CHAPTER OVERVIEW

Section 11: Distribution

Learning Objectives

After completing this lesson, you will be able to:

- Explain distribution and its role in toxicokinetics.
- Describe the impact of exposure route on distribution.
- Describe three models of disposition.
- Identify structural barriers to distribution.

In this section...

Topics include:

Section 11: Key Points

What We've Covered

This section made the following main points:

- Distribution is the process in which an absorbed chemical moves away from the site of absorption to other areas of the body.
- An absorbed chemical passes through cell linings of the absorbing organ (skin, lung, or gastrointestinal tract) into the interstitial fluid of that organ.
- The toxicant can leave the interstitial fluid by entering local tissue cells, blood capillaries and the blood circulatory system, or the lymphatic system.
- If the toxicant gains entrance into the blood plasma, it:
  - Travels bound or unbound along with the blood.
  - May be excreted, stored, or biotransformed, or may interact or bind with cellular components.
- The volume of distribution (VD) is the total volume (in liters) of body fluids in which a toxicant is distributed.
- The route of exposure is an important factor affecting the concentration of the toxicant or its metabolites at any specific location within the blood or lymph.
  - Toxicants entering from the GI tract or peritoneum are immediately subject to biotransformation or excretion by the liver and elimination by the lung (this is often called the "first-pass effect").
  - Toxicants absorbed through the lung or skin enter the blood and go directly to the heart and systemic circulation, thus being distributed to various organs before going to the liver (not subject to the first-pass effect).
  - Toxicants that enter the lymph will not go to the liver first, but will slowly enter systemic circulation.
  - The blood level of a toxicant depends on the site of absorption and the rate of biotransformation and excretion.
- Disposition is the combined processes of distirbution, biotransformation, and elimination. Disposition models can be:

- One-Compartment Open Model — disposition of a substance introduced and distributed instantaneously and evenly in the body and eliminated proportionally to the amount left in the body ("first-order" rate).
- Two-Compartment Open Model — the chemical enters and distributes in the first compartment (usually blood), then distributed to another compartment where it can be eliminated or may return to the first compartment.
  - The biological half-life, the most commonly used measure of the kinetic behavior of a xenobiotic, is the half-life for a chemical in a two-compartment model.
- Multiple Compartment Model — the chemical involves several peripheral body compartments, including long-term storage, or biotransformation and elimination at varying rates as blood levels change.

- Organs or tissues differ in the amount of a chemical they may receive, depending on:
  - Volume of blood — organs that receive larger blood volumes potentially accumulate more of a given toxicant.
  - Tissue affinity — some tissues have a higher affinity for specific chemicals, accumulating a toxicant in great concentrations despite a rather low flow of blood.
- Structural barriers to distribution include the blood-brain barrier and the placental barrier.
- Toxicants can also be stored:
  - When bound to plasma proteins in the blood
  - In adipose tissues
  - In bone
  - In the liver
  - In the kidneys
