Many body nutrients, such as sugars and amino acids, are transported across the membranes of the gastrointestinal tract by carrier processes. Certain vitamins, such as thiamine, niacin, riboflavin, and pyridoxine, and drug substances, such as methyldopa and 5-fluorouracil, require active transport mechanisms for their absorption.

Investigations of intestinal transport have often used in situ (at the site) or in vivo (in the body) animal models or ex vivo (outside the body) transport models; however, recently cell culture models of human small intestine absorptive cells have become available to investigate transport across intestinal epithelium (1). Both passive and transport-mediated studies have been conducted to investigate mechanisms and rates of transport.

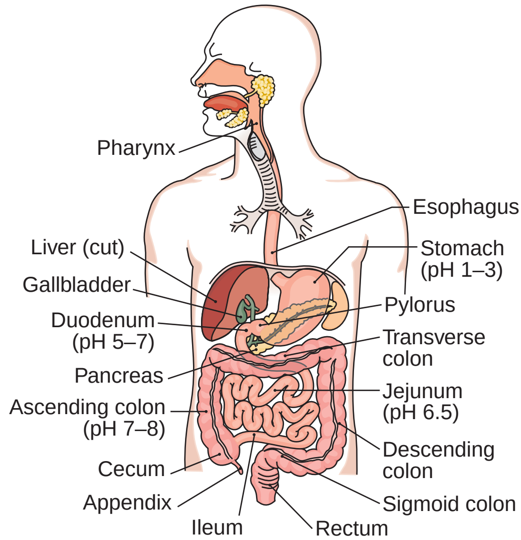

FIGURE 5.3 The digestive system, including the locations of drug absorption and their respective pH values. (Adapted with permission from Cohen BJ, Wood DL. Memmler's the Human Body in Health and Disease. 11th Ed. Baltimore, MD: Lippincott Williams & Wilkins, 2009.)

DISSOLUTION AND DRUG ABSORPTION

For a drug to be absorbed, it must first be dissolved in the fluid at the absorption site. For instance, a drug administered orally in tablet or capsule form cannot be absorbed until the drug particles are dissolved by the fluids in the gastrointestinal tract. When the solubility of a drug depends on either an acidic or basic medium, the drug dissolves in the stomach or intestines, respectively (Fig. 5.3). The process by which a drug particle dissolves is termed *dissolution*.

As a drug particle undergoes dissolution, the drug molecules on the surface are the first to enter into solution, creating a saturated layer of drug solution that envelops the surface of the solid drug particle. This layer of solution is the *diffusion layer*. From this diffusion layer, the drug molecules pass throughout the dissolving fluid and make contact with the biologic membranes, and absorption ensues. As the molecules of drug continue to leave the diffusion layer, the layer is replenished with dissolved drug from the surface of the drug particle, and the process of absorption continues.

If the dissolution of a given drug particle is rapid or if the drug is administered as a solution and remains present in the body as such, the rate at which the drug becomes absorbed depends mainly on its ability to traverse the membrane barrier. However, if the rate of dissolution for a drug particle is slow because of the physicochemical characteristics of the drug substance or the dosage form, dissolution itself is a rate-limiting step in absorption. Slowly soluble drugs such as digoxin may not only be absorbed at a slow rate; they may be incompletely absorbed or in some cases largely unabsorbed following oral administration because of the natural limitation of time that they may remain within the stomach or the intestinal tract. Thus, poorly soluble drugs or poorly formulated drug products may be incompletely absorbed and pass unchanged out of the system via the feces.

Under normal circumstances, a drug may be expected to remain in the stomach for 2 to 4 hours (*gastric emptying time*) and in the small intestine for 4 to 10 hours, although there is substantial variation between people and even in the same person on different occasions. Various techniques have been used to determine gastric emptying time and the gastrointestinal passage of drug from various oral dosage forms, including tracking