



# PHARMACOKINETICS (DRUG EXCRETION)

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Pharmacology, MA 411  
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# Outline

- Drug excretion

# Objectives

**At the end of the lesson, the students should be able to understand:**

1. Describe drug excretion.
2. Learn about factors affecting excretion.
3. Being familiar with organs have role in drug excretion.
4. Describe drug clearance
5. Describe elimination half-life of drugs

# Introduction to drug excretion



- Drug excretion refers to the process by which the body eliminates drugs and their metabolites (products of metabolism).
- Drug excretion is the **final step** in the pharmacokinetic process.
- This process is essential for the
  1. Termination of a drug's action
  2. Preventing toxic buildup in the body.

# Factors affecting excretion



**Excretion is influenced by factors like**

1. Age
2. The drug's chemical properties
3. Metabolism of drugs
4. The functioning of organs responsible for elimination

# Elimination of drugs



➤ **The body eliminates drugs and their metabolites (products of metabolism)**

**through:**

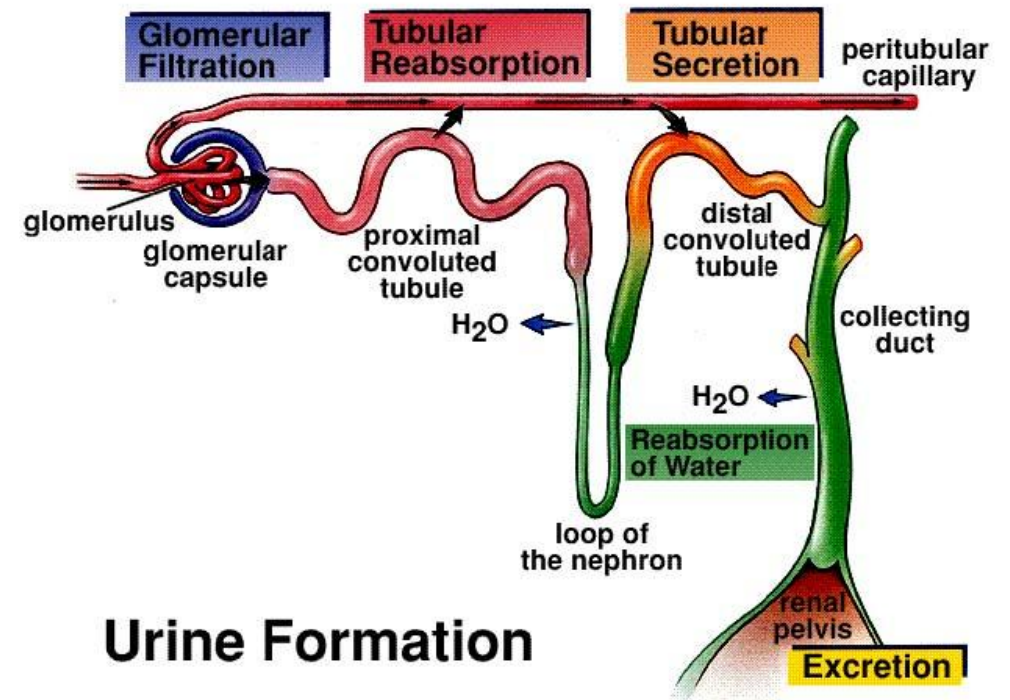
1. Renal excretion
2. Biliary excretion
3. Excretion from the lungs
4. Artificial excretion ways

# Renal excretion

➤ Drugs and metabolites are excreted from the kidneys by 2 ways.

1. Glomerular filtration

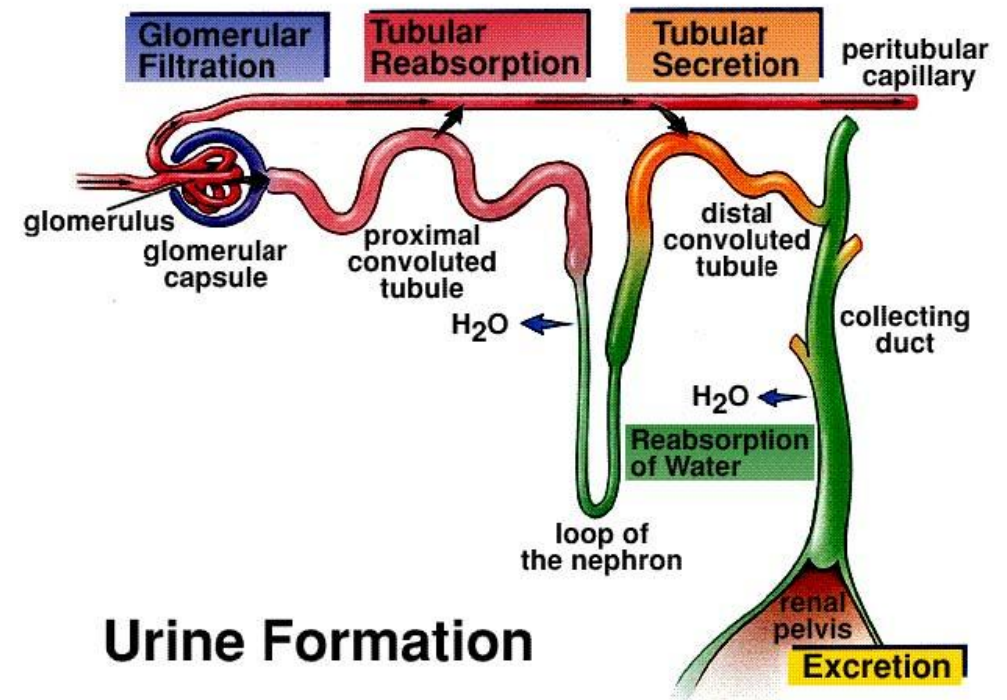
2. Tubular secretion



# Renal excretion

## 1. Glomerular filtration

- Simple passive diffusion play role in glomerular filtration.
- The filtration rate is **110-130 ml/min**.
- Drugs are filtered from the **glomerulus** into **proximal tubules** except the bound fraction of drug molecules to the plasma proteins.



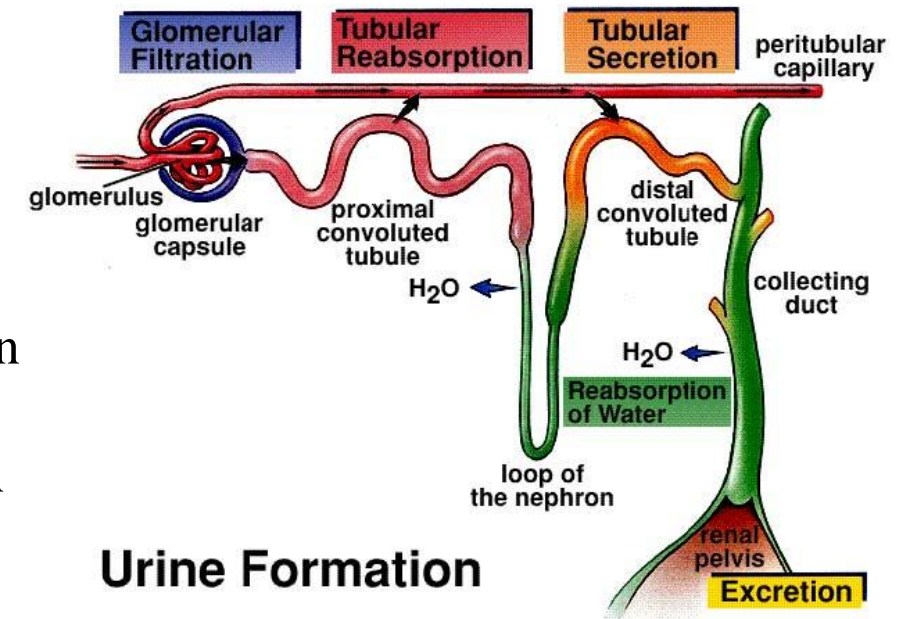
Urine Formation



# Renal excretion

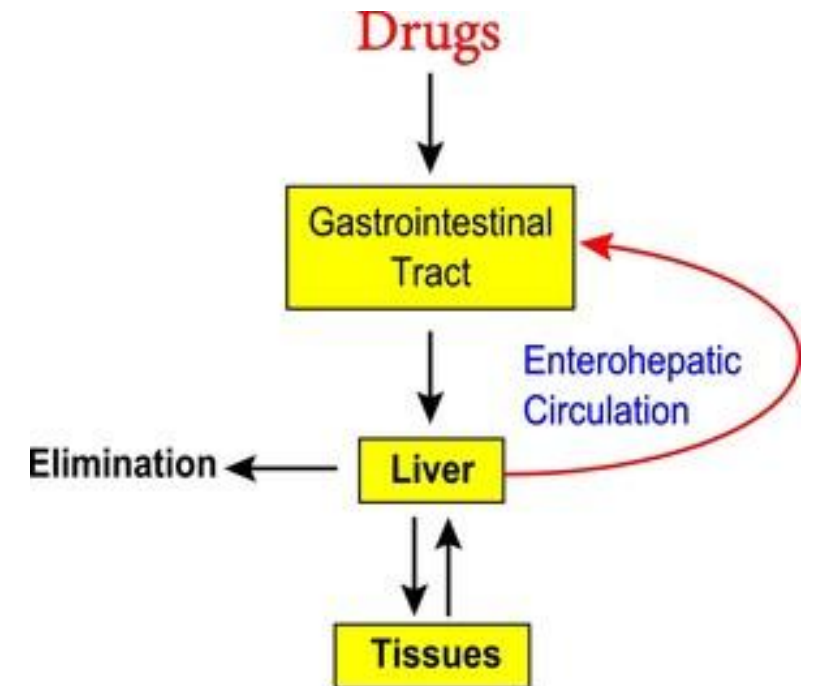
## 2. Tubular secretion:

- Tubular secretion occurs mainly in the **proximal convoluted tubules**.
- **Active transport** is the main mechanism for tubular secretion.
- The efficiency (performance) of the excretion by tubular secretion is **higher** than glomerular filtration route. Clearance maximum in glomerular filtration is approximately **120 ml/min**, whereas the clearance maximum of tubular secretion is about **600 ml/min**.



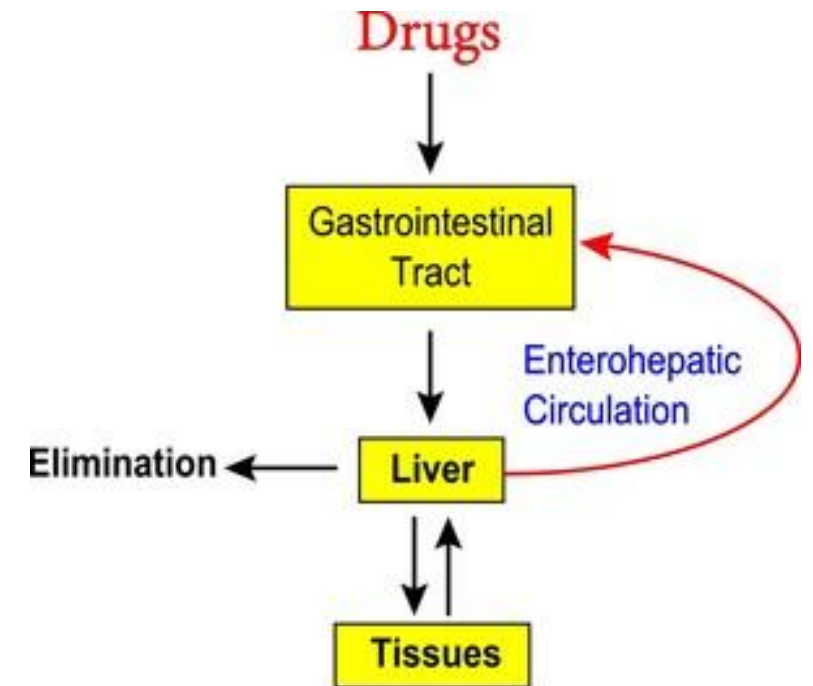
# Biliary excretion

- After biotransformation, metabolites are drained into the **small intestine by biliary duct.**
- Drug metabolites in the small intestine are broken down again in the small intestine and reabsorbed back reaching the liver by **portal vein again.**
- This cycle between the liver and small intestine is called the **enterohepatic cycle.**



# Biliary excretion

- This is **important**, because enterohepatic cycle prolongs the duration of stay of the drugs in our body which leads an increase in the duration of their effect.
- Drug examples that go under the enterohepatic cycle in remarkable amounts.
- Digitoxin
- Chloramphenicol



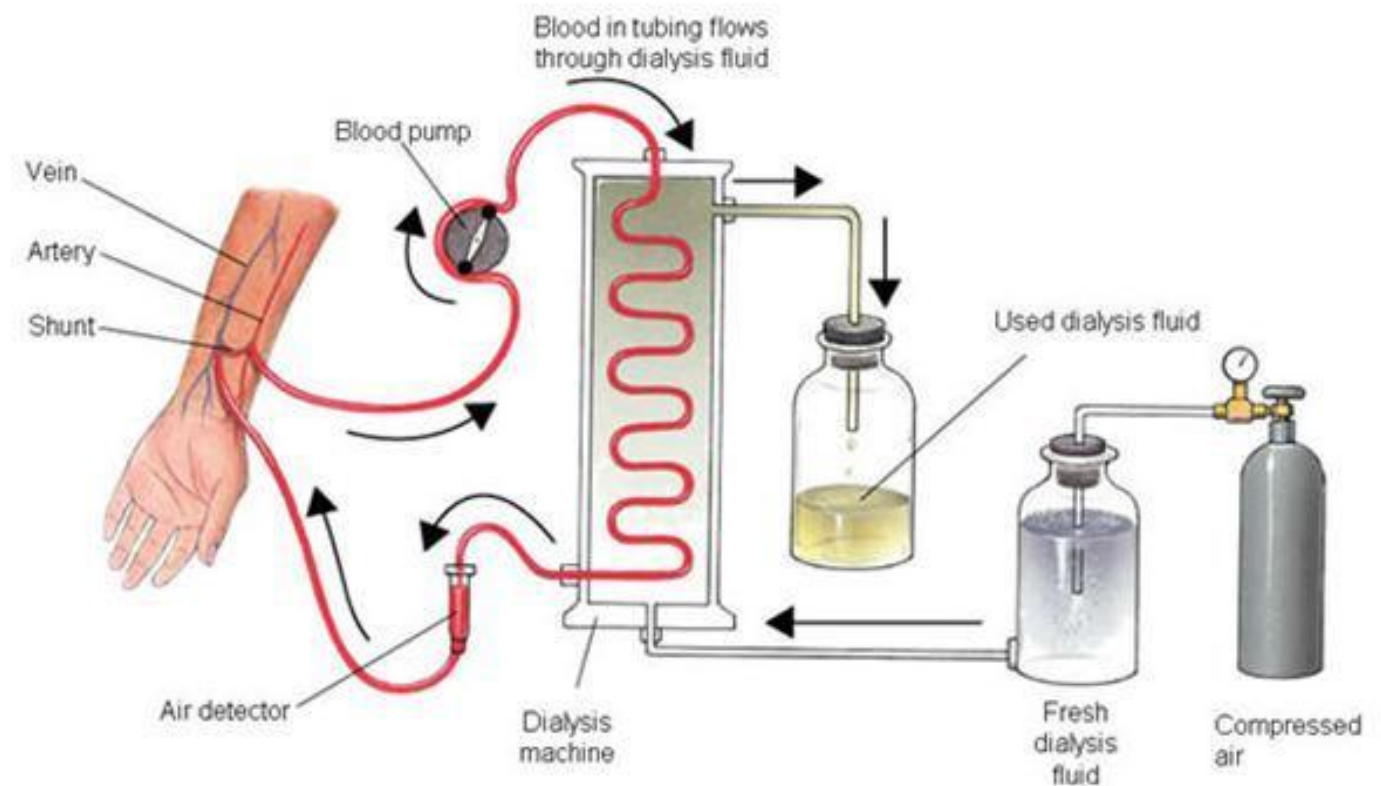
# Excretion from the lungs



- **Gaseous or the volatile substances** can pass from the blood circulation into the **alveoli** by passing across the endothelium and epithelium of the alveolar membrane.
- **Simple passive diffusion** is the main mechanism for this transport.
- After passing into the alveoli, these substances can be excreted by **exhalation**.

# Artificial excretion ways

- Hemodialysis is one of the options among the artificial excretion way for the drugs.
- It is used especially for the treatment of **acute drug intoxications** to eliminate the drug from the body.



# Artificial excretion ways



**For the achievement of this system, there are some requirements:**

1. Plasma protein binding of the drug should be low (bound fraction should be low).
2. Drug should not be stored in tissues

# Clearance



- **Clearance** can be described as the volume of plasma cleared from the drug per unit time (ml/min).
- **Renal clearance:** It can be described as the rate of the excretion of a drug from kidneys. So in other words, renal clearance is the volume of plasma cleared from the non-metabolized (unchanged) drug via the excretion by kidneys per minute.

# Factors that affect the renal clearance



➤ **There are four important factors that affect the renal clearance of the drugs:**

1. Plasma protein binding of the drug.
2. Glomerular filtration ratio of the drug.
3. Tubular reabsorption ratio of the drug.
4. Tubular secretion ratio of the drug.



## Elimination half-life ( $t_{1/2}$ ):



- It is the time it takes for the plasma concentration or the amount of drug in the body to be reduced by **50%** via different elimination mechanisms.
- Elimination half-life is inversely (negatively) proportional with the clearance.