FARMACOCINETICA

Studio del movimento dei farmaci nel corpo

Caratteristiche delle vie di somministrazione usate più frequentemente

- Enterali
  - Orale (PO)
  - Rettale
  - Sublinguale
- Parenterali
  - Endovenosa (IV)
  - Sottocutanea (subQ)
  - Intramuscolare (IM)

Orale

- **Barriere all'assorbimento**
  - Cellule epiteliali
  - Parete capillare
- **Ritmo dell'assorbimento**
  - Altamente variabile
- **Movimento del farmaco dopo l'assorbimento**
- **Vantaggi**
  - Farmaci scarsamente solubili
  - Preparazioni depot
- **Svantaggi**
  - Disagio

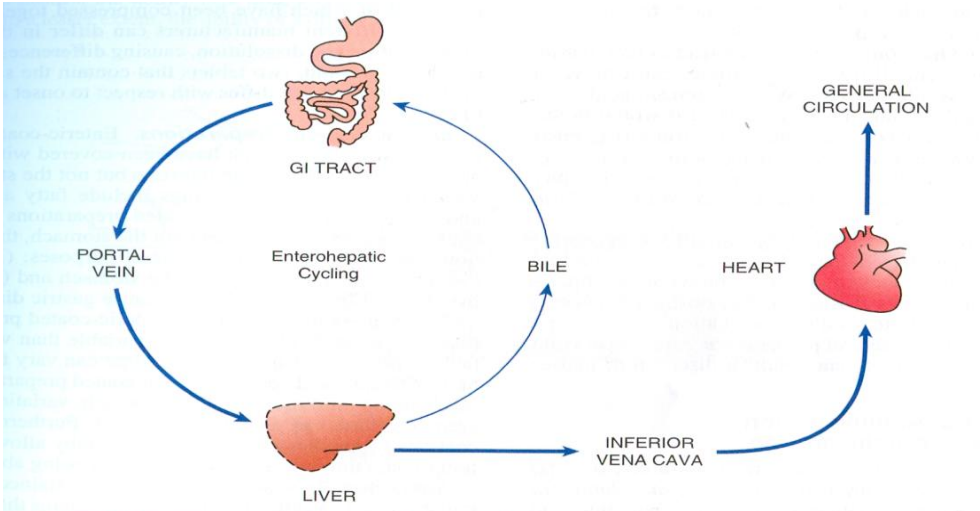

Figure 4–8 ▪ Movement of drugs following GI absorption.
All drugs absorbed from sites along the GI tract—stomach, small intestine, large intestine (but not the oral mucosa or distal rectum)—must go through the liver, via the portal vein, on their way toward the heart and the general circulation. For some drugs, passage is uneventful. Others undergo extensive metabolism. Still others undergo excretion into the bile, after which they re-enter the small intestine (via the bile duct), and then either (1) undergo reabsorption into the portal blood, thereby creating a cycle known as *enterohepatic recirculation,* or (2) exit the body in the stool (not shown).

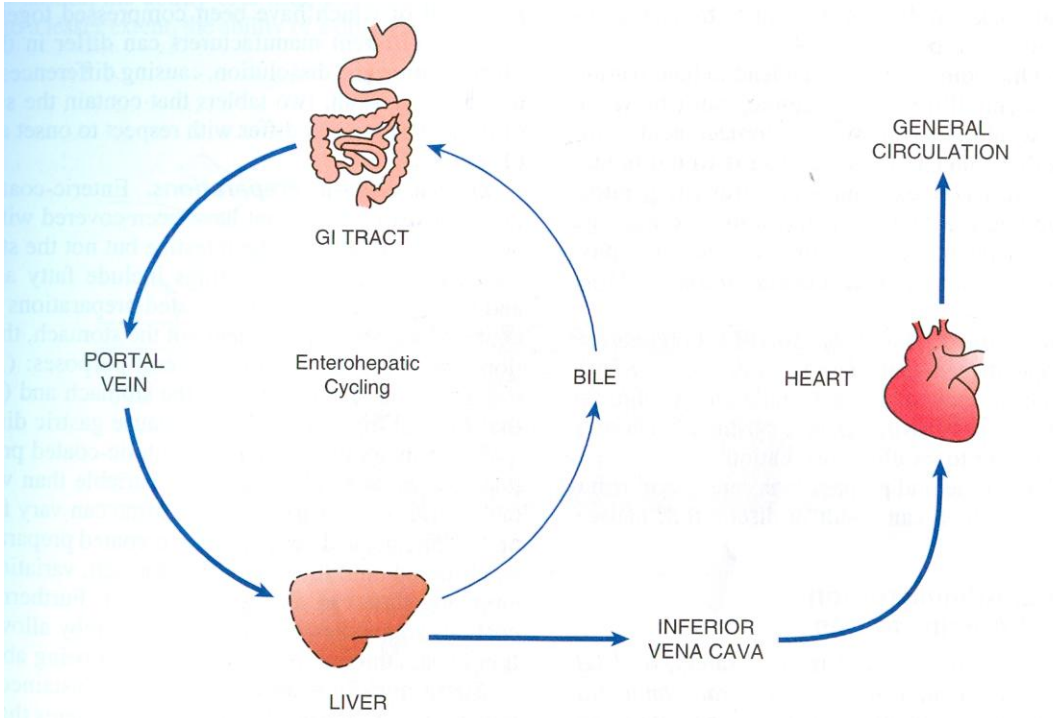

Figure 4–8 ■ Movement of drugs following GI absorption.
All drugs absorbed from sites along the GI tract—stomach, small intestine, large intestine (but not the oral mucosa or distal rectum)—must go through the liver, via the portal vein, on their way toward the heart and the general circulation. For some drugs, passage is uneventful. Others undergo extensive metabolism. Still others undergo excretion into the bile, after which they re-enter the small intestine (via the bile duct), and then either (1) undergo reabsorption into the portal blood, thereby creating a cycle known as *enterohepatic recirculation,* or (2) exit the body in the stool (not shown).

Endovenosa

- Barriere all'assorbimento
  - Nessuna barriera
- Quadro dell'assorbimento
  - Istantaneo e completo
- Vantaggi
  - Inizio rapido
  - Controllo
  - Uso di grandi volumi di liquido
  - Uso di farmaci irritanti
- Svantaggi
  - Costo elevato, difficoltà, disagio
  - Irreversibilità
  - Eccesso di liquido
  - Infezione
  - Embolia
  - Importanza della lettura dell'etichetta

Intramuscolare

- **Barriere all'assorbimento**
  - Parete capillare
- **Ritmo dell'assorbimento**
- **Vantaggi**
  - Farmaci scarsamente solubili
  - Preparazioni depot
- **Svantaggi**
  - Disagio

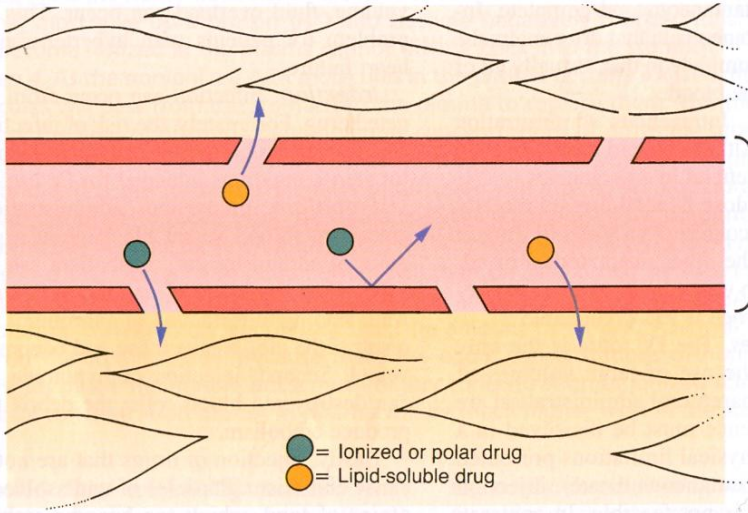

Figure 4–7 ■ Drug movement at typical capillary beds.
In most capillary beds, "large" gaps exist between the cells that compose the capillary wall. Drugs and other molecules can pass freely into and out of the bloodstream through these gaps. As illustrated, lipid-soluble compounds can also pass directly through the cells of the capillary wall.

I QUATTRO PROCESSI FARMACOCINETICI BASILARI

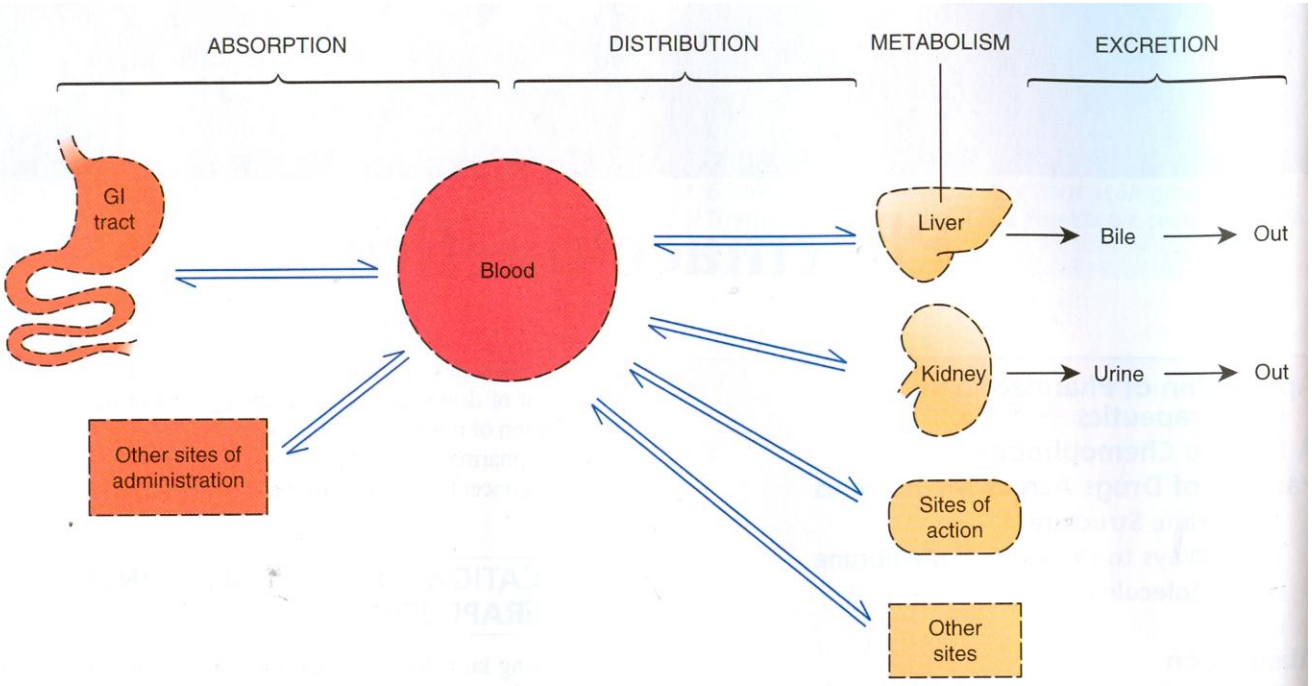

Figure 4–1 ■ **The four basic pharmacokinetic processes.**
Dotted lines represent membranes that must be crossed as drugs move throughout the body.

STRUTTURA DELLA MEMBRANA CELLULARE

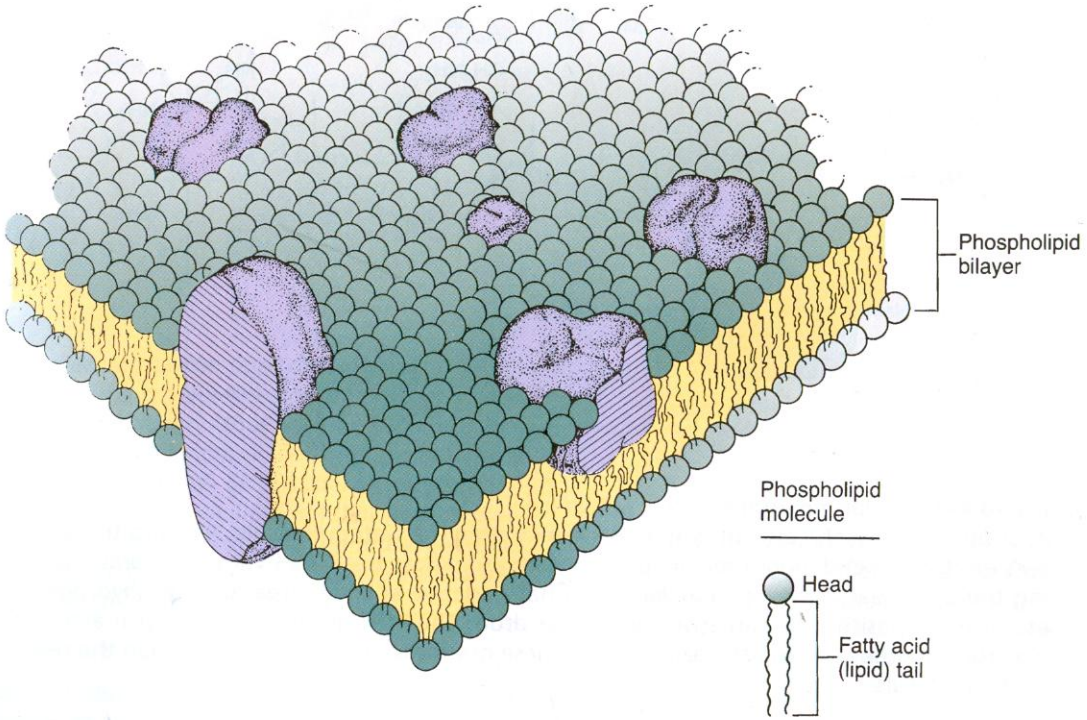

Figure 4–2 ▪ **Structure of the cell membrane.**
The cell membrane consists primarily of a double layer of phospholipid molecules. The large globular structures represent protein molecules imbedded in the lipid bilayer. (Modified from Singer SJ, Nicolson GL: The fluid mosaic model of the structure of cell membranes. Science 175:720, 1972.)

Passaggio dei farmaci attraverso la membrana

- Canali e pori
- Sistemi di trasporto
  - P-Glicoproteine
- Penetrazione diretta della membrana

Molecole polari

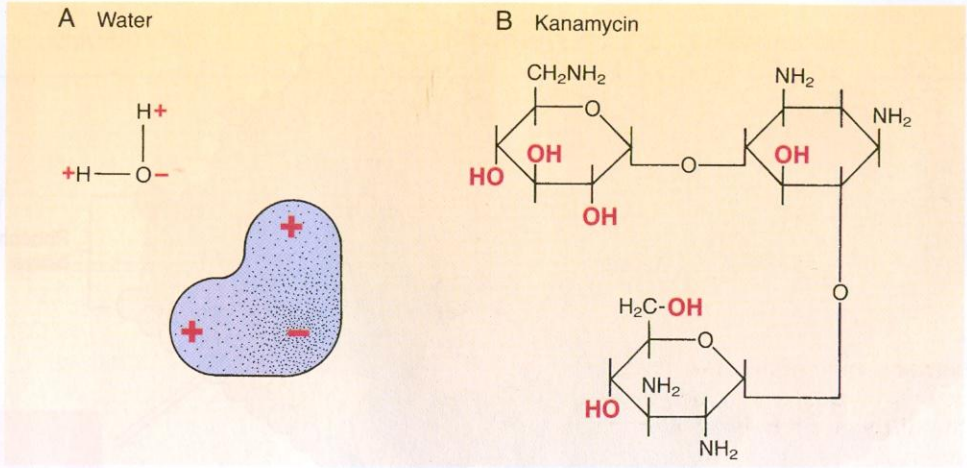

Figure 4–3 ■ **Polar molecules.**
A, Stippling shows the distribution of electrons within the water molecule. As indicated, water's electrons spend more time near the oxygen atom than near the hydrogen atoms, making the area near the oxygen atom somewhat negative and the area near the hydrogen atoms more positive. *B,* Kanamycin is a polar drug. The –OH groups of kanamycin attract electrons, thereby causing the area around these groups to be more negative than the rest of the molecule.

Ioni e ionizzazione

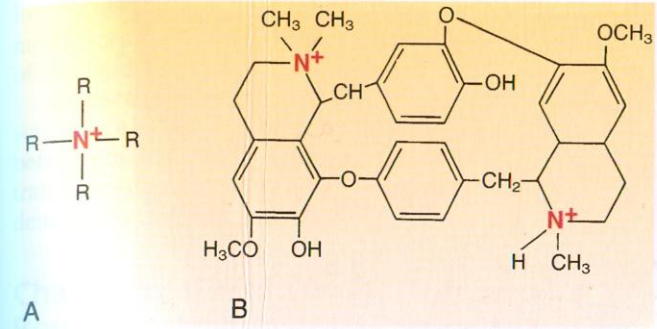

Figure 4–4 ▪ Quaternary ammonium compounds.
A, The basic structure of quaternary ammonium compounds. Because the nitrogen atom has bonds to four organic radicals, quaternary ammonium compounds always carry a positive charge. Because of this charge, quaternary ammonium compounds are not lipid soluble and cannot cross most membranes. *B,* Tubocurarine is a representative quaternary ammonium compound. Note that tubocurarine contains two "quaternized" nitrogen atoms.

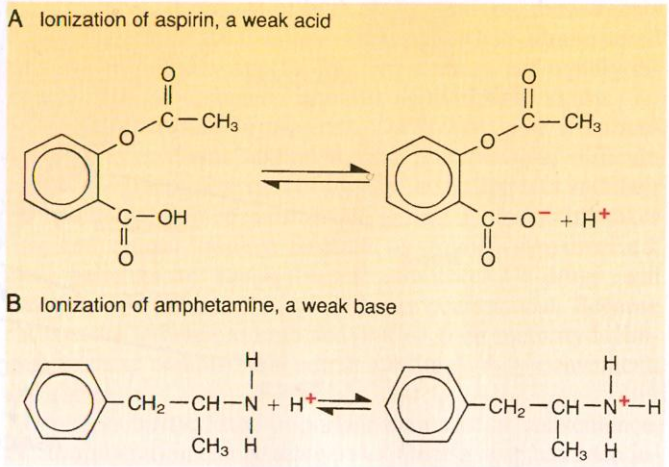

Figure 4–5 ▪ Ionization of weak acids and weak bases.
The extent of ionization of weak acids (*A*) and weak bases (*B*) depends on the pH of their surroundings. The ionized (charged) forms of acids and bases are not lipid soluble and hence do not readily cross membranes. Note that acids ionize by giving up a proton and that bases ionize by taking on a proton.

Gli acidi tendono a ionizzarsi in mezzi basici
Le basi tendono a ionizzarsi in mezzi acidi

Intrappolamento ionico (riapartizione da pH)

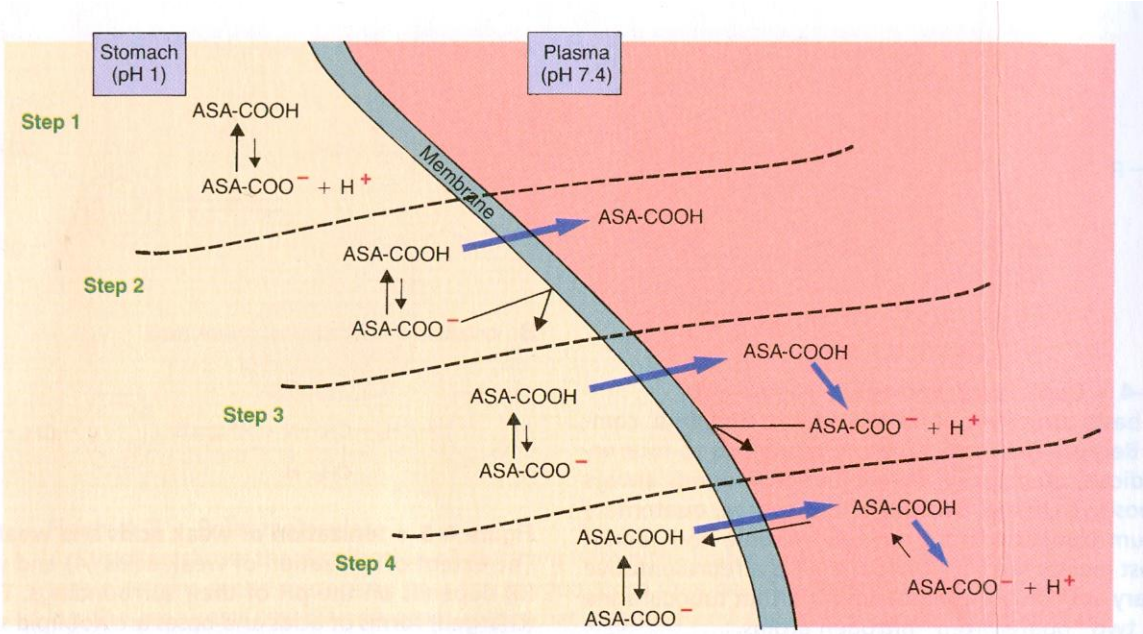

Figure 4–6 ▪ **Ion trapping of drugs.**
This figure demonstrates ion trapping using aspirin as an example. Because aspirin is an acidic drug, it will be nonionized in acid media and ionized in alkaline media. As indicated, ion trapping causes molecules of orally administered aspirin to move from the acidic (pH 1) environment of the stomach to the more alkaline (pH 7.4) environment of the plasma, thereby causing aspirin to accumulate in the blood. In the figure, aspirin (acetylsalicylic acid) is depicted as ASA with its COOH (carboxylic acid) group attached.

Step 1, Once ingested, ASA dissolves in the stomach contents, after which some ASA molecules give up a proton and become ionized. However, most of the ASA in the stomach remains nonionized. Why? Because the stomach is acidic, and acidic drugs don't ionize in acidic media.

Assorbimento

Movimento di un farmaco dal suo sito di assorbimento al sangue

Fattori che influenzano l'assorbimento dei farmaci

- Ritmo di dissoluzione
- Area della superficie
- Flusso sanguigno
- Liposolubilità
- Ripartizione da pH

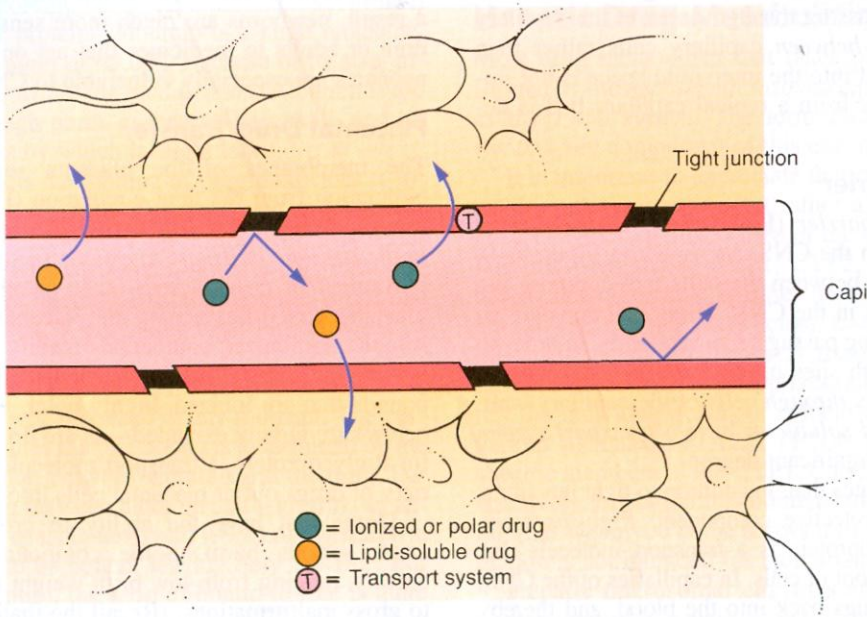

Figure 4–9 ■ Drug movement across the blood-brain barrier.
Tight junctions between cells that compose the walls of capillaries in the CNS prevent drugs from passing between cells to exit the vascular system. Consequently, in order to reach sites of action within the brain, a drug must pass directly through cells of the capillary wall. To do this, the drug must be lipid soluble or be able to use an existing transport system.

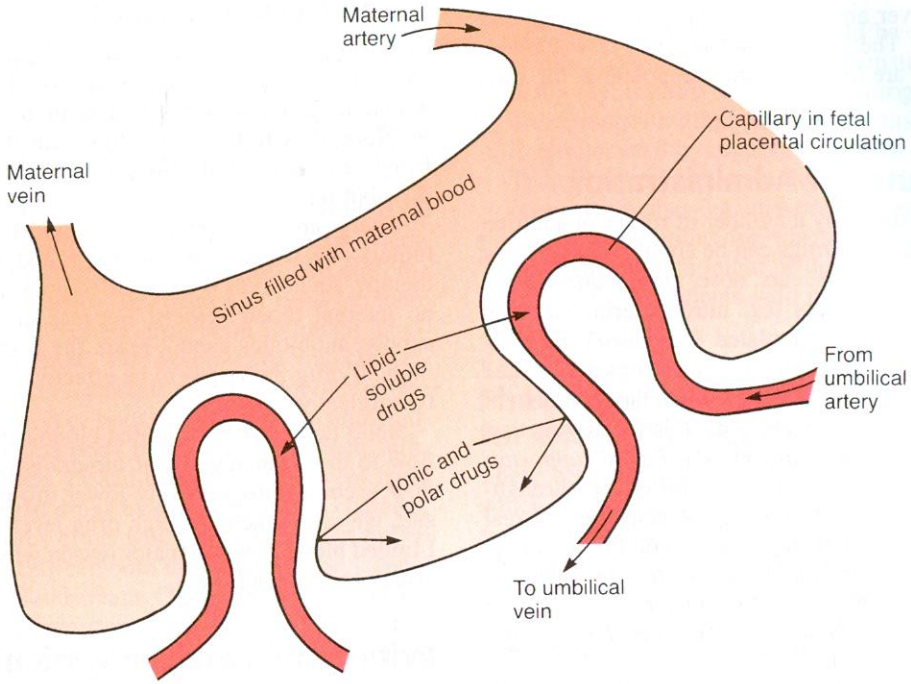

Figure 4–10 ■ **Placental drug transfer.**
To enter the fetal circulation, drugs must cross membranes of the maternal and fetal vascular systems. Lipid-soluble drugs can readily cross these membranes and enter the fetal blood, whereas ions and polar molecules are prevented from reaching the fetal blood.

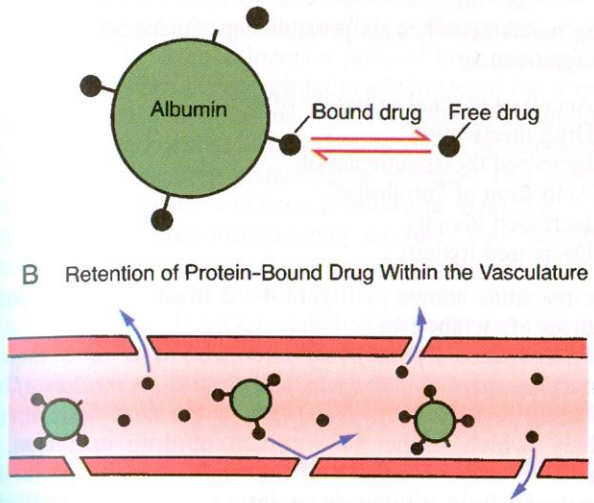

Figure 4–11 ▪ Protein binding of drugs.
A, Albumin is the most prevalent protein in plasma and the most important of the proteins to which drugs bind. *B,* Only unbound (free) drug molecules can leave the vascular system. Bound molecules are too large to fit through the pores in the capillary wall.

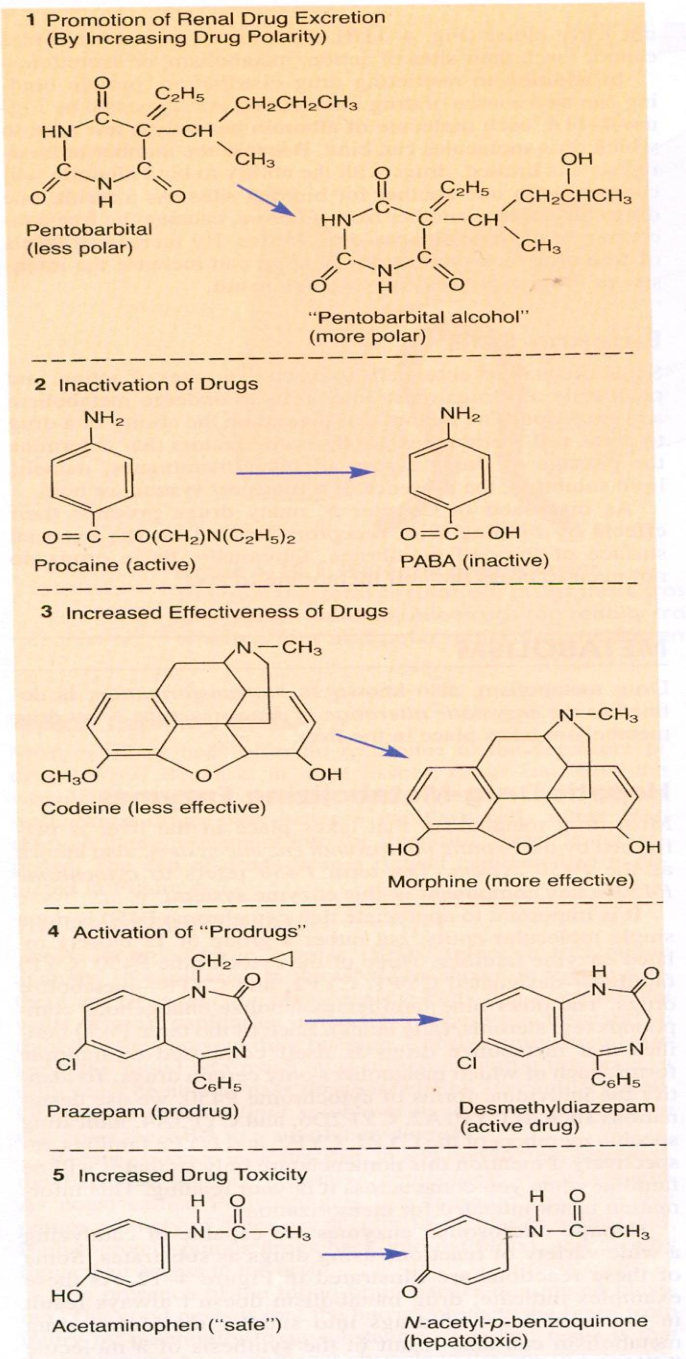

Figure 4–12 ■ **Therapeutic consequences of drug metabolism.** (See text for details.)

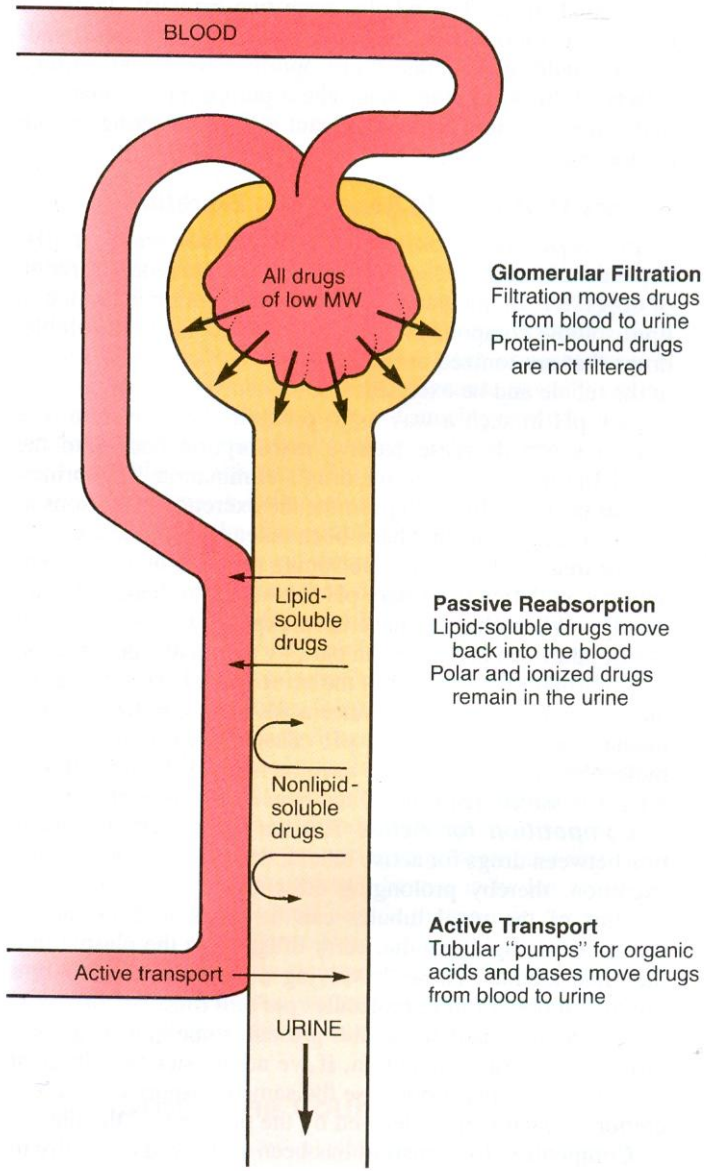

Figure 4–13 ■ **Renal drug excretion.**
(MW = molecular weight.) (Redrawn from Binns TB [ed]: Absorption and Distribution of Drugs. Edinburgh: Churchill Livingstone, 1964.)

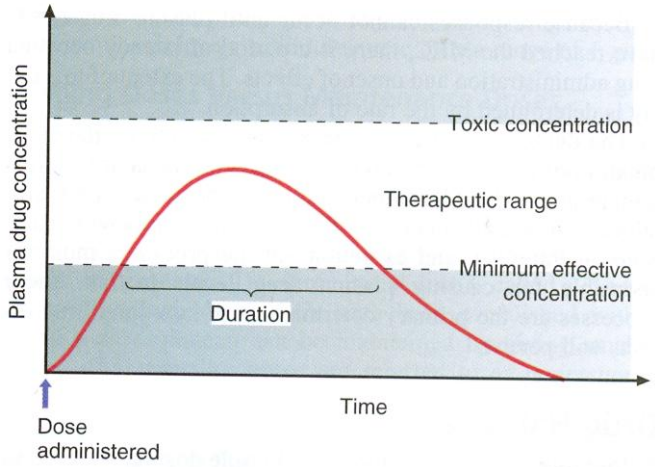

Figure 4–14 ■ **Single-dose time course.**

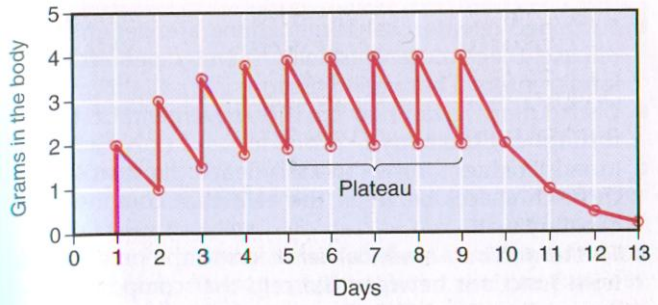

Figure 4–15 ■ **Drug accumulation with repeated administration.**