Metabolism is a general biological term that may refer to different processes. Two of those processes are listed below.

- **Catabolism** – converting food into useful energy (e.g., glycolysis or the citric acid cycle)
- **Anabolism** – using energy to synthesize proteins and other necessary molecules

In the context of drug discovery, metabolism refers to the body's ability to break down foreign molecules, called **xenobiotics**. Almost all drugs are examples of xenobiotics. Drugs are not metabolized for their energy or utility; they are metabolized so that the molecules and their effects may be eliminated from the body. Metabolic reactions are typically performed by liver enzymes.

Once a drug has entered the body, the drug can undergo a number of different metabolic processes. A drug's metabolism may be irreversible, reversible with both the forward and backward reactions being performed by the same enzyme, and reversible with the forward and backward reactions being performed by different enzymes. The metabolism products, called **metabolites**, are generally excreted by the kidneys. Metabolites may themselves be further metabolized before being removed by the kidneys. Sometimes drugs are excreted in unchanged form by the kidneys. This fate of a drug falls outside the category of metabolism.

Drugs are carefully designed to distribute in the body in a manner that is ideal for the action of a drug. Metabolites, however, have been chemically modified from the original drug and therefore can have very different properties from the original drug. In general, metabolic reactions on a drug cause the metabolite to be more polar than the original drug. As polarity increases, $V_d$ normally decreases. With a lower $V_d$, the metabolite concentrates in the plasma and is more prone to be cleared by the kidneys. Metabolic reactions, therefore, do help remove a drug from the body more quickly.

Metabolic reactions are normally divided into two categories – **phase I** and **phase II**. (Do not confuse these terms with the different stages of clinical trials.) Phase I metabolism includes oxidations, reductions, and hydrolyses. Phase II metabolism involves the connection or
conjugation of small polar molecules to a compound. These two processes often work together. A drug will undergo phase I metabolism to form a new metabolite. The new metabolite then undergoes phase II metabolism and is linked to a polar group. The final metabolite is highly polar, concentrated in the plasma (low $V_d$), and readily excreted by the kidneys (high $CL_R$). According to our pharmacokinetic equations in the previous chapter, the end result is a metabolite with a short half-life.

$$t_{1/2} \propto \frac{V_d}{CL}$$