

the blood components or with circulation and therefore, with few exceptions, are aqueous solutions.

### *Subcutaneous Injections*

The subcutaneous (hypodermic) administration of drugs entails injection through the skin into the loose subcutaneous tissue. Subcutaneous injections are prepared as aqueous solutions or as suspensions and are administered in relatively small volumes, 2 mL or less. Insulin is an example of a drug administered by the subcutaneous route. Subcutaneous injections are generally given in the forearm, upper arm, thigh, or buttocks. If the patient is to receive frequent injections, it is best to alternate injection sites to reduce tissue irritation. After injection, the drug comes into the immediate vicinity of blood capillaries and permeates them by diffusion or filtration. The capillary wall is an example of a membrane that behaves as a lipid pore barrier, with lipid-soluble substances penetrating the membrane at rates varying with their oil-water partition coefficients. Lipid-insoluble (generally more water soluble) drugs penetrate the capillary membrane at rates that appear to be inversely related to their molecular size, with smaller molecules penetrating much more rapidly than larger ones. All substances, whether lipid soluble or not, cross the capillary membrane much more rapidly than other body membranes. The blood supply to the site of injection is an important factor in considering the rate of drug absorption; consequently, the closer capillaries are to the site of injection, the more prompt is the drug's entrance into the circulation. Also, the more the capillaries, the more surface area for absorption and the faster the rate of absorption. Some substances modify the rate of drug absorption from a subcutaneous site of injection. The addition of a vasoconstrictor to the injection formulation (or its prior injection) will generally diminish the rate of drug absorption by causing constriction of the blood vessels in the area of injection and thereby reducing blood flow and the capacity for absorption. This principle is used in the administration of local anesthetics by use of the vasoconstrictor epinephrine. Conversely, vasodilators may

be used to enhance subcutaneous absorption by increasing blood flow to the area. Physical exercise can also influence the absorption of drug from an injection site. Diabetic patients who rotate subcutaneous injection sites and then do physical exercise such as jogging must realize that the onset of insulin activity may be influenced by the selected site of administration. Because of the movement of the leg and blood circulation to it during running, the absorption of insulin from a thigh injection site can be expected to be faster than from an abdominal injection site.

### *Intramuscular Injections*

Intramuscular injections are performed deep into the skeletal muscles, generally the gluteal or lumbar muscles. The selected site is where the danger of hitting a nerve or blood vessel is minimal. Aqueous or oleaginous solutions or suspensions may be used intramuscularly. Certain drugs, because of their inherent low solubility, provide sustained drug action after an intramuscular injection. For instance, one deep intramuscular injection of a suspension of penicillin G benzathine results in effective blood levels of the drug for 7 to 10 days. The addition of the decanoate ester decreases the solubility of haloperidol and, consequently, extends haloperidol's  $t_{1/2}$  from 18 hours orally to 3 weeks, an advantage in antipsychotic drug therapy.

Drugs that are irritating to subcutaneous tissue are often administered intramuscularly. Also, greater volumes (2 to 5 mL) may be administered intramuscularly than subcutaneously. When a volume greater than 5 mL is to be injected, it is frequently administered in divided doses to two injection sites. Injection sites are best rotated when a patient is receiving repeated injections over time.

### *Intravenous Injections*

In the intravenous administration of drugs, an aqueous solution is injected directly into the vein at a rate commensurate with efficiency, safety, comfort to the patient, and the desired duration of drug response. Drugs may be administered intravenously as a single, small-volume injection or as a large-volume slow intravenous drip infusion (as is