ADME is a universally used acronym in medicinal chemistry. The four letters stand for absorption, distribution, metabolism, and excretion. Collectively, these four topics cover the major areas of the field pharmacokinetics. In covering these topics we will prepare for the next chapter, which is a quantitative treatment of pharmacokinetics.

**Absorption** describes the movement of a drug from its site of administration to the bloodstream. The US Food and Drug Administration recognizes over 100 different routes of administration, but we will focus upon just two – intravenous (IV) and oral.

IV administration bypasses the absorption step altogether because the drug is administered directly into the circulatory system through a vein. In oral administration, however, a drug is absorbed by crossing membranes from the digestive tract to the bloodstream. The digestive tract, especially the small intestine, is designed to absorb nutrients from food. Properly designed drugs can readily exploit this fact and gain access to the bloodstream via the digestive system.

**Distribution** covers the travel of a drug from the bloodstream to the various tissues and organs of the body. Each drug has its own unique properties, and those properties determine the degree to which the drug spreads from the circulatory system to the muscles, fatty tissue, or the even the brain.

**Metabolism** refers to the chemical modification of a drug by the body. While a drug may be metabolized almost anywhere that the drug has been distributed, most metabolism occurs in the liver. The liver contains a host of enzymes that can perform chemical reactions on the different functional groups found in drugs. The net effect of metabolism is that the concentration of the original, unchanged drug in the bloodstream is decreased, and therefore the effect of the drug is diminished. Processes that decrease the amount of drug in the body fall under the larger category of **elimination**. We will expand upon metabolism in Chapter 8.

Metabolism by the liver has a significant influence upon drugs. All oral drugs, once they are absorbed from the bloodstream, enter a specific part of the circulatory system called the **hepatic portal system**. All blood and its contents in the hepatic portal system must pass through the liver before reaching the general circulatory system and accessing the body as a whole. By passing through the liver before reaching the body, a fraction of a drug's dose will be broken down by the liver before it even has a chance to reach the circulatory system. This initial loss of drug by the action of the liver is called the **first pass effect**.

A drug's **bioavailability** is the fraction of an administered dose of the drug that reaches the general circulatory system. The variable for bioavailability is $F$. IV drugs, which are directly placed in the bloodstream, have 100% bioavailability ($F = 1.00$). The bioavailability of an oral drug depends upon its absorption from the gastrointestinal tract as well as its resistance to being metabolized by the liver. If a drug has a low bioavailability, researchers can find clues to the problem. If a drug is poorly absorbed, it will likely be found in the feces. If a drug is absent from the feces and still shows a low bioavailability, then the drug is likely broken down extensively by the liver.

**Excretion** refers to the removal of waste and unwanted materials by an organism. Excretion
can be performed by many organs through a variety of processes (e.g., sweating from the skin and exhalation of CO$_2$ by the lungs), but the major method of excretion for drugs is through filtration of drug from the blood by the kidneys. Like metabolism, excretion reduces the concentration of a drug in the blood and therefore falls under the broader category of elimination.

The kidneys initially filter whole blood. A fraction of the particles smaller than the blood proteins are temporarily removed from whole blood. The list of affected molecules includes water, electrolytes, small molecules (including almost all drugs), and waste. The filtered fluid, or filtrate, is essentially protein-free plasma. Through the process of reabsorption, the kidneys draw valuable water, electrolytes, and sugars from the filtered fluid to be returned to the blood. Some filtered drugs are also largely returned to the blood. Similarly, through a process called secretion, small molecules that were missed in the initial filtration have a second chance to enter the filtrate by crossing a membrane separating the filtrate and whole blood. The end result is urine – an aqueous fluid that is highly concentrated in waste molecules and possibly a drug and its metabolites.