Pharmacokinetics
(Excretion of Drugs and factors affecting Excretion)

LEARNING OBJECTIVES
By the completion of lecture, the student should be able to:
Explain the basic principles by which drugs are excreted from the body.
What are the routes of drug elimination.

EXCRETION OF DRUGS
• Drugs are eliminated from the body either unchanged as the parent drug or as metabolites (a changed form of the drug).

EXCRETION OF DRUGS
• Organs that excrete drugs eliminate polar compounds (water soluble) more readily than components with high lipid (fat) solubility. (Lungs Excluded).

SOURCES OF EXCRETION
• Lipid soluble drugs are not readily eliminated until they are metabolized to more polar compounds.
Possible sources of excretion include:
• Breath
• Urine
• Saliva
• Perspiration
• Feces
• Milk
• Bile
• Hair

Kidney
• The kidney is the most important organ involved in the elimination of drugs and their metabolites.
• Substances excreted in the feces usually involve orally ingested unabsorbed drugs or metabolites excreted in the bile that are not reabsorbed from the intestinal tract.
Elimination

- Kidneys = primary site
  - Mechanisms dependent upon:
    - Passive glomerular filtration
    - Active tubular transport
  - Partial reabsorption
  - Hemodialysis

Renal disease

- Slows excretion

- Prolongs effects

Active Tubular Transport

Probenecid is moved into the urine by the same transport pump that moves many antibiotics. Why Probenecid is sometimes given as an adjunct to antibiotic therapy?

It competes with the antibiotic at the pump and slows its excretion.

Urine pH and Elimination

A patient has overdosed on phenobarbital. Phenobarbital is an acid. If we ‘alkalinalize’ the urine by giving bicarbonate what will happen to the phenobarbital molecules as they are filtered through the renal tubules?

They will ionize...

How will this affect phenobarbital
How will this affect phenobarbital reabsorption by the kidney?

- Increased elimination
- Decreased reabsorption

Biliary and fecal excretion

- Many metabolites of drugs created in the liver are excreted into the intestinal tract in the bile.
- Hence the intestine is not only a site of absorption but it is also a site of excretion.

**ENTEROHEPATIC CYCLING**

- Net excretion by intestine may be greatly reduced by subsequent reabsorption into the bloodstream of fat-soluble compounds further along the intestines.
- In this case drugs will undergo the process of excretion all over again and the drug effect is prolonged.
- This excretion/reabsorption phenomenon is called enterohepatic cycling.

Biliary and fecal excretion

- Metabolites may be excreted in the feces. More commonly, they are
reabsorbed into the blood and ultimately excreted in the urine.

ELIMINATION BY OTHER ROUTES:
- Minute amounts of drugs are excreted into sweat, saliva and tears.
- Drugs excreted into the saliva enter the mouth, where they are usually swallowed.
- Their fate thereafter is the same as drugs taken orally.
- Some drug concentrations in saliva parallel those found in the plasma.

ELIMINATION BY OTHER ROUTES:
- Since breast milk is more acidic than blood plasma, basic compounds may become slightly concentrated.
- Although excretion into hair and skin occurs in small quantities, it does have forensic significance.