LESSON ASSIGNMENT

LESSON 4
Antifungals, Antihistamines, and Antimalarial Agents.

TEXT ASSIGNMENT
Paragraphs 4-1 through 4-15.

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

4-1. Given the trade or generic name of a drug used to treat fungi, select the fungus or fungi treated with that drug.

4-2. Given the trade or generic name of a drug used to treat fungi, select the side effects associated with the use of the given drug.

4-3. Given the trade name of a drug used to treat allergies and a list of generic names, select the generic name that corresponds to the trade name.

4-4. Given a list of uses of drugs, select the uses for antihistamines.

4-5. Given the name of an antihistamine and a list of uses, select the use for that antihistamine.

4-6. Given the trade or generic name of an antihistamine and a group of statements describing uses, cautions, and warnings or adverse reactions, select the statement that describes the given drug.

4-7. Given the trade or generic name of a drug used to treat malaria, select the form of malaria treated with that drug.

4-8. Given the name of an antimalarial agent and a list of side effects or cautions and warnings, select the one associated with that agent.

4-9. Given the name of an antifungal antihistamine or antimalarial agent and a list of routes of administration, select the route of administration that can be used for that drug.

SUGGESTION
After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 4

ANTIFUNGALS, ANTIHISTAMINES, AND ANTIMALARIAL AGENTS

Section I. ANTIFUNGALS

4-1. INTRODUCTION

A fungus is a plant-like organism of the same class to which mushrooms and molds belong. They are everywhere in our environment, and those that cause systemic infection are often geographically limited. Although fungi are common plant pathogens, only about 50 of the thousands of known species are pathogenic to humans. An antifungal is an agent that destroys or prevents the growth of fungi. Some agents are used topically while others are reused systemically. The successful treatment of fungal infections depends on accurate identification of the offending fungus, followed by proper selection and use of an antifungal drug. Most superficial infections can be adequately treated with topical therapy. Deep seated infections of the hair or nails generally require systemic therapy. Systemic fungal infections require the use of orally or intravenously administered drugs, some of which are toxic.

4-2. SPECIFIC AGENTS

Various drugs are used to treat fungus.

a. Tolnaftate (Tinactin®). This agent is a topical antifungal and is used in the treatment of athlete's foot, jock itch, and ringworm. The dosage of the drug depends on the extent of the affected area. Tolnaftate is available as a solution, cream, powder, and aerosol powder. All containers should be labeled "FOR EXTERNAL USE ONLY."

b. Nystatin (Mycostatin®). Nystatin is active in vitro against a number of yeasts and molds that cause "diaper rash", thrush, and vaginal candidiasis. Nystatin is relatively nontoxic, but nausea, vomiting, and diarrhea may occur with oral therapy. This drug has staining properties, and patients using the drug should be cautioned. Nystatin is available as an ointment, in oral suspension, vaginal cream, vaginal tablets, and oral tablets.

c. Undecylenic Acid (Desenex®). This drug is an antifungal agent employed in the treatment of superficial fungus infections of the skin. Since it is only fungistatic and not fungicidal, attention must be given to other forms of hygiene. This agent may cause irritation on raw lesions; therefore, astringents are used to assist in reducing the rawness and irritation. An example of such an astringent is zinc, which may be incorporated into ointments, powders, and aerosols.
d. **Griseofulvin (Gris-Peg®).** This agent is very effective in the treatment of superficial fungus infections. It is fungistatic, not fungicidal, and is administered systemically with the dosage varying with the severity and type of infection. Griseofulvin may cause nausea and vomiting, which may be avoided by taking the drug with or shortly after a meal. Headaches are also relatively frequent. This drug is available in tablets, capsules, and in suspension.

e. **Ketoconazole (Nizoral®).** This drug is a broad-spectrum synthetic antifungal agent. It is used as a systemic agent in the treatment of candidiasis, oral thrush, histoplasmosis, and blastomycosis. Ketoconazole may produce nausea and vomiting. Occasionally, potentially fatal liver disorders may occur unless they are properly recognized and managed. The agent should be taken with meals; the patient should be cautioned against using antacids and other drugs that inhibit gastric acid, as gastric acid is necessary for the absorption of ketoconazole. This drug is available only in tablet form.

f. **Selenium Sulfide (Selsun®).** This agent is a topical antifungal used in the treatment of dandruff and seborrheic dermatitis. Oiliness or dryness of the scalp and hair may occur following use, and there have been reported cases of increased normal hair loss. This agent may also discolor the hair; thorough rinsing of the hair can minimize discoloring. Selsun, a prescription drug, is intended for external use only, as is Selsun Blue, an over the counter product.

g. **Clotrimazole (Lotrimin®).** This drug is a broad spectrum antifungal effective as a topical agent in the treatment of infections caused by pathogenic fungi and in the treatment of infections caused by Candida albicans. Side effects associated with the use of this product include itching, burning, peeling, blisters, and erythema. When used as a vaginal cream, it may cause staining of undergarments. Clotrimazole is available in tablets, creams, and in solution.

h. **Miconazole Nitrate (Monistat-Derm®, Monistat-7®).** Miconazole is a synthetic antifungal effective against the common skin fungi and vaginal candidiasis. The side effects for miconazole are the same as for clotrimazole. This product is available in cream form for either topical or vaginal application, vaginal suppositories, lotions for topical application, and in an injectable form.

i. **Fluconazole (Diflucan®).** Fluconazole is a synthetic broad-spectrum antifungal agent. It is used in the treatment of candidiasis and cryptococcal meningitis. The side effects include nausea, vomiting, headache, skin rash, abdominal pain, and diarrhea. Additionally, fluconazole has several significant drug interactions. Diflucan is available as tablets, powder for suspension, and injection.

j. **Econazole (Spectazole®).** Econazole is a topical antifungal that is used to treat tinea cruris, T. pedis, T. corporis, T. rubrum and T. versicolor. Side effects include burning, itching, and stinging. Spectazole is available as a one-percent cream that is applied once to twice daily.
k. Amphotericin B (Fungizone®). This agent is an antibiotic with antifungal activity and is used both topically and systemically. Amphotericin B may exert a "drying" effect on the skin, and in some cases, may stain the nails. This drug is available as a cream, ointment, and parenteral injection.

Section II. ANTIHISTAMINES

4-3. INTRODUCTION

Surely, you know several people who are allergic to pollen, feathers, dogs, and other things. These people may break out in hives, sneeze, or have runny noses and other conditions consequently. These symptoms are annoying, but some allergic reactions can prove to be fatal, as in the case of anaphylactic shock, which can lead to death in a few minutes. The group of drugs known as antihistamines is used primarily in allergic reactions, as sedatives, and in the treatment of certain specified disorders. To fully understand the action of these drugs, it is necessary to look at allergies and how they are caused.

4-4. IMPORTANT TERMS AND DEFINITIONS PERTAINING TO ALLERGIES

a. Allergy. Allergy is defined as the abnormal or altered reaction to an antigen. Certain individuals have an excessive or exaggerated sensitivity to a substance that does not affect a normal individual. Allergy may also be thought of as a side effect of immunity. In immunity, the antigen-antibody reactions take place in the circulatory system. In allergy, however, the antigen antibody reactions take place in contact with the cells.

b. Allergic Reaction. The allergic reaction begins with the introduction of an antigen into the body of an individual. Abnormal (incomplete univalent) antibodies are then formed by the plasma cells and are found in great numbers around tissue cells. When the antigen is again introduced into the body, the antigen antibody reaction occurs in contact with the cells. This reaction damages cells, the cells swell and burst; consequently, large amounts of a chemical called histamine, are released in the body. Mast cells, which contain large amounts of histamine, are found around capillary walls. These cells are particularly susceptible to damage caused by the antigen antibody reaction.
4-5. IMPORTANT CONSIDERATIONS ABOUT ALLERGIC REACTIONS

a. Effects of an Allergic Reaction. An allergic reaction has several effects on the body. These effects occur mainly because of the large concentration of histamine that is released. Peripheral vasodilatation occurs, and capillaries become more permeable. Here, blood plasma "leaks" from the capillaries; the capillary blood volume drops because peripheral vasodilatation and increased permeability of the capillaries. Consequently, there is a decrease in blood pressure. Bronchoconstriction, which can interfere greatly with breathing, may occur. The histamine release may also cause severe rash or hives.

b. Types of Allergic Reactions. There are several types of allergic reactions. One type of allergy is the mild local reaction to general antigens. These reactions are not severe. The antigen producing the reaction can be anything from chicken egg white to horse dander. Allergic rhinitis is an antigen antibody reaction with symptoms occurring in the nasal mucosa. When the antigen is pollen, then it is called hay fever. Hay fever is characterized by edema (swelling), sneezing, itching, and increased mucous secretions. Asthma is characterized by bronchoconstriction as well as wheezing, dyspnea, and coughing. The cause of asthma is frequently an allergic reaction to airborne antigens (it may also be caused by non-allergy related factors). Urticaria (or hives) is characterized by wheals (edema), erythema, and itching of the skin. Foods, drugs, clothing, parasites, and many other substances may cause urticaria.

c. Allergic Reactions from Drugs. Allergy can also involve mild local and systemic drug hypersensitivity reactions. The drugs that commonly cause these reactions include biologicals and antibiotics. Hives (urticaria) (swollen red areas on the skin) and swollen eyelids and lips are outstanding features here. In addition, swelling and pain that occur in joints and muscles when a patient is taking a drug, it is a possible indication the patient is allergic to the drug. An elevated temperature is the third indication that an allergic reaction may be occurring. The lymphatic hypersensitivity reaction is swelling. The respiratory system reaction is bronchoconstriction, while the nasal reaction is a runny nose. Jaundice is a symptom of the hepatic reaction, while vasodilation and increased permeability of the blood vessels are the circulatory system hypersensitivity reaction.

d. Systemic Reactions from Drugs. In addition, systemic reactions occur whenever a drug or an antigen that reacts with abnormal anti-bodies is introduced into the body. One type of systemic reaction is serum sickness. The signs and symptoms of mild drug hypersensitivity and serum sickness may be identical. Serum sickness occurs several days after an injection of a foreign protein, such as horse serum, into a patient that is not already immune. Antibodies are not released into the tissues until 7 to 10 days later. After this period, the reaction between the newly formed antibodies and the still present protein of the horse serum results in an allergic reaction throughout the body. It is similar to anaphylaxis, except in serum sickness the reactions are slow in occurring. The patient usually recovers without complications.
e. **Anaphylactic Shock.** Anaphylactic shock is the most serious type of allergic reaction. The antigen that produces the response can range from a bee sting toxin to an antibiotic. Again, this response is produced by an antigen-antibody reaction characterized by the sudden overwhelming release of histamine in the body. Therefore, one would expect the effects of histamine on the body to be demonstrated. Two main effects of anaphylactic shock on the body are severe drops in blood pressure and impaired respiration. The drastic drop in blood pressure develops from the severe peripheral vasodilation and the increased permeability of the capillaries. The impaired breathing arises from bronchoconstriction. The anaphylactic reaction occurs very rapidly after the introduction of the antigen into the patient. Unless prompt action is taken by medically trained personnel, the patient will die in a matter of minutes.

f. **Prevention or Control of Symptoms of Allergic Reactions.** It is possible to decrease or even prevent the symptoms of an allergic reaction. For a very severe allergic reaction like anaphylactic shock, a drug that will stop the effects of histamine on the body must be used. Moreover, the drug must produce positive physiological effects on the body. The drug used for anaphylactic shock is epinephrine.

g. **Desensitization.** In some instances, it may be advantageous to prevent an allergic reaction from occurring. Since the production of abnormal antibodies by the plasma cells is the real beginning of the potential allergic reaction, it makes sense that if the abnormal antibodies were not produced, a reaction would not occur when the antigen again enters the body. The answer would then be to have only complete (divalent) antibodies produced in the body. This is the basis of treatment to prevent an allergic reaction. The treatment is referred to as desensitization. Here, extracts of substances such as pollen or drugs are given to the patient in small, but increasing doses. In time, the body produces complete antibodies, and the allergic reaction does not occur.

4-6. **MECHANISM OF ACTION OF ANTIHISTAMINES**

a. Antihistamines are drugs that compete with histamines for their receptor sites, known as H1 and H2 receptor sites. These receptor sites are found in tissue cells, with H1 receptors located throughout the body and H2 receptor sites found in the gastric mucosa. The majority of available antihistamines are H1 antagonists.

b. H1 antagonists are believed to act not by opposing but by preventing the physiologic action of histamine. This occurs because anti-histamine molecules are chemically similar to histamine molecules. When the antihistamine binds itself to the H1 receptor site, it prevents histamine from doing the same, which effectively eliminates histamine action.
4-7. INDICATIONS FOR USE OF ANTIHISTAMINES

The antihistamines are used primarily in allergic reactions, as sedatives, and in the treatment/prevention of motion sickness and drug-induced Parkinsonism. These preparations do not immunize the patient or protect him over a long period. Their benefits are comparatively short-lived, provide only symptomatic relief, and do not correct the underlying disorder.

4-8. CAUTIONS AND WARNINGS

The most common side effect of these preparations is drowsiness, which may become so marked that deep sleep occurs. Other reactions include dizziness, dryness of mouth and throat, nausea, muscular weakness, and gastrointestinal disturbances. Patients receiving these products should be cautioned against drinking alcohol to avoid the associated drowsiness.

4-9. GENERAL ANTIHISTAMINE PREPARATION

a. Diphenhydramine (Benadryl®). This preparation is used for its antihistamine, anti-Parkinson, and sedative properties. The usual dose varies according to the age of the patient and the condition being treated. Diphenhydramine is available in capsules, as an elixir, or in an injectable form.

b. Chlorpheniramine (Chlor-Trimeton®). This product is used exclusively for its antihistamine properties. It is available in tablets and as syrup.

c. Loratadine (Claritin) and Fexofenadine (Allegra®). These products are used to treat allergic reactions such as seasonal allergies. They do not cause drowsiness

d. Additional Products. Other antihistamines commonly available include Brompheniramine (Dimetane®) and promethazine hydrochloride (Phenergan®). These products have similar properties, side effects, and dosage forms.

4-10. COMBINATION PREPARATION

a. Brompheniramine, Phenylpropanolamine (Dimetapp®). This product is used for its antihistaminic and decongestant properties. The dose depends on the form in which it is taken and the patient's age. It is available in tablet and elixir form.

b. Other Preparations. Other combination preparations that are available include dextromethorphan and ephedrine (Drixoral®), tripolidine and pseudoephedrine (Actifed®), and phenylpropanolamine and chlorpheniramine (Ornade®).
4-11. ANTIPRURITIC PREPARATIONS

a. Cyproheptadine (Periactin®). This drug is used to control itching caused by allergic reactions. It causes drowsiness and should not be taken with alcohol. Periactin® is available in tablet and syrup form.

b. Other Preparations. Other antipruritic preparations include trimeprazine tartrate (Temaril®) and hydroxyzine hydrochloride (Atarax®).

4-12. HISTAMINE INHIBITORS

a. Cromolyn sodium (Intal®) is a successful anti-asthma prophylactic drug that was produced as a result of knowledge of the mechanisms of allergic reactions. It acts by inhibiting the granulation of pulmonary mast cells, thereby preventing the release of histamine responsible for causing asthmatic symptoms; it has no value in stopping an allergic attack already in progress.

b. Cromolyn sodium is administered by inhalation and is used in the management of patients with severe bronchial asthma. It is also indicated in certain patients to prevent exercise-induced bronchospasm.

c. Following therapy, cromolyn sodium may cause mild throat irritation, coughing, and hoarseness. On occasion, it has been known to produce bronchospasms. Esophageal irritation is relieved by antacids or by drinking a glass of milk before each treatment to protect the gastrointestinal mucosa from direct contact with the drug. The drug demonstrates a low level of toxicity, but some hypersensitivity and allergy have occurred.

4-13. H2 ANTAGONISTS

a. Cimetidine (Tagamet®) is an antihistamine that selectively and competitively inhibits the action of histamine by occupying the H2 receptors of the gastrointestinal mucosa. This action inhibits basal gastric ulcers and controls pathogenic hypersecretory conditions.

b. The drug is available in tablet and syrup form for oral administration or may be administered intramuscularly or intravenously. It may be essential to administer antacids with cimetidine as needed for relief of pain. However, they should not be given simultaneously.

c. Side effects include mild transient diarrhea, muscular pain, dizziness, and skin rashes. A few cases of reversible confusion states have been reported in the elderly, probably because of overdose. Mild gynecomastia been observed in patients treated with this drug for one month or longer. It is relatively nontoxic. Cimetidine does not cause drowsiness like the H1 antagonists.
Section III. ANTIMALARIAL AGENTS

4-14. INTRODUCTION

Malaria has been a critical problem for the American fighting man for decades. Even with the pharmacological advances of today's modern medicine, strains of resistant malaria are now rapidly spreading throughout endemic areas of the world. The treatment of malaria requires extensive chemotherapy that is aimed at interrupting the life cycle of the disease in man.

4-15. SPECIAL AGENTS

Several significant drugs have successfully treated forms of malaria. The agents listed below work on either the blood or liver stages of malaria.

a. **Chloroquine (Aralen®)**. This drug acts only on the blood stages of the parasite. It is the drug of choice for treatment of acute attacks in all types of malaria except drug resistant strains of *P. falciparum*. Chloroquine is also very effective in the prophylaxis of malaria. Side effects associated with the use of this agent are gastrointestinal disturbances, anal pruritis, and visual disturbances. The visual disturbances occur with prolonged use of the drug, which causes damage to the cornea and retina.

b. **Primaquine**. Primaquine is an antimalarial agent used for the radical cure of the relapsing forms of malaria caused by *P. vivax* or *P. ovale*. It is effective against these types of malaria because it acts on the tissue stages of the parasite in the liver. It is the presence of the parasite in the liver which, when not treated, may cause relapses of the disease. The main side effect associated with this drug is hemolytic anemia. This condition is frequently seen in patients lacking the G-6-PD enzyme, a genetic defect that often occurs in dark skinned individuals and those of Mediterranean descent. GI upset and visual disturbances have also occurred.

c. **Chloroquine and Primaquine® (CP®)**. This agent is a combination drug suitable for prophylaxis (prevention) of all types of malaria. Chloroquine and Primaquine® should not be given for acute attacks due to severe primaquine toxicity if more than 26.3 mg of primaquine is given daily. Chloroquine and Primaquine® tablets are no longer the drug of choice for routine prophylaxis of malaria. The side effects of CP® are the same as those for the individual ingredients.

d. **Pyrimethamine and Sulfadoxine (Fansidar®)**. This combination is used in the prophylaxis and treatment of malaria caused by organisms resistant to chloroquine. Some of the side effects associated with this drug are hemolytic anemia and gastrointestinal irritation. This drug should not be dispensed to pregnant or lactating women.
e. **Quinine**: Quinine is an alternative drug in the treatment of malaria strains resistant to other modes of treatment. This agent acts only on the blood stages of the parasite. Side effects include gastrointestinal irritation, tinnitus, vertigo, headache, and drug hypersensitivity.

f. **Doxycycline (Vibramycin®)**. Doxycycline is use prophylactically for *P. falciparum* in short-term travelers to areas with chloroquine resistant strains. Side effects include GI upset and superinfection.

Continue with Exercises

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EXERCISES, LESSON 4

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

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

1. Tolnaftate (Tinactin®) is used for the treatment of:
   a. Athlete's foot
   b. Jock itch
   c. Ringworm
   d. All of the above

2. Selenium sulfide is used for the treatment of:
   a. Diaper rash
   b. Dandruff
   c. Vaginal candidiasis
   d. All of the above

3. Cimetidine is used for the treatment of:
   a. Mild allergic reactions
   b. Severe allergic reactions
   c. Gastric ulcers
   d. Thrush
4. Chloroquine and primaquine tablets (CP® tablets) are used in the treatment of active attacks of what type of malaria?
   a. P. falciparum
   b. P. vivax
   c. All types of malaria
   d. Not used to treat active malaria

5. A patient receiving antihistamines should be cautioned about:
   a. Taking the medication with food or milk
   b. Avoiding antacids
   c. Avoiding iron preparations
   d. Drowsiness

6. A patient taking cromolyn sodium (Intal®) that might have of the following side effects.
   a. Throat irritation
   b. Coughing
   c. Hoarseness
   d. All of the above

7. Which of the following is a side effect of Fansidar®?
   a. Hemolytic anemia
   b. Drowsiness
   c. Cough
   d. All of the above
8. Antihistamines are used for:
   a. Treatment of allergic reactions
   b. Sedatives
   c. Treatment/prevention of motion sickness
   d. All of the above

9. Cromolyn sodium is used to treat:
   a. Anaphylactic shock
   b. Asthma
   c. Motion sickness
   d. Drug induced Parkinsonism

10. Which of the following is used for its antipruritic activity?
    a. Cyproheptadine
    b. Trimeprazine tartrate
    c. Hydroxyzine hydrochloride
    d. All of the above

Check Your Answers on Next Page
SOLUTIONS TO EXERCISES, LESSON 4

1. d (para 4-2a)
2. b (para 4-2f)
3. c (para 4-13a)
4. d (para 4-15c)
5. d (para 4-8)
6. d (para 4-12c)
7. a (para 4-15d)
8. d (para 4-7)
9. b (para 4-12b)
10. d (para 4-11)

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