

13.3: Fecal Excretion

Fecal Excretion

Elimination of toxicants in the feces occurs from two processes:

1. Excretion in bile, which then enters the intestine ("biliary excretion").
2. Direct excretion into the lumen of the gastrointestinal tract ("intestinal excretion").

Biliary Excretion

The **biliary route** is an important mechanism for fecal excretion of xenobiotics and is even more important for the excretion of their metabolites. This route generally involves active secretion rather than passive diffusion. Specific transport systems appear to exist for certain types of substances, for example, organic bases, organic acids, and neutral substances. Some heavy metals are excreted in the bile, for example, arsenic, lead, and mercury. However, the most likely substances to be excreted via the bile are comparatively large, ionized molecules, such as those having a large molecular weight (conjugates greater than 300).

Once a substance has been excreted by the liver into the bile, and then into the intestinal tract, it can be eliminated from the body in the feces, or it may be reabsorbed. Since most of the substances excreted in the bile are water soluble, they are not likely to be reabsorbed as such. However, enzymes in the intestinal flora are capable of hydrolyzing some glucuronide and sulfate conjugates, which can release the less polar compounds that may then be reabsorbed. This process of excretion into the intestinal tract via the bile and reabsorption and return to the liver by the portal circulation is known as the **enterohepatic circulation** (Figure 1).

Enterohepatic circulation prolongs the life of the xenobiotic in the body. In some cases, the metabolite is more toxic than the excreted conjugate. Continuous enterohepatic recycling can occur and lead to very long half-lives of some substances. For this reason, drugs may be given orally to bind substances excreted in the bile.

- For example, a resin can be taken orally to bind with dimethylmercury, which had been secreted in the bile. The binding of the resin to dimethylmercury prevents its reabsorption and further toxicity.

Changes in the production and flow of bile into the liver affect the efficiency of biliary excretion.

- Liver disease usually causes a decrease in bile flow.
- Some drugs such as phenobarbital can produce an increase in bile flow rate. Administration of phenobarbital has been shown to enhance the excretion of methylmercury by this mechanism.

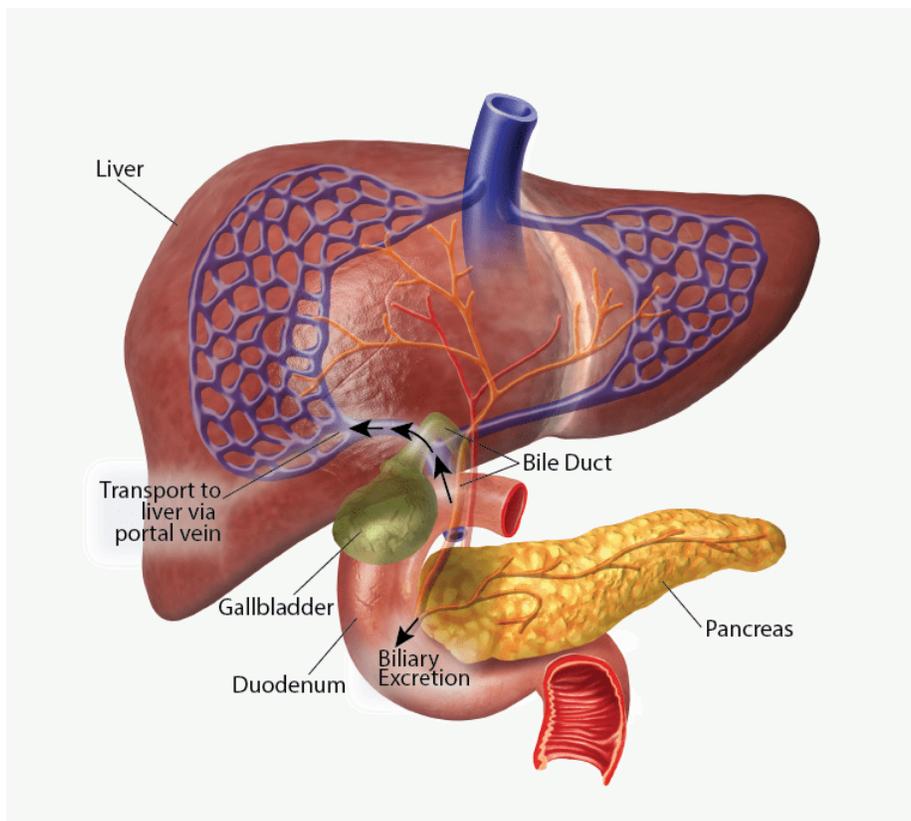


Figure 13.3.1 Biliary excretion and enterohepatic circulation
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Intestinal Excretion

Another way that xenobiotics can be eliminated via the feces is by direct **intestinal excretion**. While this is not a major route of elimination, a large number of substances can be excreted into the intestinal tract and eliminated via feces. Some substances, especially those that are poorly ionized in plasma (such as weak bases), may passively diffuse through the walls of the capillaries, through the intestinal submucosa, and into the intestinal lumen to be eliminated in feces.

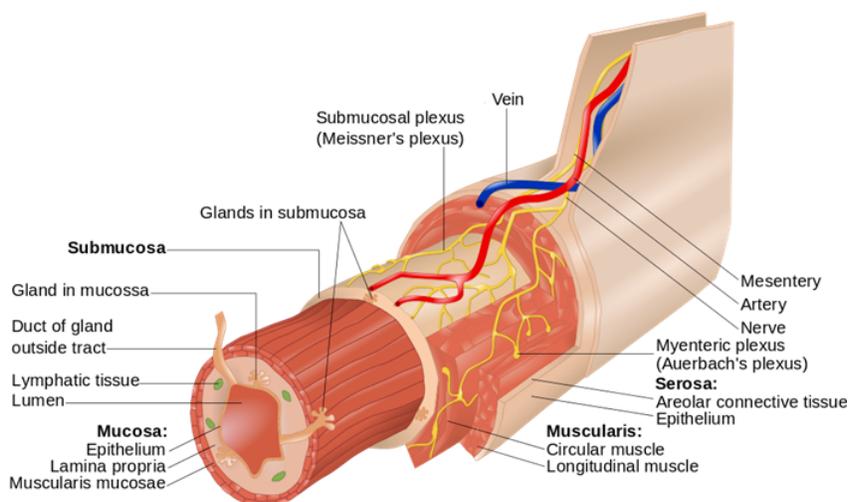


Figure 13.3.2 Layers of the Alimentary Canal

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Intestinal excretion is a relatively slow process and therefore, it is an important elimination route only for those xenobiotics that have slow biotransformation, or slow urinary or biliary excretion. Increasing the lipid content of the intestinal tract can enhance intestinal excretion of some lipophilic substances. For this reason, mineral oil (liquid paraffin, derived from petroleum) is sometimes added to the diet to help eliminate toxic substances, which are known to be excreted directly into the intestinal tract.

Knowledge Check

1) Substances excreted in the bile are primarily:

- a) Small, lipid soluble molecules
- b) Comparatively large, ionized molecules
- c) Large, lipid soluble molecules

Answer

Comparatively large, ionized molecules - **This is the correct answer.**

The most likely substances to be excreted via the bile are comparatively large, ionized molecules, such as large molecular weight (greater than 300) conjugates.

2) Many substances excreted in bile undergo enterohepatic circulation, which involves:

- a) Excretion of substances into the circulating system rather than into the intestine
- b) Excretion into the intestinal tract and reabsorption and return to the liver by the portal circulation
- c) The recycling of xenobiotics between the liver and gall bladder

Answer

Excretion into the intestinal tract and reabsorption and return to the liver by the portal circulation - **This is the correct answer.**

The process of excretion into the intestinal tract via the bile and reabsorption and return to the liver by the portal circulation is known as the enterohepatic circulation. The effect of this enterohepatic circulation is to prolong the life of the xenobiotic in the body.

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