Figure 4-1AB

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Figure 4-1D
Phagocytosis

Pinocytosis
Figure 4-2

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Blood pH = 7.4

Stomach pH 2–3

Aspirin

○ = Nonionized aspirin
+= Ionized aspirin

Figure 4-3
Copyright © 2011 Delmar, Cengage Learning
Drug swallowed and disintegrated → Not dissolved, lost in feces

Drug dissolved in gastrointestinal fluids → Lost in stomach acid

Dissolved drug reaches intestine → Lost in food, stomach acid, digestion

Drug absorbed and enters portal system

Drug in liver → Biotransformed to noneffective state

Drug in circulation → Bound to plasma proteins (not available until free)

Drug distributed throughout body → Reaches reactive tissue

Drug causes desired effect

Drug excreted by kidneys, lungs, skin, etc.

Bound to fat tissue
Figure 4-5

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Figure 4-6

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Figure 4-7
Copyright © 2011 Delmar, Cengage Learning
Figure 4-8
Less concentrated
More concentrated
Figure 4-10

Glomerular filtration
Bowman’s capsule
Proximal convoluted tubule
Distal convoluted tubule
Loop of Henle
Collecting Duct

Drugs
Amino acids
Glucose
Uric acid
Urea
H₂O

Salts

H₂O
Na⁺
Cl⁻

Drugs
(highly lipid soluble)

H₂O
Na⁺
Cl⁻

H₂O
Nh₄⁺
Creatinine

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Figure 4-11A
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Figure 4-11B

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Figure 4-11C

Minimum toxic concentration (MTC)

Minimum effective concentration (MEC)

Drug concentration in plasma

Time (hours)
Figure 4-13

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Tissue sites of action (therapeutic, toxic)

Tissue storage sites (fat, protein)

Drug dose administered into:
- GI tract
- Muscle
- Subcutaneous tissue etc.

Drug bound to plasma proteins (albumin)

Absorption

Distribution

Plasma

Drug

Distribution

Metabolites

Biotransformation in:
- Liver
- Kidneys
- Plasma etc.

Reabsorption

Excretion by:
- Kidney
- Bile
- Lungs etc.

Figure 4-14
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### Table 4-1  Mechanisms of Drug Movement

<table>
<thead>
<tr>
<th>Type of Movement</th>
<th>Energy</th>
<th>Carrier</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Passive diffusion: random movement of molecules from an area of high concentration of molecules to an area of low concentration of molecules</td>
<td>−−</td>
<td>−−</td>
<td>• Rapid for nonionic, lipophilic, small molecules</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Slow for large, ionic, hydrophilic molecules</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Lower temperatures slow the rate of diffusion; higher temperatures speed the rate of diffusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Thick cell membranes slow the rate of diffusion; thin cell membranes do not slow the rate of diffusion</td>
</tr>
<tr>
<td>Facilitated diffusion: passive movement with special molecules within the membrane that carry the molecules through the membrane</td>
<td>−−</td>
<td>++</td>
<td>• Like passive diffusion except uses a carrier molecule</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Cannot concentrate molecules on one side or the other</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Entry of glucose into the cells occurs by facilitated diffusion with the help of insulin molecules</td>
</tr>
<tr>
<td>Active transport: movement of molecules across membranes involving a carrier molecule that pumps the molecule against a concentration gradient</td>
<td>++</td>
<td>++</td>
<td>• Like facilitated diffusion but needs energy (ATP)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Movement of strongly acidic or basic substances into urine usually occurs by active transport</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• pH gradient in body systems usually occurs by active transport</td>
</tr>
<tr>
<td>Pinocytosis/phagocytosis: cell drinking or cell eating in which cellular membrane surrounds the molecule and takes it into the cell</td>
<td>++</td>
<td>−−</td>
<td>• Large drug molecules, such as proteins, are usually involved in these processes</td>
</tr>
</tbody>
</table>
### Table 4-2 Drug Factors that Affect Drug Absorption

| Drug Chemistry       | • Lipophilic drugs dissolve in oil-based fluids. Lipophilic drugs are absorbed well across phospholipid-based cell membranes.  
|                      | • Hydrophilic drugs dissolve readily in water (tissue, fluid, and lymph). Tissue fluid is water soluble; therefore, drugs that are hydrophilic dissolve in and diffuse through tissue fluid quite well. |
| Drug Size            | • Molecular size of the drug: Small molecules can pass more readily through cell membranes. |
| Ionization of the Drug | • Nonionized or neutral drugs are lipophilic and can pass through phospholipid cell membranes.  
|                      | • Ionized or charged drugs are hydrophilic and dissolve in and diffuse through tissue fluid.  
|                      | • Ionization of the drug depends on the drug pH and the environmental pH. |
| Acid-Base Characteristics | • pH of drug: Drugs may change their form when the pH of the environment changes. Weak acids become more ionized as the pH of the environment increases. Weak bases become more ionized as the pH of the environment decreases. |
| Ion Trapping         | • Drugs can pass from one compartment to another compartment with a different pH. When the drug changes compartments, it may become ionized and become trapped in its new environment |
| Drug Form            | **Oral** drugs must be in lipophilic form to penetrate the GI mucosa. They must be small to dissolve in the membrane.  
|                      | • Tablets must dissolve into smaller particles. Liquid drugs do not have a dissolution step; therefore, oral liquid drugs have a quicker onset of action than pills.  
|                      | • The drug (enteric coating) or special construction of the tablet (sustained-release) may alter dissolution and/or absorption.  
|                      | • Decreased gastric motility lengthens the time it takes for the drug to reach the absorption site.  
|                      | • Increased gastric motility shortens the time the drug remains in the GI tract. This time may not be long enough to allow drug dissolution, and the drug may pass unused in the feces.  
|                      | • The drug must be able to survive first-pass effect or detoxification by the liver. Remember that a drug is absorbed from the intestine and passes through the liver before it enters the systemic circulation.  
|                      | • The presence of food may interfere with the dissolution and absorption of certain drugs.  
|                      | **Parenteral** drugs must be in hydrophilic form.  
|                      | • Anything that interferes with diffusion of the drug from the administration site or alters blood flow to the injection site will delay absorption.  
|                      | • Some drugs are formulated to have a delayed absorption (repository or depot injections).  
|                      | • If there is limited blood flow in the injection site, absorption will be slowed (fat is poorly perfused, muscle is richly perfused).  
|                      | • Temperature may result in vasoconstriction or vasodilation, and affect blood flow to the administration site.  
|                      | • Other drugs may affect blood flow as well (e.g., lidocaine). |
### Table 4-3 Patient Factors that Affect Drug Absorption

<table>
<thead>
<tr>
<th>ANIMAL FACTOR</th>
<th>EXAMPLE OF EFFECT</th>
</tr>
</thead>
</table>
| Age | • Young animals may not have well-developed gastrointestinal tracts.  
• Young animals may have less active enzyme systems. |
| Health | • Fever may cause molecules to move faster and increase absorption.  
• Disease signs like diarrhea may speed the drug through the gastrointestinal tract and not allow enough time for proper absorption.  
• Disease signs like vomiting may affect the time the drug is in the stomach, hindering absorption.  
• Poor circulation due to a variety of disease conditions hampers drug absorption. |
| Metabolic rate | • Animals with a high basal metabolic rate may metabolize and/or eliminate drugs more rapidly than those with a normal metabolic rate. |
| Genetic factors | • Individual variation in response to drugs may occur because of genetic differences between animals. For example, one animal may metabolize a drug more slowly due to a genetically based enzyme deficiency. |
| Sex | • Male and female animals have different body compositions. The proportion of fat to lean body mass may influence the action and distribution of drugs throughout the animal's body. |
| Species | • Drugs and food may stay in the rumen for longer periods of time, which may delay drug absorption.  
• Herbivores that continuously graze may have altered drug absorption due to the presence of food in the gastrointestinal tract. |
### Table 4-4  Factors Affecting Biotransformation

<table>
<thead>
<tr>
<th>FACTOR</th>
<th>HOW BIOTRANSFORMATION IS AFFECTED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma protein binding</td>
<td>Less plasma protein binding allows excretion of drug</td>
</tr>
<tr>
<td>Storage in tissue and fat depots</td>
<td>Fat and tissue storage decrease the rate of metabolism</td>
</tr>
<tr>
<td>Liver disease</td>
<td>Affects cytochrome P450 production</td>
</tr>
<tr>
<td>Age of patient</td>
<td>Young animals have decreased metabolic pathways (except horses), a blood-brain barrier that is not yet well established, and higher percent of body water that affects volume of distribution</td>
</tr>
<tr>
<td>Nutritional status of patient</td>
<td>Poor nutrition yields inadequate plasma proteins</td>
</tr>
<tr>
<td>Species and individual variation</td>
<td>Cats have a reduced ability to biotransform aspirin</td>
</tr>
<tr>
<td>Body temperature</td>
<td>Increased body temperature increases rate of drug metabolism</td>
</tr>
<tr>
<td>Route of administration</td>
<td>Some drugs given parenterally have an effect, but when given orally have no effect (e.g., apomorphine)</td>
</tr>
</tbody>
</table>