Allergic drug reactions should be considered when new signs and symptoms develop or when they differ from the usual manifestations of the illness being treated, especially if a reaction:

- Follows ingestion of a drug, especially one known to produce allergic reactions
- Is unpredictable and occurs in only a few clients when many clients receive the suspected drug
- Occurs approximately 7 to 10 days after initial exposure to the suspected drug (to allow antibody production)
- Follows a previous exposure to the same or similar drug (sensitizing exposure)
- Occurs minutes or hours after a second or subsequent exposure
- Occurs after small doses (reduces the likelihood that the reaction is due to dose-related drug toxicity)
- Occurs with other drugs that are chemically or immunologically similar to the suspected drug
- Produces signs and symptoms that differ from the usual pharmacologic actions of the suspected drug
- Produces signs and symptoms usually considered allergic in nature (eg, anaphylaxis, urticaria, serum sickness)
- Produces similar signs and symptoms to previous allergic reactions to the same or a similar drug
- Increases eosinophils in blood or tissue
- Resolves within a few days of discontinuing the suspected drug

Virtually all drugs have been implicated in **anaphylactic reactions.** Penicillins and other antimicrobials, radiocontrast media, aspirin and other nonsteroidal anti-inflammatory drugs, and antineoplastics such as asparaginase and cisplatin are more common offenders. Less common causes include anesthetics (local and general), opioid analgesics, skeletal muscle relaxants used with general anesthetics, and vaccines. Approximately 10% of severe anaphylactic reactions are fatal. In many cases, it is unknown whether clinical manifestations are immunologic or nonimmunologic in origin.

Serum sickness is a delayed hypersensitivity reaction most often caused by drugs, such as antimicrobials. In addition, many drugs that produce anaphylaxis also produce serum sickness. With initial exposure to the antigen, symptoms usually develop within 7 to 10 days and include urticaria, lymphadenopathy, myalgia, arthralgia, and fever. The reaction usually resolves within a few days but may be severe or even fatal. With repeated exposure to the antigen, after prior sensitization of the host, accelerated serum sickness may develop within 2 to 4 days, with similar but often more severe signs and symptoms.

Systemic lupus erythematosus (SLE) is an autoimmune disorder that may be induced by hydralazine, procainamide, isoniazid, and other drugs. Clinical manifestations vary greatly, depending on the location and severity of the inflammatory and immune processes, and may include skin lesions, fever, pneumonia, anemia, arthralgia, arthritis, nephritis and others. Drug-induced lupus produces less renal and CNS involvement than idiopathic SLE.

Fever often occurs with allergic drug reactions. It may occur alone, with a skin rash and eosinophilia, or with other drug-induced allergic reactions such as serum sickness, SLE, vasculitis, and hepatitis.

Dermatologic conditions (eg, skin rash, urticaria, inflammation) commonly occur with allergic drug reactions and may be the first and most visible manifestations.

Pseudoallergic Drug Reactions

Pseudoallergic drug reactions resemble immune responses (because histamine and other chemical mediators are released) but they do not produce antibodies or sensitized T lymphocytes. **Anaphylactoid reactions** are like anaphylaxis in terms of immediate occurrence, symptoms, and life-threatening severity. The main difference is that they are not antigen–antibody reactions and therefore may occur on first exposure to the causative agent. The drugs bind directly to mast cells, activate the cells, and cause the release of histamine and other vasoactive chemical mediators. Contrast media for radiologic diagnostic tests are often implicated.

ANTIHISTAMINES

The term *antihistamines* generally indicates classic or traditional drugs. With increased knowledge about histamine receptors, these drugs are often called H_1 receptor antagonists. These drugs prevent or reduce most of the physiologic effects that histamine normally induces at H_1 receptor sites. Thus, they:

- Inhibit smooth muscle constriction in blood vessels and the respiratory and GI tracts
- Decrease capillary permeability
- Decrease salivation and tear formation

The drugs are similar in effectiveness as histamine antagonists but differ in adverse effects. These are the antihistamines discussed in this chapter. Cimetidine (Tagamet), ranitidine (Zantac), famotidine (Pepcid), and nizatidine (Axid) are H_2 receptor antagonists or blocking agents used to prevent or treat peptic ulcer disease. These are discussed in Chapter 60. Selected H_1 antagonists are described in the following sections and in Drugs at a Glance: Commonly Used Antihistamines.

First-Generation H_1 Receptor Antagonists

These chemically diverse antihistamines (also called nonselective or sedating agents) bind to both central and peripheral H_1 receptors and can cause CNS depression or stimulation. They usually cause CNS depression (drowsiness, sedation) with therapeutic doses and may cause CNS stimulation (anxiety, agitation) with excessive doses, especially in children. They also have substantial anticholinergic effects (eg, cause dry mouth, urinary retention, constipation, blurred vision).