Environmental Toxicology
Teacher's Guide

- Introduction to Environmental Toxicology
- Principles of Toxicology
- Ecotoxicology
- Chemical Carcinogenesis
- Target Organ Toxicology: Responses to Environmental Toxicants
- Pesticides and Industrial Chemicals
- Risk Assessment and Risk Management
- Environmental Epidemiology

ABSORPTION, DISTRIBUTION AND EXCRETION

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ABSORPTION, DISTRIBUTION AND EXCRETION

DISCUSSION ON HOW CHEMICALS :

- **ENTER THE BODY**
- **MOVE AROUND IN THE BODY TO DIFFERENT ORGANS**
- **STORED IN THE BODY**
- **REMOVED FROM THE BODY**

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BIOLOGICAL RESPONSE IS DIRECTLY DEPENDENT UPON DOSE

THE CHEMICAL REACTION PRODUCED BY A TOXICANT IS DEPENDENT UPON THE CONCENTRATION OF THAT CHEMICAL ON THE TARGET CELL.

THE BIOLOGICAL RESPONSE (TOXICITY) DEPENDS ON THE CHEMICAL REACTION.

THE DOSE DETERMINED WHETEHR A TOXIC RESPONSE WILL OCCUR.

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EXPOSURE AND DOSE

EXPOSURE IS THE PRESENTATION OF THE TOXICANT TO THE INDIVIDUAL PERSON OR ANIMAL

- **parts per million**
- **milligrams per cubic meter of air**
- **micrograms per liter of water**

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EXPOSURE AND DOSE

DOSE IS THE AMOUNT OF TOXICANT THAT REACHES THE TARGET ORGAN TO ELICIT A RESPONSE THAT IS THE RESULT OF A CHEMICAL REACTION BETWEEN THE TOXICANT AND AN ENDOGENOUS COMPOUND IN OR ON THE TARGET CELL

- **milligrams per kilogram body weight**

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ABSORPTION, DISTRIBUTION AND EXCRETION

ABSORPTION :

- **transfer across cells composing the body surfaces**

DISTRIBUTION :

- **toxicant passes to some, several, or all of the tissues of the body**

EXCRETION :

- **formation of urine and bile**
- **exhalation of volatile chemicals**

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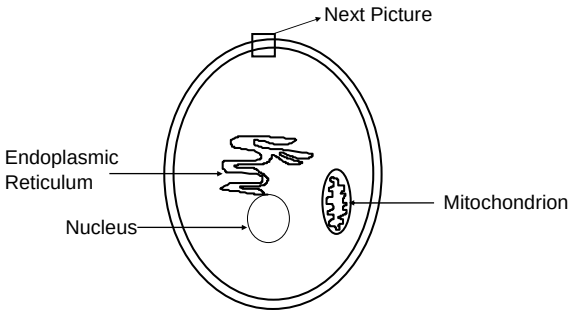
THE CELL MEMBRANE



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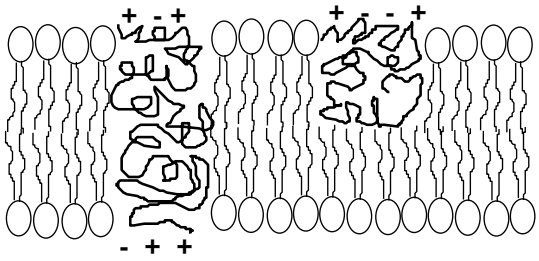
THE CELL MEMBRANE



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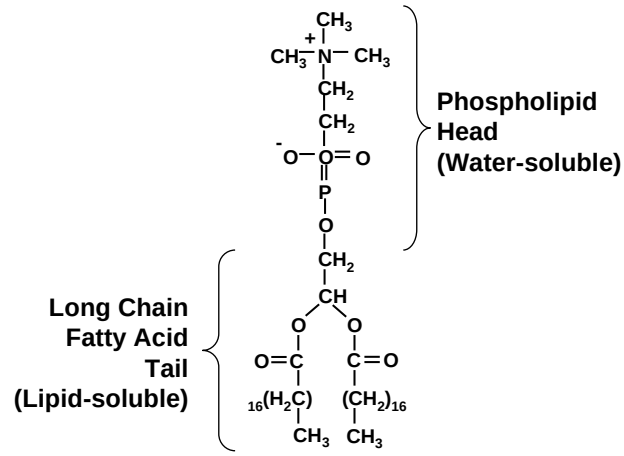

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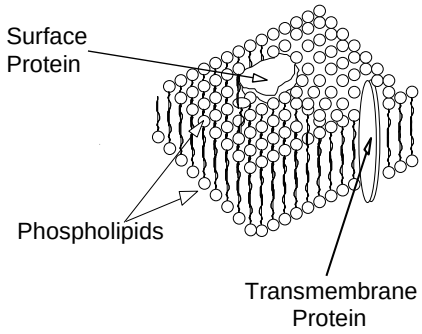
Structure of Mammalian Cell Membrane



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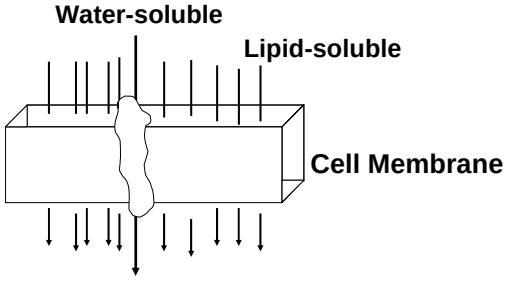
SMALL LIPID-SOLUBLE COMPOUNDS ARE USUALLY ABSORBED INTO CELLS FASTER THAN WATER-SOLUBLE COMPOUNDS



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CELL MEMBRANE PROTEINS CAN ACT AS RECEPTORS

Some surface proteins have specialized functions; toxicants can bind to these proteins to effect a biological response.

Such proteins are called receptors.

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ABSORPTION OF THE TOXICANTS

Major routes of absorption of environmental toxicants are :

- **skin**
- **lungs**
- **gastrointestinal tract**

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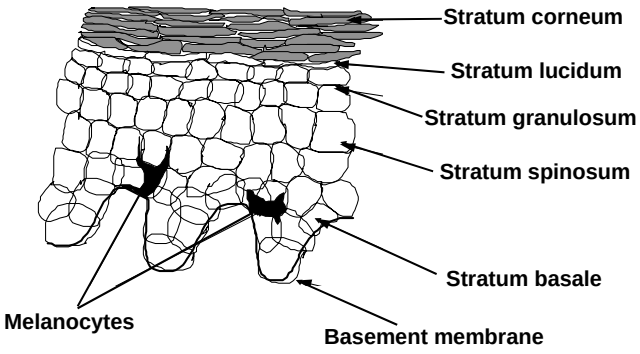

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SKIN ABSORPTION DEPENDS ON SEVERAL FACTORS

- **Thickness of Skin**
- **Effective Blood Flow**
- **Interstitial Fluid Movement**
- **Lymphatics**
- **Temperature**
- **Extent of Hydration**

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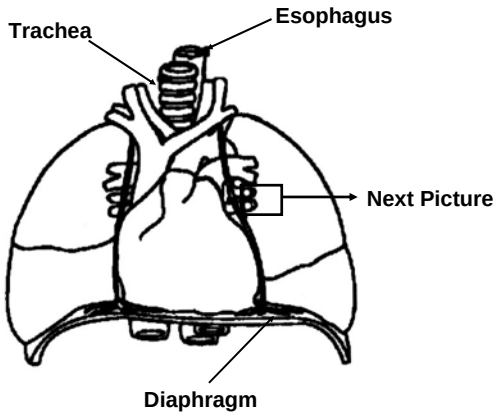

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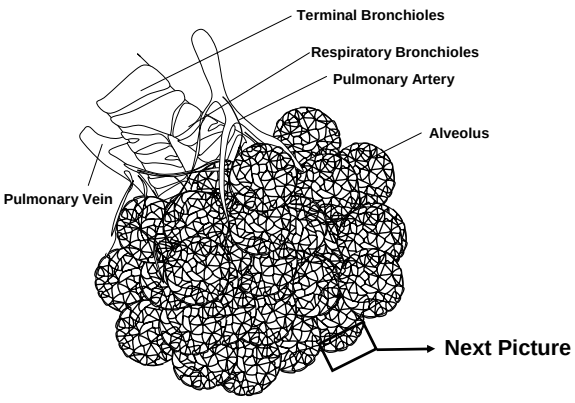

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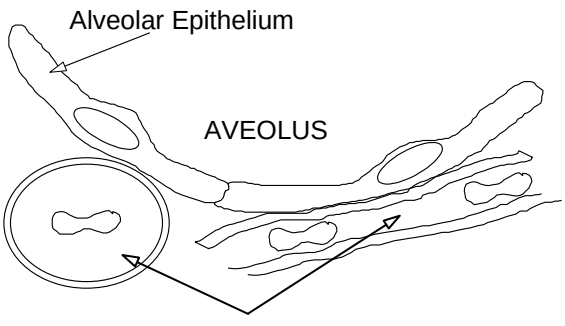

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ABSORPTION OF GASES

Water-soluble gases dissolve in the mucus lining

Lipid-soluble gases diffuse across the alveolar membrane

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DISTRIBUTION OF AEROSOLS

Aerodynamic properties particle size :

>10 microns : impact upper airways

1-5 microns : bronchioles and alveolar ducts

<1 micron : alveolar sacs

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CILIARY TRANSPORT OF PARTICLES

Above terminal bronchioles, cilia on epithelial cells move particles up the airway toward the mouth; particles can be swallowed or expectorated.

Ciliary transport can be rapid; more than 90% of the particles deposited on the mucosa can be cleared in an hour.

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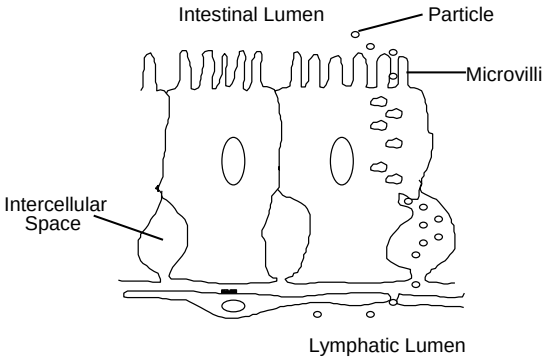
PASSAGE OF PARTICLES THROUGH INTESTINAL EPITHELIUM (VILLUS)



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PASSAGE OF PARTICLES THROUGH INTESTINAL EPITHELIUM

Most toxicants are absorbed passively.

Some toxicants are absorbed by active transport pathways.

Particles can enter epithelium.

Weak acids and bases are absorbed faster as unionized molecules.

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WEAK ACIDS AND BASES

Weak acid : hydrogen ion (H^+) donor

Weak base : hydrogen ion receiver

Handerson-Hasselbach equation :

$$pH = pKa + \log \frac{[base]}{[acid]}$$

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IONIZED ACIDS AND BASES ARE ABSORBED FASTER

	Low pH	High pH
weak acid	unionized	ionized
weak base	ionized	unionized

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DISTRIBUTION AND EXCRETION OF TOXICANTS DEPENDS ON MANY FACTORS

- water and lipid compartments
- macromolecular binding
- passage through placenta
- passage into brain and CSF
- ventilation rate (pulmonary excretion)
- rate of urine formation (renal excretion)
- rate of bile formation (biliary excretion)
- metabolism
- others

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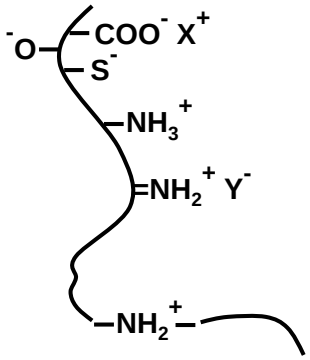
TOXICANTS CAN BIND TO PLASMA PROTEINS



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EXCRETION OF TOXICANTS

Water-soluble compounds can be rapidly excreted by the kidney via the urine.

Large water-soluble compounds can be excreted by the liver in the bile.

Lipid-soluble compounds can enter the urine and bile, but are rapidly reabsorbed back into the kidney and liver tissue, and therefore, not excreted.

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RATE OF ABSORPTION

In most cases, the rate of absorption is dependent upon the concentration gradient between the site of absorption and the blood.

$$\log M = \log M_o - \frac{k_a}{2.30}$$

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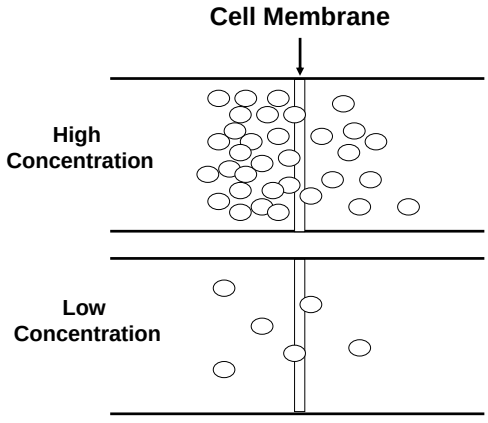

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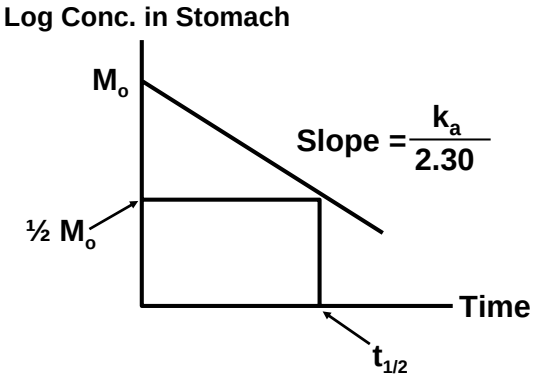
CONCENTRATION OF ASPIRIN IN STOMACH



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SUMMARY

- Exposure to a xenobiotic via air, food, or water, or by contact with the skin can lead to transfer of that xenobiotic to the blood and circulation to the tissues of the body.
- Lipid-soluble compounds are usually absorbed faster than water-soluble xenobiotics because the cell (plasma) membrane is more lipoid than aqueous.
- Xenobiotics can be held in the body by being stored in the fatty tissues and by being bound to proteins.

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SUMMARY

- The body can excrete only water-soluble xenobiotics in the urine and bile; lipid-soluble xenobiotics can be excreted via the lung only if they are highly volatile.
- The concentration of a xenobiotic in the blood determines in large part the concentration of that xenobiotic in most tissues.
- Fast rates of absorption into the blood and slow rates of excretion from the body can lead to high concentrations of xenobiotics in the body.

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