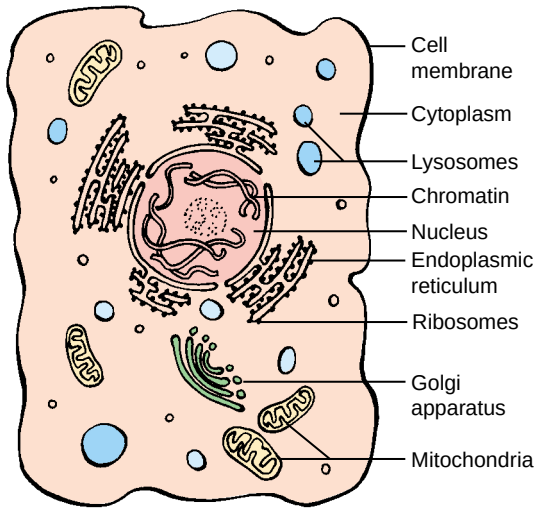

Figure 2–1 Schematic diagram of cell highlighting cytoplasmic organelles.

- Exchange materials with their immediate environment
- Obtain energy from nutrients
- Synthesize hormones, neurotransmitters, enzymes, structural proteins, and other complex molecules
- Duplicate themselves (reproduce)
- Communicate with each other via various biologic chemicals, such as neurotransmitters and hormones

DRUG TRANSPORT THROUGH CELL MEMBRANES

Drugs, as well as physiologic substances such as hormones and neurotransmitters, must reach and interact with or cross the cell membrane in order to stimulate or inhibit cellular function. Most drugs are given for effects on body cells that are distant from the sites of administration (ie, systemic effects). To move through the body and reach their sites of action, metabolism, and excretion (Fig. 2–2), drug molecules must cross numerous cell membranes. For example, molecules of most oral drugs must cross the membranes of cells in the gastrointestinal (GI) tract, liver, and capillaries to reach the bloodstream, circulate to their target cells, leave the bloodstream and attach to receptors on cells, perform their action, return to the bloodstream, circulate to the liver, reach drug-metabolizing enzymes in liver cells, re-enter the bloodstream (usually as metabolites), circulate to the kidneys, and be excreted in urine. Several transport pathways and mechanisms are used to move drug molecules through the body (Fig. 2–3 and Box 2–2).

PHARMACOKINETICS

Pharmacokinetics involves drug movement through the body (ie, "what the body does to the drug") to reach sites of action, metabolism, and excretion. Specific processes are absorption, distribution, metabolism (biotransformation), and excretion. Overall, these processes largely determine serum drug levels, onset, peak and duration of drug actions, drug half-life, therapeutic and adverse drug effects, and other important aspects of drug therapy.

Absorption

Absorption is the process that occurs from the time a drug enters the body to the time it enters the bloodstream to be circulated. Onset of drug action is largely determined by the rate of absorption; intensity is determined by the extent of absorption. Numerous factors affect the rate and extent of drug absorption, including dosage form, route of administration, blood flow to the site of administration, GI function, the presence of food or other drugs, and other variables. Dosage form is a major determinant of a drug's bioavailability (the portion of a dose that reaches the systemic circulation and is available to act on body cells). An intravenous drug is virtually 100% bioavailable; an oral drug is virtually always less than 100% bioavailable because some is not absorbed from the GI tract and some goes to the liver and is partially metabolized before reaching the systemic circulation.

Most oral drugs must be swallowed, dissolved in gastric fluid, and delivered to the small intestine (which has a large surface area for absorption of nutrients and drugs) before they are absorbed. Liquid medications are absorbed faster than tablets or capsules because they need not be dissolved. Rapid movement through the stomach and small intestine may increase drug absorption by promoting contact with absorptive mucous membrane; it also may decrease absorption because some drugs may move through the small intestine too rapidly to be absorbed. For many drugs, the presence of food in the stomach slows the rate of absorption and may decrease the amount of drug absorbed.

Drugs injected into subcutaneous (SC) or intramuscular (IM) tissues are usually absorbed more rapidly than oral drugs because they move directly from the injection site to the bloodstream. Absorption is rapid from IM sites because muscle tissue has an abundant blood supply. Drugs injected intravenously (IV) do not need to be absorbed because they are placed directly into the bloodstream.

Other absorptive sites include the skin, mucous membranes, and lungs. Most drugs applied to the skin are given for local effects (eg, sunscreens). Systemic absorption is minimal from intact skin but may be considerable when the skin is inflamed or damaged. Also, a number of drugs have been formulated in adhesive skin patches for absorption through the skin (eg, clonidine, estrogen, fentanyl, nitroglycerin, scopolamine). Some drugs applied to mucous membranes also are given for local effects. However, systemic absorption occurs from the mucosa of the oral cavity, nose, eye, vagina, and rectum. Drugs absorbed through mucous membranes pass directly into the bloodstream. The lungs have a large surface area for absorption of anesthetic gases and a few other drugs.