, skin, urinary tract infections	tablets, injection	Every 24 hours

Generations

Just as with the cephalosporins, fluoroquinolones have been divided into generations. Ciprofloxacin is a first generation and levofloxacin is a third. As with the cephalosporins, the spectrum of activity is expanded with each generation. Gram-negative and anaerobes are covered as the second and third generation drugs come on. Recently, a fourth generation of fluoroquinolones was added with an extremely broad spectrum and very little resistance develops to gram-positive infections. These fourth generation drugs include gatifloxacin, moxifloxacin, and trovafloxacin. They are reserved for serious, life-threatening infections to reduce, even further, the incidence of resistance.

Contraindications

A hypersensitivity to the fluoroquinolones or quinolone class of antibiotics is a contraindication for the use of these drugs.

Warnings

Photosensitivity

Moderate-to-severe phototoxic reactions have occurred in patients exposed to direct or indirect sunlight or to artificial ultraviolet light (e.g., sunlamps) during or following treatment with fluoroquinolones. These reactions have also occurred in patients exposed to shaded or diffuse light, including exposure through glass. Advise patients to discontinue therapy at the first signs or symptoms of a phototoxicity reaction such as a sensation of skin burning, redness, swelling, blisters, rash, itching, or dermatitis. These reactions have occurred with and without the use of sunscreens or sunblocks and with single doses of fluoroquinolones. In a few cases, recovery was prolonged for several weeks. As with some other types of phototoxicity, there is the potential for exacerbation of the reaction on re-exposure to sunlight or artificial ultraviolet light prior to complete recovery from the reaction. In rare cases, reactions have recurred up to several weeks after stopping therapy.

Convulsions

Increased intracranial pressure and toxic psychosis have occurred. CNS stimulation may also occur, which may lead to tremor, restlessness, lightheadedness, confusion, and hallucinations.

Pregnancy

Fluoroquinolones are in pregnancy category C; do not use in pregnant women. There are no adequate and well-controlled studies in pregnant women. Use during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation

Norfloxacin was not detected in breast milk following the administration of 20 mg to nursing mothers; however, this was a low dose. Ciprofloxacin is excreted in breast milk; however, the amount ingested by the infant appears to be low. Ofloxacin as a single 200-mg dose resulted in breast milk concentrations in nursing females that were similar to those found in plasma. It is not known if lomefloxacin is excreted in breast milk.

Drug interactions

The next table lists the drug interactions for the fluorquinolones.

Drug	Interaction
Antacids Sucralfate Iron salts	Interference of GI absorption of the fluoroquinolones, resulting in decreased serum levels may occur, avoid simultaneous use. Administer antacids two to four hours before or after the fluoroquinolone.
Antineoplastic agents	Fluoroquinolone serum levels may be decreased.
Cimetidine	Cimetidine may interfere with the elimination of the fluoroquinolones.
Nitrofurantoin	Antibacterial effect of fluoroquinolones in the urinary tract may be antagonized.
Probenecid	Ciprofloxacin renal clearance is reduced 50 percent, and its serum concentration is increased 50 percent.
Hydantoins	Phenytoin serum levels may be reduced, producing a decrease in therapeutic effects.
Anticoagulants	The effects of the anticoagulant may be increased.
Theophylline	Decreased clearance and increased plasma levels and toxicity of theophylline have occurred with concurrent fluoroquinolone use.

Patient information

1. Drink fluids liberally while taking fluoroquinolones.
2. Do not take antacids containing magnesium or aluminum or products containing iron or zinc simultaneously or within four hours before or two hours after dosing.

3. May cause dizziness or lightheadedness; observe caution while driving or performing other tasks requiring alertness, coordination, or physical dexterity. CNS stimulation may occur (e.g., tremor, restlessness, and confusion); use with caution in patients predisposed to seizures or with other CNS disorders.
4. Take norfloxacin and enoxacin one hour before or two hours after meals. Do not take ofloxacin with food. Ciprofloxacin and lomefloxacin can be taken without regard to meals; however, the preferred time of ciprofloxacin dosing is two hours after a meal.
5. Hypersensitivity reactions may occur, even following the first dose; discontinue the drug at the first sign of skin rash or other allergic reaction.
6. Avoid excessive sunlight/artificial ultraviolet light; discontinue drug if phototoxicity occurs. Avoid re-exposure to ultraviolet light. Reactions may recur up to several weeks after stopping therapy.

Aminoglycosides

Aminoglycosides are bactericidal antibiotics used primarily in the treatment of gram-negative infections. They irreversibly bind to the bacterial ribosomes, blocking the recognition step in protein synthesis and causing misreading of the genetic code. The ribosomes separate from messenger RNA causing cell death. Oral aminoglycosides are poorly absorbed and therefore are used only for suppression of GI bacterial flora. The small absorbed fraction is rapidly excreted with normal kidney function. The unabsorbed drug is eliminated unchanged in the feces. Most intestinal bacteria are rapidly eliminated with bacterial suppression persisting for 48 to 72 hours. Absorption from IM injection is rapid, with peak blood levels achieved within one hour. Our discussion will focus on the injectable aminoglycoside gentamycin and ophthalmic uses for both gentamycin and tobramycin.

Gentamycin for injection

Gentamycin for injection is probably the most widely used parental aminoglycoside. In the past, peak and trough level monitoring was extremely important because of the possibility of ototoxicity and nephrotoxicity. Recent studies have shown that a mega-dose given once daily will gradually dissipate to the proper trough level and reduce the incidence of toxic reactions.

Indications and dosage

Gentamycin is indicated for treating bacterial neonatal sepsis, bacterial septicemia, serious bacterial infections of the CNS (meningitis), urinary tract, respiratory tract, GI tract (including peritonitis), skin, and bone and soft tissue (including burns).

Gentamycin may be given IM or IV. For patients with serious infections and normal renal function, give 3 mg/kg/day in 3 equal doses every eight hours. For patients with life-threatening infections, administer up to 5 mg/kg/day in 3 or 4 equal doses. Reduce dosage to 3 mg/kg/day as soon as clinically indicated. Gentamycin is available in 40 mg/ml vials and syringes and 10 mg/ml vials.

Contraindications

Gentamycin is contraindicated in patients who have had reactions previously to gentamycin or other aminoglycosides. Gentamycin is not indicated for long-term therapy because of the ototoxic and nephrotoxic hazards of extended administration.

Warnings

Aminoglycosides are associated with significant nephrotoxicity or ototoxicity. These agents are excreted primarily by glomerular filtration so, the serum half-life will be prolonged and significant accumulation will occur in patients with impaired renal function.

Drug interactions

The following table lists the drug interactions with aminoglycoside antibiotics.

Drug	Interaction
Cephalosporins	The risk of nephrotoxicity may increase above that with aminoglycoside alone. The bactericidal activity against certain pathogens may also be enhanced.
Loop Diuretics	Auditory toxicity appears to increase during concomitant use. Hearing loss of varying degrees may occur; it may be irreversible.
Penicillins	Synergism of these agents is well documented; however, certain penicillins may inactivate certain aminoglycosides.

Patient information

Since this is an IV/IM medication and is used only in the in-patient setting, there are no patient information statements.

Ophthalmic uses for aminoglycoside antibiotics

Gentamycin and tobramycin are also indicated for ophthalmic use. These two antibiotics are indicated for the treatment of superficial ocular infections involving the conjunctiva or cornea. These are very superficial infections. Anything of a deeper nature should be treated with systemic antibiotics and supplemented with ophthalmics. Tobramycin is often combined with dexamethasone for inflammatory conditions, along with infections of the conjunctiva or cornea.

Contraindications

Any previous sensitivity to these agents through either ophthalmic or systemic use is a contraindication for their ophthalmic use. Any fungal infection is also a contraindication.

Warnings

Sensitization from the topical use of an antibiotic may contraindicate the drug's later systemic use in serious infections.

Condition	Description
Pregnancy	Tobramycin is in pregnancy category B and gentamycin is in C. The safety of these drugs has not been established and they should only be used during pregnancy if the potential benefits outweigh the risks to the fetus.
Lactation	There are possible risks in using these drugs in lactating women. A decision to continue the medication or breastfeeding should be made.

Drug interactions

Since these are topical medications, no interactions are listed.

Patient information

1. Tilt head back, place medication in conjunctival sac and close eyes. Apply light finger pressure on lacrimal sac for one minute following instillation.
2. May cause temporary blurring of vision or stinging following administration. Notify physician if stinging, burning, or itching becomes pronounced or if redness, irritation, swelling, decreasing vision, or pain persists or worsens.
3. To avoid contamination, do not touch tip of container to any surface. Replace cap after using.
4. In general, patients being treated for bacterial conjunctivitis should not wear contact lens; however, if the physician considers contact lens use appropriate, wait at least 15 minutes after using any solutions containing benzalkonium chloride before inserting the lens, as it may be absorbed by the lens.

Urinary tract anti-infectives

Urinary tract infections (UTI) are treated with antiseptics and anti-infectives that inhibit bacterial proliferation in the urinary tract. Many antibiotics with more general usefulness are also used in treating UTIs. Our focus is going to be on only one anti-infective, routinely used for UTIs—nitrofurantoin.

Nitrofurantoin is an antibacterial agent that is specifically used to treat UTIs caused by many gram-negative and some gram-positive bacteria. Nitrofurantoin is a synthetic nitrofuran that is bacteriostatic in low concentrations and bactericidal in higher concentrations. Nitrofurantoin may inhibit acetylcoenzyme A, interfering with bacterial carbohydrate metabolism. It may also disrupt bacterial cell wall formation.

Indications and dosage

Nitrofurantoin is indicated for the treatment of urinary tract infections due to susceptible strains of *E coli*, enterococci, *S aureus*, and certain strains of *Klebsiella* and *Enterobacter* species. The dosing for nitrofurantoin can seem a little confusing, but I'll try to keep it simple. First, nitrofurantoin should be given with food or milk to improve absorption and, in some patients, tolerance. Therapy should be continued for at least one week, or three days after sterile urine is obtained. The normal adult dosing for nitrofurantoin is 50 to 100 mg four times daily, with meals and at bedtime. For long-term suppressive therapy, the dosage is reduced to 50–100 mg at bedtime. Now for the confusing part, nitrofurantoin is available in three different chemical structures, nitrofurantoin microcrystals, nitrofurantoin macrocrystals, and nitrofurantoin monohydrate. The microcrystal and macrocrystal are equivalent in dosing with the macrocrystal being digested slower, therefore easier on the GI system. The nitrofurantoin monohydrate, when mixed with digestive fluids, forms a thick, gel-like substance that gives the drug delayed release properties and allows for twice-daily dosing.

Contraindications

Nitrofurantoin is contraindicated in patients with renal function impairment, and those suffering from anuria or oliguria (treatment is much less effective and carries an increased risk of toxicity because of impaired excretion of the drug). As usual, any hypersensitivity to nitrofurantoin is a contraindication.

Nitrofurantoin is also contraindicated in pregnant patients at term, during labor and delivery, or when the onset of labor is imminent. It is also contraindicated in infants under one month of age.

Warnings

This antibiotic has the same acute warnings as all of the others. Hypersensitivity reactions may include the sudden onset of dyspnea, chest pain, cough, fever, and chills. These symptoms normally resolve within 24–48 hours after discontinuation of therapy.

There are chronic symptoms that occur due to prolonged use of this medication. These reactions are characterized by insidious development of dyspnea, nonproductive cough, and malaise after 1–6 months of therapy. The symptoms will regress after a few weeks of discontinuation of therapy, however the pulmonary function may be permanently impaired.

Pregnancy

Nitrofurantoin is in pregnancy category B. Tests in animals have resulted in growth retardation and minor malformations. Safety for use in pregnancy has not been established. Use in women of childbearing potential only when clearly needed and when the potential benefits outweigh the potential hazards to the fetus.

Lactation

Nitrofurantoin is excreted into breast milk in very low concentrations, but could affect infants with G6PD deficiency. Safety for use in the nursing mother has not been established.

Drug interactions

1. Anticholinergics increase nitrofurantoin bioavailability by delaying gastric emptying and increasing absorption.
2. Magnesium salts may delay or decrease the absorption of nitrofurantoin.
3. Administration of high doses of probenecid with nitrofurantoin decreases renal clearance and increases serum levels of nitrofurantoin. The result could be increased toxic effects.

Patient information

1. Complete the full course of therapy; do not discontinue without notifying physician.
2. Nitrofurantoin may cause GI upset; take with food or milk.
3. Nitrofurantoin may cause brown discoloration of the urine.
4. Notify your physician if fever, chills, cough, chest pain, difficult breathing, skin rash, numbness, or tingling of the fingers or toes, or intolerable GI upset occurs.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

800. Antimicrobial action

1. What is the goal of antimicrobial therapy?
2. What is the difference between bacteriostatic and bactericidal?
3. What factors should be considered before beginning antimicrobial therapy?

801. Penicillins and cephalosporins

1. What are the four groupings of penicillins?
2. What are the disadvantages to using penicillin?
3. What interaction occurs between penicillins and oral contraceptives?
4. Into what types of groupings are cephalosporins divided?
5. Why is caution used when giving cephalosporins to penicillin sensitive patients?

6. What interaction occurs between cephalosporins and iron supplements?

802. Macrolides and tetracyclines

1. How do macrolides produce their action?
2. Why does pseudomembranous colitis sometimes occur in macrolide treated patients?
3. What interaction occurs between macrolides and cyclosporine?
4. How do tetracyclines produce their action?
5. In which disease states and circumstances may tetracyclines replace penicillin?
6. What may happen when tetracyclines are given during the period of a child's tooth development?

803. Sulfonamides, fluoroquinolones, aminoglycosides, and urinary tract anti-infectives

1. What type of microorganisms is not susceptible to sulfonamides?
2. What warning is given concerning sulfamethoxazole-trimethoprim and nursing mothers?
3. How does trimethoprim interact with digoxin?
4. How does sulfisoxazole interact with warfarin?
5. Describe the implications of the addition of a fluorine molecule to that of a quinolone antibiotic.
6. What do fluoroquinolones and cephalosporins have in common?

7. How do fluoroquinolones affect photosensitivity?
8. How do fluoroquinolones interact with anticoagulants?
9. Why do oral aminoglycosides have such a limited use?
10. Why shouldn't gentamycin be used for long-term therapy?
11. Can ophthalmic antibiotics affect the usage of systemic antibiotics? If so, how?
12. What are the three chemical structures of nitrofurantoin?
13. What chronic symptoms may occur with long-term nitrofurantoin use?

1-2. Miscellaneous Drug Therapy and Herbal Medications

This section covers those drugs that just didn't fit nicely into other categories. However they all have their specific niche. Each lesson in this section discusses a drug category in general, followed by a discussion of the drugs within that category. Each drug is covered like the drugs in your previous lessons: indications, contraindications, drug interactions, warnings, and patient information. This section will cover antimalarials, anthelmintics, and antivirals. After that we'll dive into the newest and least regulated medicines on the market—herbals.

804. Antimalarials

Malaria has been one of the most fatal diseases in human history from ancient times to the present. It has been a major factor in a number of wars. As recently as the nineteenth century, it was widespread in Canada and the United States. Though it is now rare in the United States, malaria is still a major disease in many tropical countries and a concern for people traveling to them.

Malaria is caused by the *Plasmodium* species of protozoa (specifically *P. vivax*, *P. ovale*, and *P. falciparum*). Sporozoites are introduced into the body through the "bite" of a female mosquito. The sporozoites travel to the liver where they develop. When they have matured to merozoites, they are released into the blood stream, and malaria symptoms appear. Drugs that are used against malaria act at the stage when the merozoites are released into the blood.

Among the antimalarial agents, the quinoline derivatives are still the most important. Quinine was the first to be discovered in the 1600s. Quinine is derived from the bark of the cinchona tree. Its isomer, quinidine, is used primarily as an antiarrhythmic agent but is also used in cases of severe malaria. Quinacrine was developed for use against malaria in World War II. Chloroquine and hydroxychloroquine were also developed during World War II and were found less toxic than

quinacrine. Mefloquine was developed during the Vietnam War to combat the now resistant *Plasmodium falciparum*. There are some non-quinoline derivatives used today to treat malaria. You may see doxycycline, clindamycin, tetracycline, and a few others; however, our focus will stay with the quinoline derivatives though. This lesson will cover three quinoline derivatives, quinine, chloroquine, and mefloquine.

Quinine, chloroquine, and mefloquine

Quinine, chloroquine, and mefloquine are synthetic antimalarial agents, active against asexual erythrocytic forms of most strains of *Plasmodium malariae*, *P. ovale*, *P. vivax*, and *P. falciparum*. They are used to treat malaria and, occasionally, rheumatoid arthritis and discoid lupus, although these conditions require much higher doses than for malaria. Hydroxychloroquine is preferred over these agents for non-malaria uses because it is less toxic. These agents are thought to work by raising intracellular pH, causing parasite death.

Indications and dosage

Quinine is indicated for treatment of chloroquine resistant malaria. Both chloroquine and mefloquine are indicated for the prophylaxis and treatment of malaria. The different agents treat different strains, however the general indication of malaria is what we need to know. The next table gives the other pertinent information about these medications.

Drug	Dosage form	Prophylactic dose	Acute Dose
Quinine	200, 260, 325 mg capsules; 260 mg tablets	N/A	260 to 650 mg three times daily for 6–12 days.
Chloroquine	250, 500 mg tablets; 5mg injection (equal to 200mg)	300 mg weekly (same day) beginning one to two weeks prior to exposure and continuing until four weeks after exposure.	600 mg initially and 300 mg six hours later. 300 mg daily for two more days.
Mefloquine	250 mg tablets	250 mg once weekly for four weeks, then 250 mg every other week; starting one week before and ending four weeks after a malarial area.	1,250 mg single dose, with food and 240 ml of water.

Contraindications

Hypersensitivity to any of the quinoline products or related compounds is the main contraindication for these medications. Also, patients who are deficient in glucose-6-phosphate dehydrogenase (G6PD), have optic neuritis, tinnitus, or a history of blackwater fever should not use these medications. Patients who experience any visual field changes should not use chloroquine.

Warnings

Repeated doses of quinine may cause cinchonism, with symptoms being tinnitus, headache, nausea, and slightly disturbed vision.

Pregnancy

Quinine is in category X. It has an oxytocic action. Chloroquine and mefloquine are in category C. There are no adequate and well-controlled studies in pregnant women. Use during pregnancy only if potential benefit justifies potential risk to the fetus. Warn women of childbearing potential traveling to areas where malaria is endemic against becoming pregnant and to practice reliable contraceptive measures during prophylaxis and for two months after the last dose.

Lactation

Quinine and chloroquine are excreted in breast milk in small amounts. No adverse effects have been reported in the nursing infant. Mefloquine is also excreted in breast milk. Because of the potential for

serious adverse reactions in nursing infants from mefloquine, the provider needs to decide whether to discontinue the drug, taking into account the importance of the drug to the mother.

Drug interactions

The following table lists the drug interactions for all three of these medications.

Drug	Drug	Interaction
Aluminum antacids	Quinine	Aluminum-containing antacids may delay or decrease absorption of concurrent quinine
Cimetidine	Quinine, chloroquine	Cimetidine may reduce quinine and chloroquine's oral clearance and increase its elimination half-life.
Oral anticoagulants	Quinine	Quinine may depress the hepatic enzyme system that synthesizes the vitamin K dependent clotting factors and thus may enhance the action of warfarin and other oral anticoagulants.
Digoxin	Quinine	Digoxin serum concentrations may be increased by concurrent quinine.
Beta-blockers	Mefloquine	ECG abnormalities or cardiac arrest may occur with concurrent mefloquine.
Valproic acid	Mefloquine	Valproic acid and concurrent mefloquine resulted in loss of seizure control and lower than expected valproic acid blood levels.
Kaolin or magnesium trisilicate	Chloroquine	GI absorption of chloroquine may be decreased by concomitant administration of these agents.

Patient information

1. Mefloquine may produce dizziness; patients should observe caution while driving or performing other tasks requiring alertness and physical dexterity.
2. Take with food or after meals to minimize GI irritation.
3. Medication may cause diarrhea, nausea, stomach cramps or pain, vomiting or ringing in the ears; notify physician if these become pronounced.
4. May produce blurred vision, vertigo, restlessness, confusion, or dizziness; patients should observe caution while driving or performing other tasks requiring alertness.
5. Stop the drug if there is any evidence of allergy such as flushing, itching, rash, fever, stomach pain, difficult breathing, ringing in the ears, and vision problems.
6. Report visual disturbances or difficulty in hearing or ringing in ears to physician.

805. Anthelmintics

The term *anthelmintic* is often restricted to drugs acting locally to expel parasites from the gastrointestinal tract. However, there are several types of worms that penetrate other tissues. The drugs that act on these parasitic infections are also known as *anthelmintics*. In addition, drugs that kill intestinal worms also are referred to as *vermicides*. Those that affect the worm in such a manner that peristaltic activity or catharsis expels it from the intestinal tract are referred to as *vermifuges*. This optional division serves no useful purpose because many anthelmintics manifest both actions, according to the dose given. Consequently, the anthelmintics are defined more properly as drugs used to combat any type of helminthiasis.

In this lesson we cover two anthelmintic agents: mebendazole and pyrantel.

Mebendazole

Mebendazole is an oral, broad-spectrum, synthetic anthelmintic agent that is structurally similar to thiabendazole. Mebendazole is particularly effective against susceptible GI nematodes, such as whipworms, pinworms, and hookworms and, along with pyrantel pamoate, is considered the drug of

choice in treating infections caused by these nematodes. Mebendazole inhibits the formation of the worms' microtubules and irreversibly blocks glucose uptake by the susceptible helminths, thereby depleting endogenous glycogen stored within the parasite that is required for survival and reproduction of the helminth. Mebendazole does not affect blood glucose concentrations in the host.

Indications and dosage

Mebendazole is indicated in the treatment of the following conditions:

1. Ascariasis (roundworm).
2. Enterobiasis (pinworm).
3. Uncinariasis (hookworm).
4. Trichuriasis (whipworm).

Dosing for mebendazole is pretty simple:

1. The same dosage schedule applies to children and adults.
2. Tablets may be chewed, swallowed, or crushed and mixed with food. No special procedures, such as fasting or purging, are required.
3. If the patient is not cured three weeks after treatment, a second treatment course is advised.

For whipworm, roundworm, and hookworm infection the dosage is one 100-mg tablet in the morning and evening for three consecutive days. For pinworm, a single 100-mg dose given once is sufficient.

Contraindications

Once again, the only contraindication to mebendazole is a hypersensitivity to the drug itself.

Warnings

Pregnancy

Mebendazole is in pregnancy category C. Animal studies have revealed embryotoxic and teratogenic effects in pregnant rats; however, in women who inadvertently ingested mebendazole during early pregnancy, fetal effects were no different than those found in the normal population. The potential risk to the fetus must be weighed against the potential benefits of using mebendazole.

Lactation

It is not known whether mebendazole is excreted in breast milk. Because many drugs are excreted in breast milk, exercise caution when mebendazole is administered to a nursing woman.

Drug interactions

Carbamazepine and hydantoin may reduce the plasma levels of concomitant mebendazole, possibly decreasing its therapeutic effect.

Patient information

This medication is not for infants under the age of two years. For all patients, convey the following directions:

1. Practice proper hygiene methods to prevent reinfection or infection of other family members. Shower and wash hands and fingernails often. Change and launder bedclothes, linens, and undergarments daily. Disinfect toilets daily, and damp mop floors often to reduce the number of worm eggs.
2. Pinworms spread easily to others. Treatment of family members is usually necessary to get rid of pinworms.
3. Take exactly as directed for the complete length of time prescribed, even if you feel better. Mebendazole works best when you keep a constant amount in your body (blood) at all times.

Try to space doses evenly throughout the day and night (if you take two doses a day, they should be spaced 12 hours apart), and take doses at the same time each day. It is very important that you complete the full course of treatment. Do not stop taking except on your health care provider's advice. Parasite (worm) death can be slow. It may take several days after treatment to remove all parasites from the intestines. Retreatment is recommended if you are not cured in three weeks.

4. Take missed doses as soon as possible after the dose was due, but do not take it if it is nearly time for your next dose; do not double your dose or take extra doses. Space missed doses four to five hours apart if you take two doses per day, or 10 to 12 hours apart if you take one dose per day. Consult your health care provider or pharmacy if you need help adjusting your dosing schedule.
5. Mebendazole works best if you chew or crush tablets before swallowing. For children, tablets may be crushed and mixed with food (like applesauce or pudding).
6. Take with food or milk. Mebendazole works best when taken with food, especially fatty foods such as whole milk, cheese, or ice cream.

Pyrantel

Pyrantel is an anthelmintic first developed for use in veterinary practice. It is effective against various intestinal helminths in both animals and humans, and very little toxicity has been associated with its use. Pyrantel is a depolarizing neuromuscular blocking agent. Its use results in spastic paralysis of the worm. It also inhibits cholinesterases. Pyrantel is available as oral tablets and as a suspension.

Indications and dosage

Pyrantel is indicated in the treatment of the following conditions:

1. Ascariasis (roundworm).
2. Enterobiasis (pinworm).
3. Trichuriasis (whipworm).
4. Uncinariasis (hookworm).

Dosing consists of a single dose of 11 mg/kg. Maximum total dose is 1 g. It may be administered without regard to ingestion of food or time of day. Purging is not necessary. Pyrantel may be taken with milk or fruit juices.

Contraindications

Pyrantel should be used with caution in patients with hepatic disease or impairment because the small amount of absorbed drug is metabolized by the liver.

Warnings

Taking pyrantel during pregnancy has not revealed any harmful fetal effects in animal studies.

Pyrantel should be used with caution in pregnant women. Pregnant women who plan to self-medicate should do so under a health care provider's supervision, and the potential risk to the fetus must be weighed against the potential benefits of using pyrantel. There are no statements concerning pyrantel use and lactation.

Drug interactions

A possible interaction occurs between pyrantel and theophylline. Theophylline levels have increased in some patients taking pyrantel.

Patient information

This medication is not for infants under the age of two years. For all patients, convey the following directions:

1. Practice proper hygiene to prevent reinfection or infection of other family members. Shower and wash hands and fingernails often. Change and launder bedclothes, linens, and undergarments daily. Disinfect toilets daily, and damp mop floors often to reduce the number of worm eggs.
2. Pinworms spread easily to others. Treatment of family members is usually necessary to get rid of pinworms. Ask your pharmacy for a patient package insert describing the symptoms, identification, treatment, and prevention of pinworms.
3. Take exactly as directed (take the entire dose of pyrantel). Pyrantel may be taken with food, milk, juice, or on an empty stomach at any time during the day. The suspension may be mixed in a beverage or semi-solid food (applesauce or pudding) just before taking.
4. Consult your health care provider if symptoms do not improve or become worse after a few days. It can take several days after treatment to remove all parasites from the intestines. Retreatment one week after the initial treatment is recommended for severe infections or if worms remain after treatment.

806. Antivirals

The number of antiviral drugs has increased dramatically over the past decade, largely in response to human immunodeficiency virus (HIV). This section will cover some of these drugs. Viruses consist of either double or single strands of DNA or RNA enclosed in a protein coat called a capsid. Some viruses also possess a lipoprotein envelope that, like the capsid, may contain antigenic proteins. Some viruses contain enzymes that initiate viral replication inside a host cell. Since viruses have no metabolic mechanisms of their own, they usurp the mechanism of the host cell. Effective antiviral agents must inhibit virus-specific replicative events or inhibit the synthesis of the virus. Our discussion of antivirals will cover two broad classes and a couple of drugs in each of those classes. First we'll look at antiherpes agents and then antiretroviral agents.

Antiherpes agents

We touched on the disease "shingles" earlier in the course, but didn't describe any therapy at that time. I reserved conversation on these agents until now because they just fit here better. Infection with herpes simplex virus type 1 (HSV-1) causes diseases of the mouth, face, skin, esophagus, or brain. Herpes simplex virus type 2 (HSV-2) usually causes infection of the genitals, rectum, skin, hands, or meninges. Our discussion of antiherpes drugs will cover acyclovir, valacyclovir, famciclovir, and penciclovir. You'll see as we go on that I'll group these logically for you.

Acyclovir and valacyclovir

These two agents are grouped together because valacyclovir is converted to acyclovir during the "first pass effect." It can also be said that valacyclovir is a *prodrug* of acyclovir. They are twice as effective against HSV-1 as they are against HSV-2. Acyclovir inhibits viral DNA synthesis through infiltrating HSV-infected cells and becoming activated by the specific cellular enzymes in these cells. The acyclovir disrupts DNA replication and the HSV infected cell dies.

Indications and dosage

These agents are indicated for the initial and recurrent treatment of HSV-1 and HSV-2. Acyclovir is also indicated for varicella zoster virus (shingles). The dosing is listed in the table below.

Drug	Indication		
	HSV-1 and 2 (initial)	HSV-1 and 2 (recurrent)	Varicella zoster
Acyclovir	200 mg every four hours, five times daily for 10 days.	400 mg twice daily for 12 months	800 mg every four hours, five times daily for 7–10 days
Valacyclovir	1 gm three times daily for seven days.	500 mg twice daily for five days.	NA

Contraindications

The listed contraindications for these drugs are hypersensitivity to acyclovir or any of its components and patients with advanced HIV infection.

Warnings

1. Testicular atrophy has occurred with long-term therapy (six months). Some recovery of potency may return 30 days after stopping medication.
2. Acyclovir is in pregnancy category C and valacyclovir is in B. There are no well-controlled studies however, fetal abnormalities and maternal toxicity has occurred when acyclovir has been used during pregnancy.
3. Acyclovir concentrations in breast milk in women following oral administration have ranged from 0.6 to 4.1 times corresponding plasma levels. These concentrations would potentially expose the nursing infant to a dose of acyclovir up to 0.3 mg/kg/day. Exercise caution when administering to a nursing woman. There is no experience with valacyclovir.

Drug interactions

There aren't many interactions for these medications, but they are different. They are explained in the following table.

Drug	Interaction
Acyclovir	Probenecid increases the bioavailability of acyclovir and may increase its half-life. Concurrent use of zidovudine and acyclovir may cause severe drowsiness and lethargy.
Valacyclovir	Administration cimetidine and probenecid, separately or together, reduced the rate, but not the extent, of conversion of valacyclovir to acyclovir. The renal clearance of acyclovir was reduced.

Patient information

1. For herpes zoster, advise patients to initiate treatment as soon as possible after a diagnosis of herpes zoster. There are no data on treatment initiated > 72 hours after onset.
2. For recurrent genital herpes, tell patients to avoid contact with lesions and to avoid intercourse when lesions or symptoms are present to avoid infecting others. If medical management of herpes recurrence is indicated, advise patients to initiate therapy at the first sign or symptom of an episode.

Famciclovir and penciclovir

Just like the previous antivirals, these two drugs are grouped together because famciclovir is the prodrug of penciclovir. Penciclovir is similar to acyclovir in its spectrum of activity and potency against HSV and varicella but it isn't absorbed well orally. These two work very similar to acyclovir in inhibiting DNA. Penciclovir isn't as potent as acyclovir, but it stays active in higher blood concentrations longer.

Indications and dosage

In its oral form famciclovir is approved for the treatment of localized herpes zoster. Famciclovir given at 500 mg three times daily for seven days is as effective as conventional acyclovir treatment. Famciclovir and topical and intravenous formulations of penciclovir are undergoing clinical trials in various herpes virus infections.

Contraindications

Once again, the only listed contraindication is in patients who have shown sensitivity to these drugs or any of their components.

Warnings

1. These drugs are in category B for pregnant women. There are no adequate and well-controlled studies in pregnant women. Use during pregnancy only if the benefit to the patient clearly exceeds the potential risk to the fetus.
2. It is not known whether famciclovir is excreted in breast milk. Because of the potential for tumorigenicity shown for famciclovir in rats, the provider must decide whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Drug interactions

1. The concurrent use of famciclovir with probenecid may result in increased levels of penciclovir.
2. After a single dose of digoxin and famciclovir, the concentration of digoxin increased by 19 percent.

Patient information

1. Famciclovir may be taken without regard to meals.
2. For herpes zoster, begin medication as soon as herpes zoster is diagnosed.
3. For genital herpes, inform patients that famciclovir is not a cure for genital herpes. There is no data evaluating whether famciclovir will prevent transmission of infection to others. As genital herpes is a sexually transmitted disease, patients should avoid contact with lesions or avoid intercourse when lesions or symptoms are present to avoid infecting partners. Genital herpes can also be transmitted in the absence of symptoms through asymptomatic viral shedding.

Antiretroviral agents

All of the currently approved antiretroviral agents are divided into two distinct mechanisms of action. The first group, the nucleoside reverse transcriptase inhibitors, acts by inhibiting the RNA-dependent DNA polymerase of HIV. This enzyme converts the viral RNA genome into a double stranded DNA copy prior to it integrating the cell during the replication cycle. This action blocks acute infection of the cells but is minimally effective in chronically infected ones. Despite their common mechanism of action, antiretroviral agents differ substantially in their pharmacologic properties, including intracellular pathways and toxicologic profiles. Available since 1987, zidovudine was the first agent shown to provide clinically important benefits. Since then, a large number of comparative and combination studies have been undertaken.

The second type of antiretroviral medication, protease inhibitors, acts by not allowing the HIV protease to work. HIV protease splits the viral polyprotein generating functional proteins that allow the virus to mature. The protease inhibitor stops the splitting, thus keeping the virus in an immature (turned-off) state. It is important to note that these agents are never used alone. Dual or triple combination "cocktails" are given to reduce the possibility of resistance.

These drugs are so complicated and so rarely used in our facilities that this is as far as we need to go. The table below lists some of the medications and their category.

Protease inhibitors	Nucleoside reverse transcriptase inhibitors
Saquinavir	Didanosine
Ritonavir	Lamivudine
Indinavir	Stavudine
Nelfinavir	Zalcitabine
Amprenavir	Zidovudine
	Abacavir

807. Herbal medications

Almost overnight, herbal remedies have become a major factor in American health care. Botanicals with names like Ginseng, St. John's Wort, and Ma huang have suddenly become household words throughout the United States. The majority of today's herbal remedies exhibit varying degrees of therapeutic value. Some seem genuinely useful, while others can be very dangerous. As the use of unfamiliar botanicals spreads, the need to steer patients towards the few truly useful preparations and warn them of ineffective and dangerous alternatives is becoming an increasingly significant priority. We don't have time nor space to cover every herbal medication in this course, so what we'll do is cover some of the most used and recognizable herbals so that you can be familiar with them. We'll talk about the herbals use, dosing, and any contraindications or side effects. As for drug interactions (e.g., alcohol may cause excessive drowsiness when taken with herbal medications) we need to know this about *ALL* herbal medications: The drug interactions for herbal medications will be extremely close to those of the prescription medications used to treat similar disorders. For example, St. John's Wort works in a similar manner to MAO inhibitors and SSRIs. It makes sense then, that the drug interactions would be very similar to drugs such as sertraline. With that said, let's jump into our discussion of some of the top herbal sellers.

Echinacea purpurea

Echinacea is an extremely popular herbal. In fact, it is the number one seller among herbal medications. It is reported to accelerate the healing of wounds and has produced immune effects when given internally or parenterally. Some of the effects include an increase in the number of white blood cells and spleen cells, increase in the capacity for phagocytosis, elevation of body temperature, reproduction of T-helper cells, and production of cytokines (helpful in treating inflammation).

Dosing

The recommended oral dose of echinacea is 300 mg three times daily.

Contraindications

Reports recommend that echinacea not be used in systemic diseases such as tuberculosis, leukosis, collagenosis, multiple sclerosis, AIDS, HIV infections, or any other autoimmune diseases.

Drug interactions

First, please refer to the general discussion on herbals. Because echinacea stimulates the immune system, it may alter the effects of these drugs:

1. Anabolic steroids.
2. Amiodarone.
3. Methotrexate.
4. Ketoconazole.
5. Cyclosporine.

St. John's Wort

St. John's Wort is used as a mild antidepressant and anxiolytic. Studies have demonstrated that the antidepressive effect may be due to the presence of a monoamine oxidase inhibiting function in the active agents. More recent studies have indicated that the antidepressive effect may be largely due to the ability of the herb to inhibit the reuptake of serotonin. Topically, St. John's Wort has shown anti-inflammatory properties due to its flavonoid content.

Indications and dosing

St. John's Wort is indicated for anxiety, depression, and inflammation of the skin. The average internal daily dosage is 2 to 4 grams, and the external dose is 0.2 to 1.0 mg of total product. At higher doses, photosensitization may occur.

Drug interactions

If St. John's Wort is taken with other photosensitizers (such as tetracycline), individuals may burn faster when exposed to the sun. Other drugs that can interact with this drug are:

1. Digoxin.
2. Cyclosporine.
3. Oral contraceptives.

Of course, we must remember our general warning; St. John's Wort has been linked with serotonin syndrome, a serious condition involving fever, sweating, dizziness, and other symptoms when taken with other Selective Serotonin Reuptake Inhibitors (sertraline, fluoxetine, paroxetine).

Ginkgo Biloba

Studies suggest that Ginkgo may improve circulation, memory, and mental function. A component of Ginkgo has a potent inhibitory effect on the platelet-activating factor by displacing it from its receptor sites. In studies Ginkgo has improved glucose utilization and membrane stabilizing and has reduced blood viscosity. Ginkgo increases blood flow to the brain and throughout the body's network of blood vessels that supply blood and oxygen to the organ systems. It increases metabolism efficiency, regulates neurotransmitters, and boosts oxygen levels in the brain which uses 20 percent of the body's oxygen.

Indications and dosage

Ginkgo's indications include

1. Organic brain dysfunction.
2. Intermittent claudication.
3. Vertigo (vascular origin).
4. Tinnitus (vascular origin).

Drug interactions

OK, let's review. Ginkgo reduces blood viscosity and inhibits platelets. What will that interact with?

1. Aspirin.
2. Dipyridamole.
3. Ticlopidine.
4. Warfarin.

Ginseng

Ginseng is the most famous Chinese herb. It is the most widely recognized plant used in traditional medicine. Various forms of ginseng have been used in medicine for more than 7,000 years. Several

species grow around the world, and though some are preferred for specific benefits, all are considered to have similar properties as an effective general rejuvenator.

Ginseng contains vitamins A, B-6 and the mineral Zinc, which aids in the production of thymic hormones, necessary for the functioning of the defense system. The main active ingredients of ginseng are the more than 25 saponin triterpenoid glycosides called "ginsenosides." These steroid-like ingredients provide the adaptogenic properties that enable ginseng to balance and counter the effects of stress. The glycosides appear to act on the adrenal glands, helping to prevent adrenal hypertrophy and excess corticosteroid production in response to physical, chemical, or biological stress.

Indications and dosage

The listed indication for Ginseng is the lack of stamina. The average daily dosage is 1 – 2 grams of ginseng root.

Drug interactions

The drug interactions for Ginseng are:

Drug	Interaction
Warfarin	It may increase anticoagulant effects.
Phenelzine	Headache, trembling, and mania may occur.
Digoxin	It may cause monitoring of digoxin response to be altered.

Kava kava

Kava kava is the most relaxing botanical herb with exception of the opium poppy. Pharmacological studies show Kava kava's active ingredients, kavalactones, produce physical and mental relaxation and a feeling of well being. It has also been used in the treatment of ailments of the genitourinary tract including vaginitis, gonorrhea, and menstrual cramps. Kava is a diuretic and an anti-inflammatory, thus useful for gout, rheumatism, bronchial congestion, cystitis, and prostatitis. It is an effective local anesthetic and pain reliever when applied externally as a liniment. The relaxed state and sharpening of senses also contribute to an aphrodisiac effect.

Contraindications, indications and dosage

This drug is contraindicated in patients with endogenous depression because it increases the danger of suicide. It is also contraindicated in pregnancy and nursing mothers. Kava kava is used for nervous anxiety, stress, and restlessness. The average daily dosage is 60 – 120 mg.

Drug interactions

Kava kava may potentiate the effectiveness of substances that act on the central nervous system such as alcohol, barbiturates, and most other psychopharmacological agents.

Saw Palmetto

Saw Palmetto inhibits androgen and estrogen receptor activity and may be beneficial for both sexes in balancing the hormones. Because of its hormonal effects it can aid the thyroid in regulating sexual development and normalizing activity of those glands and organs.

For men, Saw Palmetto treats an enlarged and weakened prostate gland. It has shown significant action in treatment of conditions associated with benign prostatic hypertrophy (BPH). Saw Palmetto extract works to prevent testosterone from converting into dihydrotestosterone, the hormone thought to cause prostrate cells to multiply, leading to an enlarged prostate. It is chiefly used as a diuretic and to tone the bladder by improving urinary flow, and relieving strain. Regular use of saw palmetto may decrease urinary frequency, especially during the night, by allowing complete bladder expulsion and reducing inflammation of the bladder and enlarged prostrate.

Women have used the herb to stimulate breast enlargement and lactation as well as treating ovarian and uterine irritability. It has been prescribed for reduced or absent sex drive, impotence, and frigidity. Because of its potential hormonal effects, pregnant women should not use it.

Indications and dosage

The listed indications for Saw Palmetto are prostate complaints and irritable bladder. The average daily dose is 1 – 2 grams of the drug or 320 mg of lipophilic ingredients (concentrated materials extracted with ethanol).

Drug interactions

There are no listed interactions for this medication. One important note however, Saw Palmetto drastically decreases the amount of prostate-specific antigens (PSA). The test for prostate cancer depends on the presence of these antigens. As men self-medicate to treat urinary conditions, they may be masking the presence of prostate cancer.

Ephedra/Ma huang

Ephedra contains two alkaloids, ephedrine and pseudoephedrine. Ephedrine, the main constituent, is a bronchodilator and stimulates the sympathetic nervous system. It has valuable antispasmodic properties, acting on the air passages by relieving swellings of the mucous membrane.

Pseudoephedrine is a nasal decongestant and has less stimulating effect on the heart and blood pressure. Physicians use these alkaloids to treat bronchial asthma, bronchitis, emphysema, persistent coughs, wheezing, and shortness of breath. Ma huang can help the body to break fevers and clear blocked sinuses. The alkaloids are also effective in treating allergic skin reactions such as hives, relieve general body pain, and treat low blood pressure, rheumatism, and narcolepsy.

Because of its stimulating effect on the nervous system, Ephedra can be found in some popular weight loss and energy products. For dieters it suppresses the appetite and stimulates the thyroid gland, which stimulates metabolism. Recently Ma huang has been the subject of scientific research for obesity because of its thermogenic fat-burning effect on dietary intake. Ephedra can cause peripheral vasoconstriction, elevation of blood pressure, and cardiac stimulation, and is often combined with other tonic herbs to help counteract these effects.

Ma huang is also found in “energy” products that may give athletes extra energy without draining their reserves. People also indicate an increase in alertness and perception. Similar to the diet formulas, it is often combined with ingredients such as kola nut or guarana, which contain caffeine. Concerns over the potency of this herb and its isolated alkaloids have prompted increased regulatory scrutiny and industry label warnings. Contraindications and possible side effects should be listed on the bottle. Contraindications include general weakness, poor digestion, high blood pressure, nervousness, sleeplessness, cardiac arrhythmia, and heart disease. It should not be used if you are pregnant or nursing.

Indications and dosage

The listed indication is cough or bronchitis. It is also used to treat asthma, stimulate cardiovascular output, and as a general stimulant. The average single dose is 15 – 30 mg with a total daily dose of 300 mg being recommended.

Contraindications

This can be a very dangerous drug when used incorrectly. Any patient suffering from anxiety, high blood pressure, closed-angle glaucoma, prostate enlargement, or any type of heart trouble should avoid this drug.

Drug interactions

Numerous reciprocal actions have occurred:

Drug	Interaction
Heart glycosides	Ephedra changes the heart rhythm.
Sympathomimetics	Ephedra causes an additive effect, possibly causing toxicity.
Blood pressure medications	Ephedra raises blood pressure.

In general, this can be a very dangerous OTC medication. Any drug effecting the CNS should be evaluated against ephedra use.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

804. Antimalarials

1. List the quinolone antimalarials.
2. Which antimalarials have a prophylactic dose?
3. What is the interaction between quinine and oral anticoagulants?

805. Anthelmintics

1. What types of infestations are treated with mebendazole?
2. What type of drugs can reduce mebendazole's effectiveness?
3. How does pyrantel work?
4. What interaction occurs with pyrantel and theophylline?

806. Antivirals

1. In general how do antivirals work?
2. What is the difference between herpes simplex virus 1 and 2?

3. How are acyclovir and valacyclovir related?
4. Which antiviral isn't available orally due to poor absorption?
5. How do protease inhibitors work?

807. Herbal medications

1. Which herbal is the number one seller among herbal medications?
2. Which herbal medication is a photosensitizer?
3. What effect does Ginkgo Biloba have on platelets?
4. What vitamins and minerals does Ginseng contain?
5. Which herbal medication is often used in weight loss products?

Answers to Self-Test Questions**800**

1. To destroy or suppress the growth of infecting microorganisms so that the body's normal defense mechanisms can gain control of the infection.
2. Bacteriostatic agents inhibit bacterial growth while bactericidal agents cause bacterial cell death.
3. Patient age, other diseases, organ impairment/insufficiency, pregnancy, allergies, other concomitant drug therapy.

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1. Natural, penicillinase resistant, aminopenicillins, extended spectrum.
2. Unpredictable oral absorption, relatively high incidence of allergic reactions, and somewhat limited antibacterial spectrum.
3. The efficacy of oral contraceptives may be reduced and increased breakthrough bleeding may occur.
4. They are divided into groups called generations.
5. There is evidence of cross-sensitivity in approximately 5 – 16 percent of patients.
6. Iron supplements and foods fortified with iron reduce the absorption of some cephalosporins.

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1. They inhibit RNA-dependent protein synthesis.
2. Treatment with macrolides alters the normal flora of the colon and may permit overgrowth of clostridia, the primary cause of antibiotic-associated colitis.
3. Cyclosporin levels become elevated increasing the risk of toxicity.
4. Tetracyclines interfere with the protein synthesis of the infectious organism halting its growth and reproduction.
5. Tetracyclines are used to treat Lyme disease, brucellosis, syphilis, and gonorrhea in patients who cannot take penicillin.
6. May cause permanent discoloration of deciduous and permanent teeth.

803

1. Microorganisms that require exogenous folic acid and do not synthesize folic acid are not susceptible to the action of sulfonamides.
2. Sulfonamides are excreted into breast milk and may cause kernicterus.
3. Trimethoprim can increase digoxin serum concentrations by reducing the secretion of digoxin.
4. Sulfisoxazole can potentiate the anticoagulant effects of warfarin.
5. The addition of a fluorine molecule provides an increased potency against gram-negative organisms and broadens the spectrum to include gram-positive organisms.
6. They are both divided into generations.
7. Moderate to severe phototoxic reactions have occurred in patients exposed to direct or indirect sunlight or to artificial ultraviolet light during or following treatment with fluoroquinolones.
8. The effects of the anticoagulant may be increased.
9. They are poorly absorbed so they are used for suppression of GI bacterial flora.
10. When used long-term, the incidence of ototoxicity and nephrotoxicity increases.
11. Yes they can. Ophthalmic antibiotics can cause sensitization, which may contraindicate a drug's later systemic use in serious infections.
12. Nitrofurantoin microcrystal, macrocrystal, and monohydrate.
13. Insidious development of dyspnea, nonproductive cough and malaise after 1 – 6 months of therapy.

804

1. Quinine, chloroquine, and mefloquine.
2. Chloroquine and mefloquine.
3. The action of the anticoagulants may be enhanced.

805

1. Ascariasis (roundworm), enterobiasis (pinworm), uncinariasis (hookworm), and trichuriasis (whipworm).
2. Carbamazepine and hydantoins.
3. It paralyzes the helminth.
4. Theophylline levels may be increased.

806

1. The replicate using the mechanism of the host cell.
2. The areas of the body that they affect. Herpes simplex type 1 affects the mouth, face, skin, esophagus, or brain. Herpes simplex type 2 affects the genitals, rectum, skin, hands, or meninges.
3. Valacyclovir is a prodrug of acyclovir.
4. Penciclovir.
5. They block the action of the HIV protease, which is vital to the maturation of the cell.

807

1. Echinacea.
2. St. John's Wort.
3. Ginkgo inhibits platelet forming by displacing it from its receptor sites.
4. Vitamins A and B-6, the mineral Zinc.
5. Ephedra.

Do the Unit Review Exercises (URE) before going to the next unit.

Unit Review Exercises

Note to Student: Consider all choices carefully, select the *best* answer to each question, and *circle* the corresponding letter. When you have completed all unit review exercises, transfer your answers to ECI Form 34, Field Scoring Answer Sheet.

Do not return your answer sheet to ECI.

1. (800) What is the goal of antimicrobial therapy?
 - a. Provide an aseptic environment in the body.
 - b. Suppress microorganism reproduction so that the infection dies off naturally.
 - c. Eradicate all microorganisms from the body so that body functions may return to normal.
 - d. Destroy or suppress the growth of infecting microorganisms so that the body's normal defenses can gain control.
2. (800) Which of the following is NOT a way that antimicrobial agents exert bacteriostatic or bactericidal effects?
 - a. Disrupting bacterial DNA.
 - b. Inhibition of protein synthesis.
 - c. Inhibition of essential metabolite synthesis.
 - d. Disrupting bacterial membrane permeability.
3. (800) What classification is given when staining dye is applied to the bacterial cell and is clearly visible under microscopic inspection?
 - a. Broad spectrum.
 - b. Narrow spectrum.
 - c. Gram positive.
 - d. Gram negative.
4. (800) Which of the following is a host factor that must be considered before initiating antimicrobial therapy?
 - a. Organ impairment.
 - b. Drug penetration.
 - c. Infection location.
 - d. Elimination rate.
5. (801) What antibiotic was the first to be commercially produced?
 - a. Penicillin.
 - b. Ampicillin.
 - c. Cephalexin.
 - d. Erythromycin.
6. (801) How are penicillins grouped?
 - a. Allergic reactions.
 - b. Rate of absorption.
 - c. Spectrum of activity.
 - d. Route of administration.
7. (801) What does beta-lactamase do?
 - a. Renders penicillin useless.
 - b. Extends the spectrum of penicillins.
 - c. Reduces allergic reactions to penicillins.
 - d. Reduces the incidence of penicillin-induced diarrhea.

8. (801) What must be present in a bacterial cell in order for penicillin to be effective?
 - a. Penicillinase.
 - b. Beta-lactamase.
 - c. Actively growing cells.
 - d. Double-stranded DNA.
9. (801) What interaction results when probenecid is given concomitantly with penicillin?
 - a. Higher and prolonged penicillin blood levels.
 - b. Decreased penicillin blood levels.
 - c. Penicillin levels approach toxicity.
 - d. Penicillin is inactivated.
10. (801) Which of the following drugs is a penicillinase resistant penicillin?
 - a. Amoxicillin.
 - b. Ampicillin.
 - c. Oxacillin.
 - d. Piperacillin.
11. (801) Which form of penicillin is the dosage form of choice in severe infections when rapid and high penicillin levels are required?
 - a. Ampicillin.
 - b. Carbenicillin.
 - c. Penicillin V.
 - d. Penicillin G.
12. (801) To which class of antibiotic does penicillin have cross-allergenicity?
 - a. Cephalosporins.
 - b. Tetracyclines.
 - c. Sulfonamides.
 - d. Macrolides.
13. (801) Which of the following cephalosporins is indicated in the treatment of otitis media?
 - a. Cephalexin.
 - b. Cefazolin.
 - c. Cephapirin.
 - d. Cefoxitin.
14. (801) Into which generation does Cefpodoxime fall?
 - a. First.
 - b. Second.
 - c. Third.
 - d. Fourth.
15. (801) What interaction occurs when cephalosporins and anticoagulants are given concomitantly?
 - a. Cephalosporins are inactivated.
 - b. Cephalosporin levels may reach toxicity.
 - c. Hypothrombinemic effects of anticoagulants may be increased.
 - d. Hypothrombinemic effects of anticoagulants may be decreased.
16. (802) Which macrolide is indicated in the treatment of UTIs?
 - a. Azithromycin.
 - b. Clarithromycin.
 - c. Dirithromycin.
 - d. Erythromycin.

17. (802) What interaction occurs between macrolides and digoxin?
 - a. Digoxin concentrations may be elevated.
 - b. Digoxin concentrations may be decreased.
 - c. Macrolides may be less effective.
 - d. Macrolide levels may reach toxicity.
18. (802) Which class of antibiotic is considered to be the first truly "broad spectrum" antibiotic?
 - a. Cephalosporins.
 - b. Macrolides.
 - c. Penicillins.
 - d. Tetracyclines.
19. (802) How do tetracyclines perform their function?
 - a. Interference with cell wall formation.
 - b. Interference with protein synthesis.
 - c. Destruction of cellular DNA.
 - d. Destruction of cellular wall.
20. (802) What effect does food and/or milk have on the GI absorption of most oral tetracyclines?
 - a. No effect on absorption.
 - b. Absorption is increased by approximately 50 percent.
 - c. Absorption is reduced by approximately 50 percent.
 - d. Absorption is nullified.
21. (802) What effect does tetracycline have on tooth development?
 - a. Temporary discoloration.
 - b. Permanent discoloration.
 - c. Improved resistance to tooth decay.
 - d. Decreased resistance to tooth decay.
22. (802) What interaction occurs when tetracyclines are given with iron preparations?
 - a. Iron toxicity may occur.
 - b. Tetracycline toxicity may occur.
 - c. Tetracycline absorption and effectiveness is increased.
 - d. Tetracycline absorption and effectiveness is decreased.
23. (803) What must an organism do to be susceptible to the actions of sulfonamides?
 - a. Synthesize folic acid.
 - b. Not synthesize folic acid.
 - c. Not require any folic acid.
 - d. Require exogenous folic acid.
24. (803) What antibiotic is combined with sulfamethoxazole to treat UTIs, bronchitis, and cholera?
 - a. Azithromycin.
 - b. Erythromycin.
 - c. Sulfisoxazole.
 - d. Trimethoprim.
25. (803) What is the main indication for erythromycin/sulfisoxazole?
 - a. UTIs.
 - b. Otitis media.
 - c. Bronchitis.
 - d. Sinusitis.

26. (803) Why should caution be used when giving sulfonamides with known allergic reactions to thiazide diuretics?
- The antibacterial action could enhance any allergic reaction.
 - The antibacterial action could inactivate any emergency medication.
 - The sulfonamides are structurally related and may cause similar reactions.
 - Genes causing diuretic allergies make patients hypersensitive to antibiotics.
27. (803) What type of molecule was added to an older medication to make fluoroquinolones?
- Fluoride.
 - Fluorine.
 - Quinine.
 - Quinam.
28. (803) How long does the post-antibiotic effect of fluoroquinolones last?
- 1 – 3 hours.
 - 2 – 6 hours.
 - 12 – 16 hours.
 - 20 – 24 hours.
29. (803) What interaction occurs with concomitant usage of fluoroquinolones and theophylline?
- Increased chance of fluoroquinolone toxicity.
 - Decreased fluoroquinolone effectiveness.
 - Increased chance of theophylline toxicity.
 - Decreased theophylline effectiveness.
30. (803) What class of bacteria do aminoglycosides primarily treat?
- Gram-positive.
 - Gram-negative.
 - Broad-spectrum.
 - Third generation.
31. (803) Which parenteral aminoglycoside is the most widely used?
- Gentamycin.
 - Lincomycin.
 - Tobramycin.
 - Vancomycin.
32. (803) Why is gentamycin not indicated for long-term therapy?
- Ototoxicity.
 - Allergic reactions.
 - Loss of effectiveness.
 - Weakening of the immune system.
33. (803) Which anti-inflammatory is often added to ophthalmic tobramycin to treat infections of the cornea or conjunctiva?
- Betamethasone.
 - Dexamethasone.
 - Fluticasone.
 - Triamcinolone.
34. (803) How does nitrofurantoin exert its bactericidal effects?
- By destroying bacterial RNA.
 - Interfering with protein synthesis.
 - By blocking the uptake of folic acid.
 - By interfering with bacterial carbohydrate metabolism.

-
35. (803) What bodily function may be permanently impaired following chronic use of nitrofurantoin for 1–6 months?
- Optic.
 - Renal.
 - Nervous.
 - Pulmonary.
36. (803) What class of drug increases nitrofurantoin bioavailability by delaying gastric emptying and increasing absorption?
- Anticholinergics.
 - Anticonvulsants.
 - Proton pump inhibitors.
 - Nonsteroidal anti-inflammatory drugs (NSAID).
37. (804) In what stage of the infection do malaria symptoms appear?
- Within six hours after exposure.
 - 24 hours after exposure.
 - When the sporozoites enter the bloodstream.
 - When the merozoites are released into the bloodstream.
38. (804) What was the first antimalaria drug to be discovered?
- Quinine.
 - Mefloquine.
 - Chloroquine.
 - Hydroxychloroquine.
39. (804) What isomer of quinine is also used as an antiarrhythmic?
- Quinidine.
 - Quinidine.
 - Chloroquine.
 - Mefloquine.
40. (804) How do quinine and oral anticoagulants interact?
- The anticoagulant action is decreased.
 - The anticoagulant action is increased.
 - Quinine action is decreased.
 - Quinine action is increased.
41. (805) What term is given to drugs that kill intestinal worms?
- Anthelmintics.
 - Pediculosides.
 - Vermicides.
 - Vermifuges.
42. (805) How does mebendazole perform its anthelmintic action?
- Paralyzation.
 - Chemical sterilization.
 - Blocks glucose uptake.
 - Inactivation of oxygen transformation.
43. (805) Treatment of which parasite consists of only one dose of mebendazole?
- Roundworm.
 - Hookworm.
 - Whipworm.
 - Pinworm.

44. (805) What interaction occurs between mebendazole and hydantoins?
- Hydantoin toxicity is increased.
 - Hydantoin effectiveness is decreased.
 - Mebendazole toxicity is increased.
 - Mebendazole effectiveness is decreased.
45. (805) How does pyrantel perform its anthelmintic action?
- Paralyzation.
 - Chemical sterilization.
 - Blocks glucose uptake.
 - Inactivation of oxygen transformation.
46. (805) What interaction may occur between pyrantel and theophylline?
- Increased theophylline levels.
 - Decreased theophylline levels.
 - Increased pyrantel toxicity.
 - Decreased pyrantel effectiveness.
47. (806) How is valacyclovir converted to acyclovir?
- Neurotransmitter conversion at receptor sites.
 - Enzyme breakdown in the stomach.
 - First pass effect in the liver.
 - Virus-cell metabolization.
48. (806) How does acyclovir cause herpes simplex virus cell death?
- Breaks down cell wall.
 - Destroys cellular RNA.
 - Disrupts cellular DNA replication.
 - Inhibits cellular protein synthesis.
49. (806) Which of the following antivirals is not used orally due to poor absorption?
- Acyclovir.
 - Famciclovir.
 - Penciclovir.
 - Valacyclovir.
50. (806) What interaction occurs between famciclovir and digoxin?
- The concentration of digoxin decreases.
 - The concentration of digoxin increases.
 - Famciclovir is inactivated.
 - Famciclovir toxicity is increased.
51. (806) Which of the following antiretroviral agents acts by inhibiting the DNA of HIV?
- Indinavir.
 - Ritonavir.
 - Zidovudine.
 - Saquinavir.
52. (807) What drug interaction information holds true for all herbal medications?
- Patients taking antibiotics should not use herbal medications.
 - Alcohol may cause excessive drowsiness when taken with herbal medications.
 - Liver toxicity is increased when taking acetaminophen concomitantly with herbal medications.
 - Drug interactions for herbal medications will be similar to prescription medications for the same disorder.

53. (807) Which of the following medications is most likely to interact with echinacea purpurea?
- a. Digoxin.
 - b. Dipyridamole.
 - c. Cyclosporine.
 - d. Oral contraceptives.
54. (807) Which herbal medication is considered to be the most relaxing?
- a. Ginseng.
 - b. Kava kava.
 - c. Ginkgo Biloba.
 - d. Saw Palmetto.
55. (807) Which herbal medication inhibits androgen and estrogen receptor activity to help balance hormones?
- a. Ginseng.
 - b. Kava kava.
 - c. Saw Palmetto.
 - d. Ginkgo Biloba.
56. (807) Which of the following is not a side effect of ephedra/ma huang?
- a. Peripheral vasoconstriction.
 - b. Blood pressure elevation.
 - c. Cardiac stimulation.
 - d. Drowsiness.

Please read the unit menu for Unit 2 and continue. →

Student Notes

Unit 2. Use of Emergency Drugs and Medical Devices

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CARDIAC arrest is an absent or inadequate ventricular contraction that immediately results in systemic circulatory failure. Symptoms include loss of consciousness, rapid, shallow breathing leading rapidly to apnea, profound arterial hypotension accompanied by nonpalpable pulses over major vessels, and absent heart sounds. Within several minutes, the resultant arterial hypoxemia leads to progressive cyanosis and loss of the pupillary light reflex (dilated pupils).

Cardiac arrest is a medical emergency taking precedence over all others except external hemorrhage to the point at which life can no longer be sustained or airway obstruction that should be controlled simultaneously. Cardiac arrest can result from cardiac causes (electrical dysfunction or mechanical failure), circulatory shock, or abnormalities in ventilation leading to cardiopulmonary arrest. Although either the heart or lungs may fail first, the two events usually are closely related.

2-1. Use of Emergency Drugs and Medical Devices

Life is not always predictable; sometimes situations occur that needs special treatment. The medications discussed in this unit primary are used for those emergency situations. Whether it's a cardiac emergency or a poisoning, the correct medication given at the correct time is critical. We will discuss those emergency medications, along with some other items that we sometime take for granted—medical devices.

In this section we discuss the drugs used in the treatment of cardiac arrest and its associated symptoms. There is also a short discussion on the use of some medical devices that we all should be familiar with.

808. Drugs for emergency situations

The drugs in this lesson are used in the treatment of ventricular fibrillation (VF), ventricular tachycardia (VT), bradycardia, asystole, electromechanical dissociation, and narcotic overdose.

Drugs for ventricular fibrillation or ventricular tachycardia

Lidocaine

Lidocaine remains the standard therapy for VF or VT and is used with countershock to convert VF. Onset of action is immediate after rapid IV administration, but a constant infusion is required to maintain therapeutic blood levels.

Lidocaine is a widely used antiarrhythmic. Administered parenterally, lidocaine is an effective antiarrhythmic agent and is considered the drug of choice in the treatment of acute, life-threatening ventricular arrhythmias. Recently, the drug has also been considered for use as a prophylactic agent in the prevention of arrhythmias following acute myocardial infarction.

Procainamide

Procainamide is used to treat VT unresponsive to lidocaine and to suppress ventricular ectopy, which can predispose to VF.

Procainamide is a potent antiarrhythmic agent used in the treatment of several cardiac arrhythmias including atrial fibrillation, atrial flutter, paroxysmal atrial tachycardia, and ventricular tachycardia. A derivative of the local anesthetic procaine, procainamide is similar in action to quinidine and disopyramide.

Epinephrine

Epinephrine is the first-line drug for VF when initial defibrillation fails. It is an endogenous catecholamine that is produced primarily in the adrenal medulla from norepinephrine. Epinephrine stimulates both alpha- and beta-adrenergic receptors. Nonspecific beta-stimulation, combined with moderate alpha agonism, results in inotropic (influencing the contractility of muscular tissue) effects equal to those of dopamine and dobutamine but greater chronotropic (affecting the rate of rhythmic movements, such as heartbeat) effects than either agent.

Bretylium

Ventricular fibrillation or tachycardia that is resistant to lidocaine and defibrillation, or is recurrent on lidocaine, may be treated with bretylium tosylate. Bretylium may be delivered by intermittent rapid IV injection or as a continuous infusion.

Bretylium is an intravenous antiarrhythmic. Bretylium is indicated for the treatment of ventricular fibrillation and unstable ventricular tachycardia, although it is not considered a first-line agent.

NOTE: The effects of procainamide and bretylium may be additive with lidocaine and direct current (DC) countershock in treating VF or VT.

Drugs for bradycardia, asystole, and electromechanical dissociation and miscellaneous emergency medications

The term *asystole* describes absent cardiac contraction and ECG evidence of cardiac electrical activity. Asystole is treated by IV or intra-airway administration of epinephrine. Atropine sulfate can also be given if rhythm is not restored. Intracardiac injection of epinephrine is not recommended unless IV and/or airway routes are inaccessible because of complications of pneumothorax, coronary artery laceration, cardiac tamponade, and prolonged interruptions of cardiopulmonary resuscitation (CPR).

Drugs used in the treatment of bradycardia, asystole, and electromechanical dissociation

Epinephrine

Epinephrine has combined alpha- and beta-adrenergic receptor properties and several beneficial effects during CPR. Alpha effects may augment peripheral and coronary diastolic pressure, thereby increasing perfusion to subendocardial regions during chest compressions. This may, in turn, generate electrical activity and increase the cardiac contractility, thus increasing cardiac output. Since good absorption of epinephrine occurs from the lungs, its administration should not be delayed if there is difficulty in starting an IV line. It can be administered through an endotracheal tube. Intravenous doses can be given every five minutes as needed, but it should not be administered concurrently in the same IV line with alkaline solutions.

Atropine

Atropine is a parasympatholytic that increases heart rate and conduction. It may be useful for bradyarrhythmias with myocardial ischemia.

Atropine is a naturally occurring tertiary amine extracted from belladonna alkaloid. Atropine is the prototype antimuscarinic from which other antimuscarinic agents were developed. Atropine has many uses, but it is most commonly used systemically to treat bradycardia and as a preoperative agent to reduce secretions prior to surgery.

Isoproterenol

Isoproterenol has beta-sympathomimetic action and is used to increase heart rate for a slow idioventricular rhythm in the absence of effective circulation or symptomatic bradycardia unresponsive to atropine. Excessive beta-adrenergic activity can increase myocardial oxygen consumption and worsen ventricular arrhythmias, especially if myocardial ischemia is present. When it is given in excessive doses, arterial hypotension may result from peripheral vasodilation.

Other medications used in cardiac emergencies

Propranolol, verapamil, sodium bicarbonate, calcium chloride, and naloxone are frequently used in emergency situations. There is also a short discussion of drugs used to treat circulatory shock.

Propranolol

Beta-adrenergic blockers can be used to control symptomatic supraventricular tachyarrhythmias. At times, malignant ventricular arrhythmias can also be controlled using beta-blockers, although extreme caution must be observed in patients with asthma, cardiac failure, or dependency on adrenergic support.

Propranolol is the beta-blocker that has been used most extensively. Some of the newer beta-blockers (e.g., esmolol) have a much shorter duration of action and may be more efficacious when the concern of adverse reactions is high. However, there has been relatively less experience with these newer agents.

Verapamil

Verapamil is the pharmacological agent of choice for the conversion of paroxysmal supraventricular tachycardia (PSVT). Hypotension from this drug may be treated with calcium chloride. Verapamil may also be useful in controlling other symptomatic supraventricular tachycardias, but has been associated with cardiovascular deterioration in sustained VT.

Sodium bicarbonate

Sodium bicarbonate is no longer recommended as initial, automatic therapy for cardiac arrest, since it may induce paradoxical acidosis of the brain and heart, hyperosmolality, hypernatremia or alkalemia, and may inhibit the release of oxygen by the blood. Other adjuncts (e.g., defibrillation, ventilation, cardiac compression, and drugs) should be tried first unless the cause of arrest is preexisting acidosis, hyperkalemia, or tricyclic overdose with complex ventricular arrhythmias. When it is used, administration should be dictated by arterial pH monitoring (q 5 min).

Calcium chloride

Calcium chloride is no longer recommended except in the case of hyperkalemia, hypocalcemia, or calcium channel blocker toxicity since high circulating levels of calcium may also have adverse effects. Other forms of calcium (e.g., calcium gluceptate or calcium gluconate) may be used. Caution is necessary when digitalis toxicity is a potential cause of the arrest.

Naloxone

The narcotic antagonist naloxone is clinically useful in the reversal of narcotic-induced respiratory depression. Naloxone, a pure narcotic antagonist, will precipitate abstinence syndrome in the presence of narcotic addiction. Because it is devoid of undesirable agonist properties, naloxone is preferred for reversal of narcotic-induced respiratory depression. Naloxone prevents or reverses opioid effects including respiratory depression, sedation and hypotension; it can reverse psychotomimetic and dysphoric effects of agonist-antagonists. The mechanism of action is not fully understood; however, evidence suggests that naloxone antagonizes the opioid effects by competing for the same receptor sites. Naloxone is an essentially pure narcotic antagonist (i.e., it does not possess "agonistic" or morphine-like properties). Naloxone does not produce respiratory depression, psychotomimetic

effects or pupillary constriction. In the absence of narcotics or agonistic effects of other narcotic antagonists, naloxone exhibits essentially no pharmacologic activity.

Drugs used to treat circulatory shock

Circulatory shock (hypotension following restoration of spontaneous circulation) after cardiac arrest is first treated by cautious IV volume infusions if left ventricular failure is not evident. For severe arterial hypotension unresponsive to volume replacement, the following drugs are useful in titrated doses by continuous infusion: dopamine (inotrope), epinephrine (inotrope and vasoconstrictor), norepinephrine (peripheral vasoconstrictors), or phenylephrine, with titration as needed to restore blood pressure (BP). Vasoactive drugs should be used in the minimal dose necessary to achieve a satisfactory BP since they may increase vascular resistance and decrease organ perfusion, especially in the mesenteric bed. Sometimes CPR must be resumed after resuscitation and continued until adequate ventilation, palpable pulse, and acceptable BP indicate stabilized cardiorespiratory function.

Epinephrine is the most valuable drug for the emergency treatment of severe allergic reactions. The vasoconstrictor effect of epinephrine on the capillary directly antagonizes the generalized vasodilation produced by histamine. Epinephrine reverses the increased permeability of dilated capillaries to plasma. The shock of severe allergic reaction is due to the loss of circulating blood volume by pooling in the dilated capillary beds and loss of plasma into the tissues. Epinephrine quickly restores circulating blood volume and blood pressure by constricting the capillary bed. The itching during episodes of hives or angioedema is promptly relieved by epinephrine.

Epinephrine is a powerful relaxer of the smooth muscles of the bronchioles, stomach, intestine, pregnant uterus, and urinary bladder wall. The bronchospasm, wheezing, and dyspnea of acute allergic reactions are relieved. Where abdominal cramping, defecation, or involuntary urination have occurred during severe allergic attacks, epinephrine rapidly produces relief. Subcutaneous or intramuscularly administered epinephrine has a rapid onset and short duration of action. Subcutaneous administration during asthma attacks can produce bronchodilation within five to 10 minutes, and maximal effects can occur within 20 minutes. There are two forms of epinephrine that are routinely dispensed to outpatients: anaphylaxis emergency treatment kits and epinephrine auto-injectors.

Anaphylaxis emergency treatment kit

An anaphylaxis emergency treatment kit contains the following items:

1. One syringe containing two single doses of epinephrine injection, USP, (1:1000) for intramuscular or subcutaneous injection only.
2. Four chlorpheniramine maleate, USP, 2 mg tablets.
3. Two sterilizing swabs, 70 percent isopropyl alcohol.
4. One tourniquet.
5. One patient direction sheet.

Indications

Anaphylaxis emergency treatment kits are indicated for use by adult and pediatric patients under the following conditions:

1. Allergic reactions including anaphylactic shock due to stinging insects (primarily bees, wasps, hornets, yellow jackets, bumble bees, and fire ants).
2. Severe allergic or anaphylactic reactions due to allergy injections, exposure to pollens, dusts, molds, foods, drugs, and exercise or unknown substances.
3. Severe, life-threatening asthma attacks characterized by wheezing, dyspnea, and inability to breathe.

Drug interactions

The effects of epinephrine may be potentiated by tricyclic antidepressants, levothyroxine, and antihistamines. Epinephrine should not be administered concomitantly with other sympathomimetic agents, since the effects are additive and may be detrimental to the patient.

Contraindications

Epinephrine is contraindicated in patients with the certain conditions.

1. Epinephrine is contraindicated in cardiac dilation; cardiogenic, traumatic, or hemorrhagic shock; cerebral arteriosclerosis; narrow-angle glaucoma; or organic brain damage.
2. Epinephrine should not be used to counteract circulatory collapse or hypertension due to phenothiazines, since such agents may reverse the pressor effect of epinephrine, leading to a further lowering of blood pressure.
3. Epinephrine must not be given intra-arterially, as marked vasoconstriction may result in gangrene.
4. This unit is not intended for intravenous use. Further dilution would be necessary and is not practical with this emergency syringe.
5. Intramuscular injections of epinephrine into the buttocks should be avoided since the vasoconstriction produced by the epinephrine reduces the oxygen tension of the tissues, enabling any anaerobic *Clostridium welchii* that may be present on the buttocks to multiply and possibly cause gangrene.

Patient information

For all patients, convey the following directions:

1. If an allergic reaction (as described by your health care provider) occurs, use the epinephrine injection immediately.
2. If you have used the epinephrine injection, be sure to tell the health care provider or go to the nearest hospital emergency room.
3. If you have been stung by an insect, remove the insect's stinger with your fingernails, if possible. Be careful not to squeeze, pinch, or push it deeper into the skin. Ice packs or baking soda soaks, if available, may then be applied to the area stung.
4. Specific directions for proper administration are provided with this kit. Please read entire direction sheet before an emergency arises.
5. This injection is for subcutaneous or intramuscular injection only. It is not intended for intravenous use.
6. Epinephrine is light sensitive and should be stored in the box provided.
7. Keep at room temperature; protect from freezing.
8. Do not try to force air out of the syringe until you are ready to use the epinephrine. This may rupture the seal and allow the epinephrine solution to contact the metal promoting deterioration.
9. Never remove the rubber protector over the needle until you are ready to use the syringe. This may cause the needle and contents to become contaminated. Any epinephrine solution in contact with the needle may cause rusting of the needle.
10. Periodically check the contents of the syringe. If discoloration or precipitate is present, DO NOT USE. Obtain a replacement syringe.
11. Periodically check the expiration date on the syringe. If expiration is near, re-order a new syringe and discard the outdated syringe after you receive a new one.

Epinephrine auto-injectors

The epinephrine auto-injectors contain 2 ml of epinephrine injection for emergency intramuscular use. Each epinephrine auto-injector delivers a single dose of 0.3 mg epinephrine from epinephrine injection, USP 1:1000 (0.3 mL) in a sterile solution. The pediatric epinephrine auto-injector delivers a single dose of 0.15 mg epinephrine from epinephrine injection, USP 1:2000 (0.3 mL) in a sterile solution. All of the indications, contraindications, and other information pertaining to the anaphylaxis kit epinephrine also apply to the auto-injector.

To use the epinephrine auto-injector:

1. Remove the gray safety cap first.
2. Place the black tip on the thigh, at a right angle to the leg.
3. Press hard into the thigh until the auto-injector functions. Hold in place for several seconds. Then remove the auto-injector and discard.
4. Massage the injection area for 10 seconds.

809. Use of selected medical devices

Medical devices were also hit hard with cutbacks in the past few years. Even though your pharmacy may not stock all of these items, the topics discussed in this lesson are still very relevant.

Diagnostic glucose monitoring

All diabetic patients should be instructed in self-glucose monitoring, and insulin-treated patients should be taught to adjust their insulin dosages accordingly. A variety of commercial reagent strips are available for determining the glucose concentrations in a drop of fingertip blood. The results are determined by comparing the strip with a color chart provided by the manufacturer or by using a reflectance meter that provides a numeric read-out. (Glucose concentration in fingertip blood is equivalent to that in venous plasma.) A spring-powered lancet is recommended to obtain the fingertip blood sample. The patient's testing technique should be evaluated at regular intervals. The frequency of testing is determined individually. Insulin-dependent diabetes mellitus (IDDM) patients usually monitor their plasma glucose fasting, one hour after each meal and at bedtime daily or at least twice weekly. It is desirable for patients with non-insulin-dependent diabetes mellitus (NIDDM) to monitor weekly in a similar way.

Patients with IDDM should be instructed in testing for urine ketones with commercially available reagent strips. They should be advised to test for urine ketones whenever they first develop symptoms of a cold, flu, or other concurrent illness; nausea, vomiting, or abdominal pain; polyuria; or if they find an unexpectedly high plasma glucose level upon self-glucose monitoring. Tests for ketones in all urine samples are recommended in IDDM patients who exhibit persistent, rapid, and marked fluctuations in their degree of hyperglycemia.

Insulin syringes

Insulin is routinely provided in preparations containing 100 units/mL (U-100 insulin). It is injected subcutaneously with disposable insulin syringes calibrated for use with U-100 insulin, which are commercially available with maximal capacities of 100 units (1 mL), 50 units (0.5 mL), and 30 units (0.3 mL). Patients who routinely inject doses of ≤ 50 units generally prefer the smaller syringes because they are more easily read and facilitate the accurate measurement of smaller insulin doses. A multiple-dose insulin injection device, commonly referred to as an insulin pen, is designed to use a cartridge containing several days' dosage of a semisynthetic human insulin preparation. Some diabetics who take multiple daily insulin injections prefer its convenience in transporting their insulin supplies. Remember, insulin should be refrigerated but never frozen; however, most insulin preparations are stable at room temperature for months, which facilitates their use at work and when traveling.

Condoms

Condom use, the third most common contraceptive method in the USA (after male/female sterilization and oral contraceptives), is the only reversible, effective male contraceptive method other than coitus interruptus (withdrawal). If used properly, the condom also provides considerable protection against sexually transmitted diseases and sexual transmission of HIV. The condom should not be applied tightly (the tip should overlap about ½ inch to collect the ejaculate), and must be removed carefully so that none of the contents is spilled. The failure rate with careful use is from 3 to 4 percent. Adding a spermicidal agent, either in the lubricant or by insertion into the vagina, may further lower this rate.

Vaginal foams, creams, suppositories, and sponges

These agents must be placed into the vagina before each coital act. They contain a spermicide, usually nonoxynol 9 that immobilizes or kills sperm on contact; they also provide a mechanical barrier to sperm. No single type of foam or suppository seems to be more effective than another, but the contraceptive sponge has the advantage of remaining effective for 24 hours. Its failure rate is about the same as that of the diaphragm. Efficacy with all these agents increases greatly as the woman's age increases; in women over 30 years of age, it is similar to that of the intrauterine device (IUD).

Drug delivery system for use with metered dose inhalers (MDI)

These portable drug delivery systems help metered dose inhalers deliver medication to the lungs. These systems are designed to improve the delivery of these medications making it easier for the patient to use them.

Some patients using MDIs may not be getting all their medication. MDIs do provide a convenient and effective method for delivering drugs, but it is not easy to use them correctly. Patients must carefully time each breath while squeezing the MDI downward. If their timing is incorrect, the full dose of medication may not be delivered deep into their lungs.

Portable drug delivery systems make it simpler to use MDIs correctly. There are three basic types of delivery systems used with MDIs.

Spacer

The simplest system is commonly called a "spacer." It isn't much more than a 6 inch tube, about 2 inches in diameter with a mouthpiece on one end and an MDI adapter on the other. The patient shoots the MDI medication into the tube; the extra space between the MDI and the patient's mouth keeps the medication from shooting against the back of the throat giving an increased chance for proper inhalation.

Valved-chamber

A valved-chamber system can be used. It is similar to the spacer in size and shape. However, on the mouthpiece end, inside the chamber is a one-way valve that allows air to pass in only one direction – out the back of the chamber. The mouthpiece is also adaptable to attach a mask to help administer medication to patients with special needs. The operation of this device is similar to the spacer. The patient releases the medication into the chamber and, after allowing the particles to suspend in the air inside the chamber, inhales deeply. The medication is well dispersed inside the chamber.

Bag device

There is the bag device system. The MDI medication container must be removed from its holder in order for this device to be used. The medication canister fits on top of the mouthpiece and then a plastic bag is attached. After the patient presses down on the metered dose inhaler, medication is released and stored in the bag, giving the patient a chance to breath in the medication in more than one breath. This does away with the need for careful coordination when taking a breath and releasing the spray. This system has a special feature to help teach patients better breathing techniques. When a patient is using this type of drug delivery system correctly (taking a slow, deep breath that helps get

the medication deep within the lungs), the bag collapses and the patient does NOT hear a whistling sound. But, if the patient breathes in too fast (a common mistake that can reduce the effectiveness of the treatment), he or she hears a whistling sound. This signals the patient to breathe slower. This slow breathing and holding one's breath after taking each dose of medication is necessary to obtain more complete relief.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

808. Drugs for emergency situations

1. What drugs are used to treat ventricular tachycardia and ventricular fibrillation?
2. What is asystole?
3. How is propranolol used to treat cardiac emergencies?
4. How does naloxone work?
5. What condition could result if epinephrine is given intra-arterially?

809. Use of selected medical devices

1. When should insulin-dependent diabetics test their urine ketones?
2. What are the three types of delivery systems for metered dose inhalers?

2-2. Drug and Chemical Poisonings, and First-aid for Poisonings

Worldwide, more than 9 million natural and synthetic chemicals have been identified. Fortunately, fewer than 3,000 cause more than 95 percent of accidental and deliberate poisonings. Identifying a poison and accurately assessing its potential toxicity are critical to a physician's successful management of poisoning. The physician must rely on simple general supportive treatment unless a specific "toxidrome" (toxicologic symptom complex) is pinpointed. Increasingly, physicians are depending on local or regional poison control centers for technical information, particularly concerning ingredient data (toxic potentials) and consultations.

Some pharmacies are very involved in drug and chemical poisonings when they occur. Other pharmacies simply restock antidote kits after they are used. Whatever your role, this section will be of

great assistance to you when you are involved in a poisoning situation—whether you are at home or at work in the hospital.

810. Types and effects of drug or chemical overdoses and poisonings

Poisoning should be considered in the differential diagnosis of any unexplained symptoms or signs, especially in children less than five years old. Similarly, in a young adult, any disparity between expected history and clinical findings should suggest poisoning. Recently, poisonings among the elderly (especially medication mix-ups), among hospitalized patients (drug errors), among workers exposed to occupational chemicals, and as a result of environmental pollution have been increasingly recognized. Often, the type and speed of onset of the total clinical picture will confirm or refute a suspicion of poisoning. Occasionally, the absence of a specific finding will be as important as its presence. Any pertinent history should be secured and the person and premises inspected for traces of drugs (i.e., imprint identifications on solid medication forms, alcohol, etc.) particularly for the unconscious patient.

Ingredients, first-aid measures, and antidotes often printed on product containers may be inaccurate or out of date. Information about household and industrial chemicals can be obtained through poison centers in all parts of the USA and Europe. Consultation with the centers is encouraged. The name of the nearest center is often listed under Emergency Numbers in the local telephone directory, or is available from the operator.

This lesson begins with a definition of toxicology. That is followed by a discussion of the types of poisons and poisonings, the local and systemic effects of poisons, and the routes of entry for poisons into the body.

Toxicology

Toxicology is the division of medical and biological science concerned with toxic substances. This includes detecting them, studying their chemistry and pharmacological action, establishing antidotes and treatment of toxic manifestations, preventing poisoning, and methods for controlling exposure to harmful substances.

Poisons

A poison is anything that chemically causes illness or death if it gets into or onto a human body in sufficient quantity.

Types of poisons

Poisons come in many forms—liquids, gases, and solids—and from many sources. They may be natural or synthetic. See their description in the following table.

Type	Description
Natural	Natural poisons include the toxic chemicals present in many types of plants and the venom produced by various animals (such as snakes and spiders). Toxic substances produced by various bacteria in food are also natural poisons.
Synthetic	Synthetic poisons include industrial chemicals and minerals, the chemicals used in household products, and all prescription and nonprescription drugs.

Types of poisonings

There are two types of poisonings: acute and chronic.

Type	Description
Acute	<p>Acute poisonings are normally the result of an accidental poisoning or a suicide attempt. An acute poisoning is a sudden poisoning. The effects of the poison on the body are immediate or occur shortly after the exposure. The symptoms run a short course and can be mild to severe, depending on several factors:</p> <ul style="list-style-type: none"> • Type of poison. • Amount of poison involved. • How the poison enters the body. • Length of time poison stays in the body. <p>Age, size, and health of the victim.</p>
Chronic	<p>Chronic poisoning normally involves repeated exposures to small doses of a poison. Symptoms may take months or years to develop. Identification of the cause of chronic poisoning can be extremely difficult—if it is even recognized as a poisoning.</p> <p>Chronic poisonings are normally the result of repeated exposures to toxic substances in the workplace or other environment. An example is lead poisoning in children. This type of poisoning is caused by ingestion of pieces of lead-based paint over a period of time.</p>

Local and systemic effects of poisons

Once in or on a victim's body, poisons cause damage in various ways. This damage can be divided into two categories: local effects and systemic effects.

Local effects

Local effects occur at the place where the poison entered or touched the body. For example, acid burns any skin or tissue it touches.

Systemic effects

Systemic effects involve the victim's central nervous system, breathing, blood circulation, or vital organs (particularly the liver, kidney, and lungs). These effects are the result of poisons being absorbed into the blood and carried through the body. Systemic effects are more serious than local effects, and some are life-threatening.

Many poisons can cause both local and systemic effects. They may cause damage entering the body and even more damage once they are inside the body. Even though most poisons affect several parts of the body, serious illness or death usually results from damage to one organ (e.g., the liver) or body function (e.g., breathing or blood circulation).

Routes of entry

Poisons can enter our bodies in four ways. They are discussed in the following table:

Route	Description
Absorption (through the skin or into the eyes)	A variety of substances cause damage when they come in contact with the skin or the eyes. Many of these substances can cause further damage if they are absorbed through the skin into the blood.
Ingestion (by mouth)	Almost 90 percent of all poisoning accidents involve ingested or swallowed poisons.
Inhalation (by nose or mouth)	Numerous types of inhaled gases, fumes, vapors, and dusts can cause injury. Some of these, like carbon monoxide, cause acute poisonings. Others, such as asbestos dust, cause chronic poisonings.
Injection (into the skin)	Health care providers use needles to inject medicinal drugs into our bodies. Snakes and insects inject poisons into our bodies when they bite or sting. The poison enters the skin through the snake's fangs or the insect's stinger. Many drug overdoses (intentional or accidental) involve injected poisons.

811. Providing first-aid for poisonings (outside the hospital setting)

The longer a poison is in or on the body, the more damage it does. Consequently, all poisonings are considered medical emergencies and require immediate attention. The damage a poison causes is, in large part, determined by how the poison enters the body, and first-aid measures differ with the route of entry.

In this lesson we describe first-aid for poisonings outside the hospital setting. We give instructions for ingested, inhaled, injected, and absorbed poisonings.

General first-aid for ingested poisonings

There are three general categories of ingested poisons:

<i>Corrosive (caustic) substances</i>	<i>Petroleum-like substances</i>	<i>Other substances (neither corrosive nor petroleum-like)</i>
<ul style="list-style-type: none"> • Antirust solutions • Drain cleaners • Fertilizers • Household bleaches • Metal polishes • Paint and varnish removers • Photographic developers • Refrigerants 	<ul style="list-style-type: none"> • Floor polish and wax • Furniture polish and wax • Gasoline • Kerosene • Lighter fluid 	<ul style="list-style-type: none"> • Medicines • Drugs • Plants • Food poisoning • Household products

Most accidentally ingested poisonings involve substances that are neither corrosive nor petroleum-like. The diversity of these substances is enormous and is not restricted to liquids. Some substances (such as plants that irritate the skin) may cause local effects, but the main concern following the ingestion of any substance is the possibility of systemic effects. The following is a list of general first-aid procedures for ingested poisons:

1. Check for breathing and open the victim's airway. Loosen any tight clothing.
2. Start CPR if the victim has stopped breathing.
3. Call for an ambulance and call the poison control center, physician, or hospital emergency room and follow all instructions.

4. Keep the victim warm.
5. If the victim is vomiting, turn his/her body and head to the side, and position the victim so the emesis runs out of the mouth instead of back into the stomach or lungs.
6. Save (and give to physician or emergency personnel) whatever caused the poisoning (medicine, parts of plants, household products). You should also save any emesis.

For ingested noncorrosive and nonpetroleum-like substances

First-aid for ingested noncorrosive and nonpetroleum-like substances is directed at getting the poison out of the body, which is best accomplished by making the victim vomit. Usually the best way to induce vomiting is with ipecac syrup. The following is a list of general first-aid procedures for ingested poisons that are neither corrosive nor petroleum-like:

1. Give 1 to 2 cups of water or milk if the victim is conscious and not having convulsions.
2. Call a poison control center, emergency room, or physician for instructions.
3. If you are instructed to do so, give the victim ipecac syrup. Save any vomit for examination.
4. If the victim does not vomit after you have given ipecac syrup twice, call the poison control center, emergency room, or physician for further advice.

For ingested corrosive and petroleum-like substances

Corrosives burn or destroy tissue through their chemical action. Swallowing a corrosive substance, such as an acid or an alkali, causes immediate local effects. These poisons burn the lips and skin around the victim's mouth, throat, and stomach. Absorbed into the blood, they may cause systemic effects. Acids, for example, can cause hemorrhages, and alkalis can cause difficult breathing.

The victim of ingested corrosive substances requires immediate medical attention. First-aid for this type of poisoning depends on what was ingested. One rule does apply to all corrosives—DO NOT MAKE THE VICTIM VOMIT!

Should the victim vomit the corrosive, it will again burn the sensitive lining of the throat and mouth. In some instances, demulcents (soothing substances), such as milk, egg white, aluminum hydroxide gel, gelatin solution, flour and water, or vegetable oil may dilute the corrosive. However, these should only be given to the victim as directed by a poison control center, physician, or hospital emergency room.

Likewise, the victim of an ingested petroleum-like substance should not be made to vomit. Petroleum-like products give off fumes that can cause a severe type of pneumonia, and these fumes may be inhaled into the lungs during vomiting.

First-aid for inhaled poisons

Inhaling some gases, vapors, fumes, and dusts may cause only irritation to the body's respiratory tract. However, some of these poisons cause systemic effects when they are absorbed from the lungs into the blood. For example, carbon monoxide gas has an effect on blood that prevents it from carrying oxygen.

The basic first-aid procedure for an inhaled poison is to get the victim to fresh air immediately. Artificial respiration may then be necessary. The following is a list of general first-aid procedures for inhaled poisons:

1. Move the victim away from the source of the poison to fresh air immediately.
2. Loosen the victim's clothing and open his/her airway.
3. If the victim is not breathing, begin CPR immediately. Do not stop until the victim is breathing well or help arrives.
4. Call a poison control center, physician, or emergency room for further instructions.

If you are attempting to rescue someone from smoke, gas, or chemical fumes, follow these precautions:

1. If you are alone, call for help before you attempt to rescue the victim. You, too, may be overcome by smoke, gas, or fumes.
2. Do not light a match, turn on a light switch, or produce a flame or spark in the presence of gas or fumes.
3. Before entering the area, take several deep breaths of fresh air. Then inhale deeply and hold your breath as you go in.
4. Do not attempt any first-aid measures until you are in the fresh air.

First-aid for injected poisons

The majority of injected poisons produce immediate local effects, such as pain, tenderness, and swelling at the site of the injection. Systemic effects take longer to develop and depend on the amount of poison that enters the blood.

The local effects of an injected poison can be treated with first-aid measures; treatment of systemic effects, however, requires expert medical attention. There is no way to get the poison out (sucking out snake venom is no longer recommended).

First-aid for absorbed poisons

Absorbed poisons, those that come in contact with the skin, usually cause immediate local effects. For example, acids burn the skin. Some chemicals, such as those found in insecticides, are rapidly absorbed into the bloodstream through the skin. Once in the blood, they can cause systemic effects.

On the skin

First-aid for absorbed poison is directed at getting the poison off the skin and diluting it. Speed is essential; a delay of only seconds may greatly increase the injury. Remove the substances as quickly as possible; water dilutes it and flushes it away, and removal of contaminated clothing takes any nonabsorbed chemicals away from the skin. The following is a list of general first-aid procedures for poisons on the skin.

1. Remove any contaminated clothing, including shoes and socks. Also remove jewelry, watches, or rings.
2. Flush the affected area immediately with large quantities of cool water from a shower, hose, faucet, or pail. Continue flushing for at least 15 minutes.
3. Cover the affected area with a loose, clean cloth.
4. Call a poison control center, physician, or emergency room for further instructions. Call even if the affected area is not large and is not causing the victim any pain.

In the eye

Again, speed is essential; a delay of only seconds may greatly increase the injury. The following is a list of general first-aid procedures for poisons in the eye:

1. Hold the victim's eyelids open with your fingers and rinse the eyes and face with a stream of water for at least 15 to 20 minutes.
2. Use water from a faucet, drinking fountain, or hose, or use a glass or other container to pour water into the eye.
3. Do not use an eyecup.
4. Remove contact lenses or slide them gently onto the white of the eye using the eyelids.
5. Do not allow the victim to rub the eyes. Do not use eye drops, drugs, or ointments.
6. Call a poison control center, physician, or emergency room for further advice—but do not delay treatment.

812. Providing first-aid for poisonings (in the hospital setting)

As you might have guessed, first-aid procedures in the hospital setting differ greatly from those outside the hospital. In this lesson we discuss immediate care of the poisoning victim: emesis versus lavage in ingested poisonings, the use of cathartics and activated charcoal, specific antidotes, continuing care, and the prevention of poisonings.

Give immediate care

This is a quick explanation of the immediate care given to a victim of poisoning when they arrive at the hospital.

1. Determine the adequacy of cardiac and respiratory function and begin resuscitation if needed.
2. Determine quickly what has happened. If possible, identify the substance ingested, its route of entry into the body, and its toxicity potential. Save any containers and appropriate specimens of the product or of emetic returns. Determine the need for medical care, recognizing that many substances need no further treatment. Always keep in mind that over-treatment may also be a hazard and is expensive.
3. Unless contraindicated, immediately dilute and remove the toxic substance from the body surface. A person who has ingested a toxic substance may also have spilled it on the skin and may be inhaling fumes as well.

Provide appropriate first-aid for ingested substances

The type of aid you administer depends on the substance. The most common types used are emesis, gastric lavage, cathartics, and activated charcoal.

Emesis

Emesis usually removes more of the toxic substance than does gastric lavage. Follow this procedure for emesis:

1. Immediately induce vomiting with ipecac syrup 15 to 30 mL (1 to 2 tablespoonfuls) for children and adults, taken with water or soft drinks (orally that is 15 mL/kg for infants, or 1 qt [1 L] for adults). The dose of ipecac may be repeated in 15 to 30 minutes if necessary.
2. If ipecac is not available, give soapy water, anionic or nonanionic detergent (handwashing liquid detergent) plus water. Try to induce vomiting by inserting a finger or blunt instrument into the patient's throat to stimulate the gag reflex. Avoid being bitten. Place a child in the head-down position. Save a portion of the vomitus for analysis.

Caution: Do not induce vomiting if the patient is comatose, is having convulsions (or is likely to), or has ingested petroleum distillates or corrosive substances. Emesis of petroleum distillates is rarely indicated unless some other compound that requires evacuation (e.g., parathion) has been dissolved in the distillates.

Gastric lavage

1. When gastric lavage is carried out (do not use lavage if the patient is convulsing or if the ingested substance is corrosive), use the largest tube appropriate for the patient.
2. Have the patient in a head-low position.
3. For adults, you may use a 0.9 percent sodium chloride solution or tap water; for children, a 0.45 percent sodium chloride solution is recommended.
4. Introduce lavage fluids in 20- to 30-mL aliquots and remove the stomach contents by siphon or syringe after each instillation.
5. Continue the rinsing procedure until washings return free of toxin.
6. After the return is clear, instill a specific antidote if one is available; otherwise instill a slurry of activated charcoal.

Cathartics

The use of cathartics remains controversial. Some evidence suggests that they may actually enhance absorption rather than promote excretion. If a cathartic is used, it is best limited to sodium sulfate 30 gm, dissolved in 250 mL water, with proportionally reduced amounts for children, or sorbitol/charcoal solutions (but use no more than two doses).

Activated charcoal

When taken internally, activated charcoal with its molecular configuration and large surface area adsorbs significant amounts of many poisons, precluding their absorption from the gut. The earlier the charcoal is used, the more effective it is. Use from five to 10 times the amount of charcoal as that of the poison that is suspected of being ingested. For children under age five, the usual dose is 10 to 25 gm; for older children and adults, 50 to 100 gm. Charcoal is administered as slurry (20 to 200 gm in water), preferably by stomach tube. It should not be administered before or immediately after syrup of ipecac has been given because ipecac induces vomiting; remember that 30 percent of patients vomit after charcoal administration alone. Charcoal is especially effective when the patient is already symptomatic and when the compound is re-excreted into the gut (e.g., glutethimide). Increasingly, charcoal is being accepted as the primary technique of management in the emergency room.

Use specific antidotes for other substances

While not numerous, specific antidotes are remarkably effective (e.g., naloxone in opioid overdoses, atropine in organophosphate encounters, methylene blue for methemoglobinemia, acetylcysteine for acetaminophen, Digibind® for digoxin). A poison center should be contacted to determine if new specific antidotes have been developed, particularly for new drugs.

For inhaled poison

Remove the patient from the contaminated environment, support his/her respiration, and protect other personnel from contamination.

For skin and eye contamination

Remove contaminated clothing (including shoes and socks). Thoroughly wash the skin and flush the eyes with water. Protect helpers from contamination.

For CNS stimulation

CNS stimulation by a poison may require sedation. Usually, diazepam or a barbiturate is used. In pure amphetamine poisoning, chlorpromazine is the drug of choice. To terminate convulsions, give a slow IV of diazepam. You may use phenobarbital IV or IM to either terminate or prevent the recurrence of a convulsion. Keep the patient oxygenated. Refractory seizures very rarely require general anesthesia. The above measures usually are satisfactory to control the hypoxic and cardiovascular consequences of convulsions.

Provide continuing care

Symptomatic and supportive treatment depends on symptoms and signs, and on anticipation of the clinical course, based upon identification of the poison. Continuation of the appropriate measures already begun and attempts to enhance the excretion of poison already absorbed are basic considerations. Stimulants are unlikely to be effective and are generally contraindicated. Severe CNS depression requires support of the circulation and of ventilation. Endotracheal intubation and, rarely, tracheostomy may be necessary. In suspected or known narcotic poisoning, you should use naloxone.

Cerebral edema is common in poisonings due to sedatives, carbon monoxide, lead, and other CNS depressants. Give a 20 percent mannitol solution slowly by IV over a 30- to 60-minute period. Corticosteroids are also used. Intracranial monitoring with hyperventilation to alter the degree of cerebral edema is enjoying less widespread use. The use of barbiturate coma in cerebral edema associated with hypoxic episodes was advocated in the past, but is not recommended now.

Renal failure may occur in poisoning, and dialysis may be required. You can sometimes hasten the elimination of poisons either by augmenting normal excretory pathways or by using artificial means such as dialysis or perfusion. The method depends upon the nature of the poisoning, the availability of the facilities, and the condition of the patient. Flushing out the poison simply by increasing urine volume is rarely helpful. Alkalinization or acidification of the urine is occasionally helpful (e.g., in acute salicylate ingestions or giving sodium bicarbonate IV augments excretion significantly). In general, weak acids are captured in alkalinized urine and weak bases in acidified urine.

Hemo- and peritoneal-dialysis have been augmented by the development of "lipid dialysis." This technique is used to remove lipid-soluble substances from the blood, and hemoperfusion provides an even more rapid and efficient clearance of toxic substances from the blood. However, these techniques are useless if the involved substance has a large apparent volume of distribution—i.e., if it is stored in fatty tissue (e.g., digitalis and tricyclic compounds) or is extensively bound to tissue protein. In select circumstances these techniques may be effective, but in many instances their yield is negligible. Thus, while digoxin is rapidly cleared from the blood via hemoperfusion, when such a small amount (3 to 5 percent) of the total body digoxin is in the blood, hemoperfusion is ineffective. Tricyclic antidepressants are also largely confined to other than the vascular compartment, and the use of hemoperfusion for overdoses is likewise not warranted.

Chelating agents are useful in treating poisoning by many metals and other toxic substances.

Prevent poisonings from happening

Widespread, voluntary, and now mandatory use of child-resistant containers (safety caps) has produced a dramatic decline in poisoning deaths—from about 500 deaths in the USA among children under five years of age in 1959 to some 30 in 1999. Labeling of household products and prescription items, use of drug imprints on solid medication forms, and improved monitoring of toxic exposures within industry and throughout the environment have been successful means of preventing poisonings. Another effective activity includes widespread public and professional education programs such as that built around the Mr. Yuk Program[®] or that of the American Association of Poison Control Centers. These programs produce intense community-wide efforts to make syrup of ipecac available in each home and to make each home aware of the nearest poison center's phone number.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

810. Types and effects of drug or chemical overdoses and poisonings

1. Define toxicology.
2. List examples of natural poisons.
3. What factors determine the severity of an acute poisoning?
4. Give an example of a local effect of a poison.

5. List the four ways in which poisons can enter our bodies.

811. Providing first-aid for poisonings (outside the hospital setting)

1. What are the three general categories of ingested poisons?
2. In a poisoning situation, what is the main concern following the ingestion of any substance?
3. When someone ingests noncorrosive and nonpetroleum-like poison, what is the best way to induce vomiting?
4. What is the basic first-aid procedure for an inhaled poison?
5. In instances of poison in the eye, how long should you rinse the eyes and face with a stream of water?

812. Providing first-aid for poisonings (in the hospital setting)

1. How much water or soft drink should you give to an adult patient who has received ipecac syrup to induce vomiting?
2. Under what circumstances should gastric lavage not be used?
3. How much activated charcoal do you give to a patient (in comparison to the amount of poison suspected of being ingested)?
4. What drug should be used in cases of suspected or known narcotic poisoning?
5. What types of drugs are useful in treating poisoning by many metals and other toxic substances?

Answers to Self-Test Questions

808

1. Lidocaine, Procainamide, Epinephrine, and Bretylium.
2. Absent cardiac contraction and ECG evidence of cardiac electrical activity.
3. To control symptomatic supraventricular tachyarrhythmias.
4. Naloxone prevents and reverses opioid effects by actively competing with the same receptor sites as the narcotic.
5. Marked vasoconstriction, resulting in gangrene may occur.

809

1. Whenever they first develop symptoms of a cold, flu, or other intercurrent illness; nausea, vomiting, or abdominal pain; polyuria; or if they find an unexpectedly high plasma glucose level upon self-glucose monitoring.
2. Spacer, valved chamber, bag device.

810

1. The division of medical and biological science concerned with toxic substances—detecting them, studying their chemistry and pharmacological action and establishing antidotes and treatment of toxic manifestations, preventing poisoning, and methods for controlling exposure to harmful substances.
2. Plants, the venom produced by various animals (such as snakes and spiders), and toxic substances produced by various bacteria in food.
3. Type of poison; amount of poison involved; how the poison enters the body; length of time it stays in the body; and the age, size, and health of the victim.
4. Acid burns on skin or tissue it touched.
5. Absorption, ingestion, inhalation, and injection.

811

1. Corrosive (caustic) substances, petroleum-like substances, and substances that are neither corrosive (caustic) nor petroleum-like.
2. The possibility of systemic effects.
3. Ipecac syrup.
4. Get the victim to fresh air immediately.
5. For at least 15 to 20 minutes.

812

1. One quart or liter.
2. If the patient is convulsing or if the ingested substance is corrosive.
3. From five to 10 times the amount of charcoal as that of the poison suspected of being ingested.
4. Naloxone.
5. Chelating agents.

Unit Review Exercises

Note to Student: Consider all choices carefully, select the *best* answer to each question, and *circle* the corresponding letter. When you have completed all unit review exercises, transfer your answers to ECI Form 34, Field Scoring Answer Sheet.

Do not return your answer sheet to ECI.

57. (808) Which emergency medication is produced in the adrenal medulla and is the first-line drug for ventricular fibrillation when defibrillation fails?
 - a. Procainamide.
 - b. Lidocaine.
 - c. Epinephrine.
 - d. Bretylium.
58. (808) Which emergency medication is used to treat ventricular fibrillation or tachycardia that is resistant to other medications and defibrillation?
 - a. Bretylium.
 - b. Epinephrine.
 - c. Lidocaine.
 - d. Procainamide.
59. (808) Which of the following emergency medications is a parasympatholytic used to treat bradycardia with myocardial ischemia?
 - a. Atropine.
 - b. Epinephrine.
 - c. Isoproterenol.
 - d. Propranolol.
60. (808) What adverse reaction may result when excessive doses of isoproterenol are administered?
 - a. Arterial hypotension.
 - b. Arterial hypertension.
 - c. Peripheral vasoconstriction.
 - d. Acute systolic bradycardia.
61. (808) Which beta-blocker is most extensively used to control symptomatic supraventricular tachyarrhythmias?
 - a. Atenolol.
 - b. Esmolol.
 - c. Levobunolol.
 - d. Propranolol.
62. (808) What is the most valuable drug for emergency treatment of severe allergic reactions?
 - a. Atropine.
 - b. Epinephrine.
 - c. Chlorpheniramine.
 - d. Diphenhydramine.
63. (808) What condition may occur if epinephrine is injected intramuscularly into the buttocks?
 - a. Paralysis.
 - b. Gangrene.
 - c. Hypertension.
 - d. Anaphylactic shock.

64. (809) When should insulin-dependent diabetics test their urine ketones?
- Weekly.
 - Monthly.
 - When self-test glucose levels are high.
 - When self-test glucose levels are low.
65. (809) When using a bag-type device with a metered dose inhaler, what signals that the patient is inhaling too quickly?
- The bag collapses on itself.
 - A bitter taste in the patient's mouth.
 - A whistling sound comes from the mouthpiece.
 - Medication will not pass through the mouthpiece.
66. (810) Which of the following is an example of a natural poison.
- Digitalis.
 - Warfarin.
 - Ammonia.
 - Snake venom.
67. (810) Which route of entry for poisons accounts for almost 90 percent of all poisoning accidents?
- Injection.
 - Ingestion.
 - Inhalation.
 - Absorption.
68. (811) Which of the following substances is an example of a petroleum-like poison?
- Fertilizer.
 - Floor polish.
 - Pain remover.
 - Photographic developer.
69. (811) Why do you not have a patient vomit after ingesting a corrosive poison?
- Vomit-inducing agents adversely react with corrosives.
 - Corrosives will not pass upward through the esophageal sphincter.
 - Corrosives are more easily inactivated in the stomach.
 - Corrosives will do more damage to the lining of the throat and mouth when vomited.
70. (811) What may occur if petroleum-like products are vomited?
- Excessive irritation of the esophagus.
 - The inhaled fumes may cause pneumonia.
 - Permanent damage to the lining of the mouth.
 - Petroleum-like products mix with digestive fluids to form a gel, possibly causing choking.
71. (811) What is the first thing you should do for an inhaled poison victim?
- Check the airway.
 - Move the victim to fresh air.
 - Call the poison control center.
 - Begin CPR.
72. (811) For an absorbed poisoning of the eye, which of the following should you NOT do?
- Use an eyecup to cleanse the eye.
 - Remove the victim's contact lenses.
 - Hold the victim's eye open to flush it.
 - Use drinking fountain water to flush the eye.

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73. (812) What amount of activated charcoal must be used to treat poisonings?
- a. One-half the suspected amount of poison.
 - b. Equal to that of the suspected amount of poison.
 - c. Twice as much as the suspected amount of poison.
 - d. Five to 10 times as much as the suspect amount of poison.
74. (812) What is the drug of choice in pure amphetamine poisoning?
- a. Diazepam.
 - b. Phenobarbital.
 - c. Chlorpromazine.
 - d. Prochlorperazine.
75. (812) What condition is common in poisonings due to sedatives, carbon monoxide, lead, and other central nervous system depressants?
- a. Cerebral edema.
 - b. Renal failure.
 - c. Liver disease.
 - d. Blindness.

Student Notes

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