The fecal excretion of drugs appears to lag behind the rate of urinary excretion, partly because a day or so elapses before the feces reach the rectum. Drugs administered orally for local activity within the gastrointestinal tract and not absorbed will be eliminated completely via the feces. Unless a drug is particularly irritating to the gastrointestinal tract, there is generally no urgency about removing unabsorbable drugs from the system by means other than normal defecation. Some drugs that are only partially absorbed after oral administration will naturally be partly eliminated through the rectum.

PHARMACOKINETIC PRINCIPLES

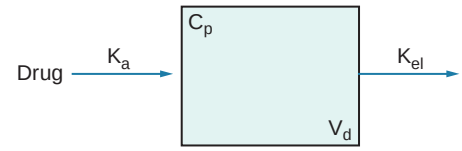
This section introduces the concept of pharmacokinetics and how it interrelates the various processes that take place when one administers a drug to a patient, that is, ADME. It is not intended to be comprehensive, and thus, for further information about the subject, the reader is referred to other appropriate literature.

A problem encountered when one needs to determine a more accurate dosage of a drug or a more meaningful interpretation of a biologic response to a dose is the inability to determine the drug concentration at the active site in the body. Consequently, the concept of compartmental analysis is used to determine what has become of the drug as a function of time from the moment it is administered until it is no longer in the body. Pharmacokinetic analysis uses mathematical models to simplify or simulate the disposition of the drug in the body. The idea is to begin with a simple model and then modify as necessary. The principal assumption is that the human body may be represented by one or more *compartments* or pools in which a drug resides in a dynamic state for a short time. A compartment is a hypothetical space bound by an unspecified membrane across which drugs are transferred (Fig. 5.12). The transfer of drugs into and out of this compartment is indicated by arrows that point in the direction of drug movement into or out of the compartment. The rate at which a drug is transferred throughout the system is designated by a symbol that usually represents an exponential rate constant. Typically, the letter K or k with numeric or alphanumeric subscripts is used.

Several assumptions are associated with modeling of drug behavior in the body. It is assumed that the volume of each compartment remains constant. Thus, an equation that describes the time course of the amount of drug in the compartment can be converted to an equation that depicts the time course of the drug concentration in the compartment by dividing both sides of the equation by the volume of the compartment. Second, it is assumed that once a drug enters the compartment, it is instantaneously and uniformly distributed throughout the entire compartment. Thus, it is assumed that a sampling of any one portion of the compartment will yield the drug concentration of the entire compartment.

In compartment models, it is assumed that drug passes freely into and out of compartments. Thus, these compartmental systems are known as open systems. Typically, drug transport between compartments follows first-order kinetics, wherein a constant fraction of drug is eliminated per unit of time and can be described by ordinary differential equations. In these linear systems, the time constants that describe the rate at which the plasma or blood concentration curve of a drug decays are independent of the dose, the volume of distribution, and the route of administration.

The simplest pharmacokinetic model is the single-compartment *open-model system*



Where:
C_p is the drug concentration in plasma
V_d is the volume of the compartment or volume of distribution

FIGURE 5.12 A one-compartment system.