11.2: Influence of Route of Exposure

Influence of Exposure Route

The **route of exposure** is an important factor that can affect the concentration of the toxicant (or its metabolites) at any specific location within the blood or lymph. This can be important since the time and path taken by the chemical as it moves through the body influences the degree of biotransformation, storage, and elimination (and thus toxicity).

For example, if a chemical goes to the liver before going to other parts of the body, much of it may be biotransformed quickly. In this case, the blood levels of the toxicant "downstream" may be diminished or eliminated. This way of processing the chemical right away can dramatically affect its potential toxicity.

Gastrointestinal Tract and Peritoneum

When toxicants are absorbed through the **gastrointestinal (GI) tract**, a similar biotransformation process occurs. Blood carries absorbed toxicants entering the vascular system of the GI tract directly to the liver via the portal system. This is also true for those drugs administered by intraperitoneal injection. Blood from most of the peritoneum also enters the portal system and goes immediately to the liver. Blood from the liver then flows to the heart and then on to the lung, before going to other organs.

Thus, 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 referred to as the "first-pass effect."

For example, first-pass biotransformation of the drug propranolol (cardiac depressant) is about 70% when given orally. This means the blood level of this medication is only about 30% of a comparable dose administered intravenously.

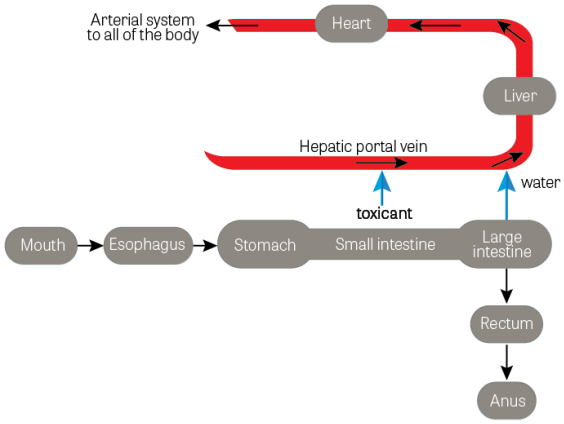

Figure 11.2.1. Movement of a toxicant through the portal system
(Image Source: Adapted from Kimball's Biology Pages. Original author: John W. Kimball, obtained under Creative Commons Attribution 3.0 Unported license, ©. View original image.)

Lung and Skin

Drugs and other substances that are absorbed through the **lungs** or **skin** enter the bloodstream to be carried throughout the body. Thus, they avoid the liver (hepatic) first-pass effect that would have occurred if they had been absorbed from the gastrointestinal tract. These substances can have local effects in the lungs or skin in addition to having systemic effects, and some cells in the lungs and skin may metabolize the drug or other substance. Examples of a "local first-pass effect" in the skin due to metabolism are when nitroglycerin and cortisol applied to the skin. Drugs administered intravenously or intramuscularly also enter the bloodstream to be carried throughout the body and avoid the liver (hepatic) first-pass effect.

Did you know?

Some advantages of transdermal drug delivery (skin patches):

- They are a better way to deliver substances that are broken down by the stomach acids, not well absorbed from the gut, or extensively broken down by the liver.
- They are a substitute for oral route.
- They permit constant dosing rather than the peaks and valley in medication level associated with orally administered medication.
- They can minimize undesirable side effects.
- They can be used to prescribe drugs that have short biological half-lives or a narrow therapeutic window.
- They can be removed, thereby terminating therapy easily.
- They are noninvasive, avoiding the inconvenience of IV therapy or injections.
- They can be used with patients who are nauseated or unconscious.
- They are cost-effective.

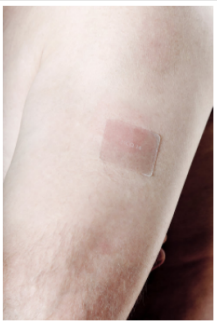

Figure 11.2.2 Nicotine patch
(Image Source: iStock Photos, ©)

Lymph

The delivery of drugs and bioactive compounds via the lymphatic system avoids first-pass metabolism by the liver and increases oral bioavailability. It is also a way to deliver drugs for diseases that spread through the lymphatic system such as certain types of cancer and the human immunodeficiency virus (HIV). For example, liposomes composed of phosphatidylethanol can enhance the oral bioavailability of poorly absorbed hydrophilic drugs such as cefotaxime.

Blood

The blood levels of a drug or other substance depend on the site of absorption, whether being absorbed after subcutaneous injection or more quickly from intramuscular injection. These blood levels also depend on the individual's rate of local and systemic biotransformation, and the rate of excretion. Uptake and release can occur in areas of the body away from the first site of absorption. Some anesthetics can be taken up by the lungs and later released, impacting blood levels. Lidocaine, given intravenously, is one example of this later release. Further, as noted elsewhere in ToxTutor, the metabolism of a substance can vary widely from person-to-person due to factors such as genetic differences, age, diet, and diseases that affect metabolism.

Some advantages of intramuscular injections:

- They are absorbed faster than subcutaneous injection, partly because muscle tissue has a larger blood supply than tissue just under the skin.
- They can hold a greater injected volume of drug (or vaccine) than a subcutaneous tissue injection can.
- They can be used instead of intravenous injection if a drug is irritating to veins or if a suitable vein cannot be located.
- They may be used instead of oral delivery if a drug is known to be degraded by stomach acids.

Knowledge Check

1) The main difference in distribution of a toxicant absorbed from the gastrointestinal tract from toxicants absorbed through the skin or from inhalation is:

a) The toxicant is distributed to more organs
b) A greater amount of the toxicant that is absorbed will be distributed to distant parts of the body
c) The toxicant enters the systemic circulatory system after first passing through the liver

Answer

The toxicant enters the systemic circulatory system after first passing through the liver - **This is the correct answer.**
Toxicants that enter the vascular system of the gastrointestinal tract are carried directly to the liver by the portal system. Thus, toxicants are immediately subject to biotransformation or excretion by the liver. This is often referred to as the "first pass effect."