

كلية الطب البيطري - جامعة تكريت
ماجستير أدوية

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3

Advanced Pharmacology

Drug Excretion

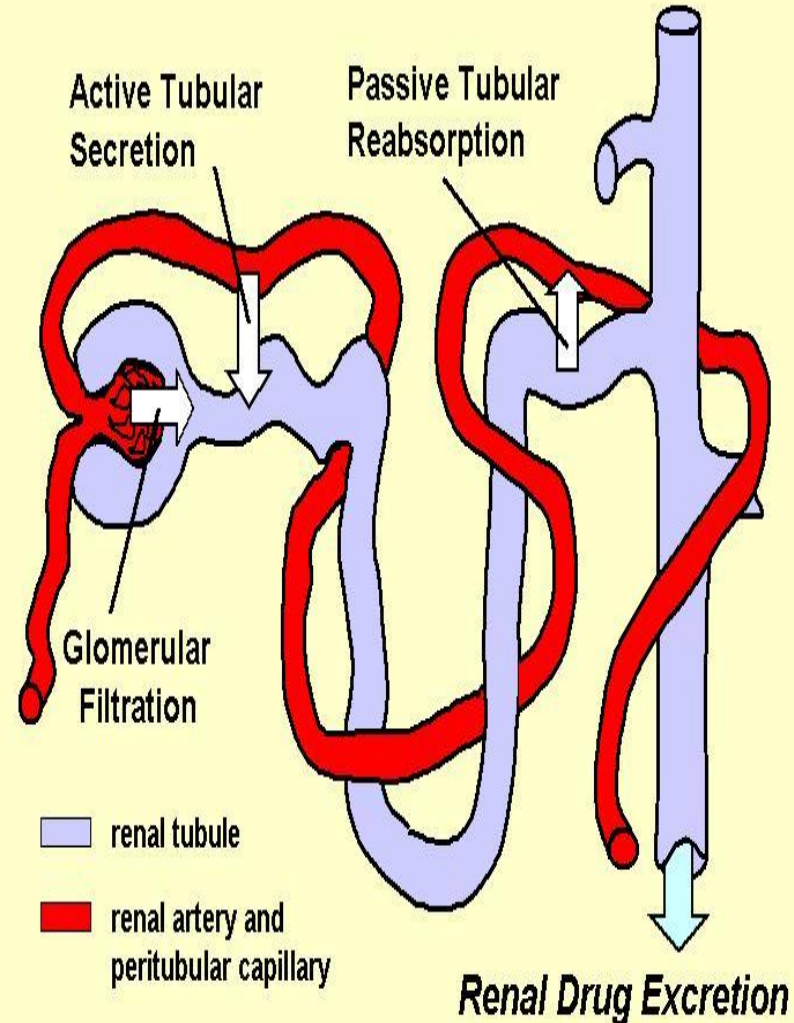
Drug Excretion

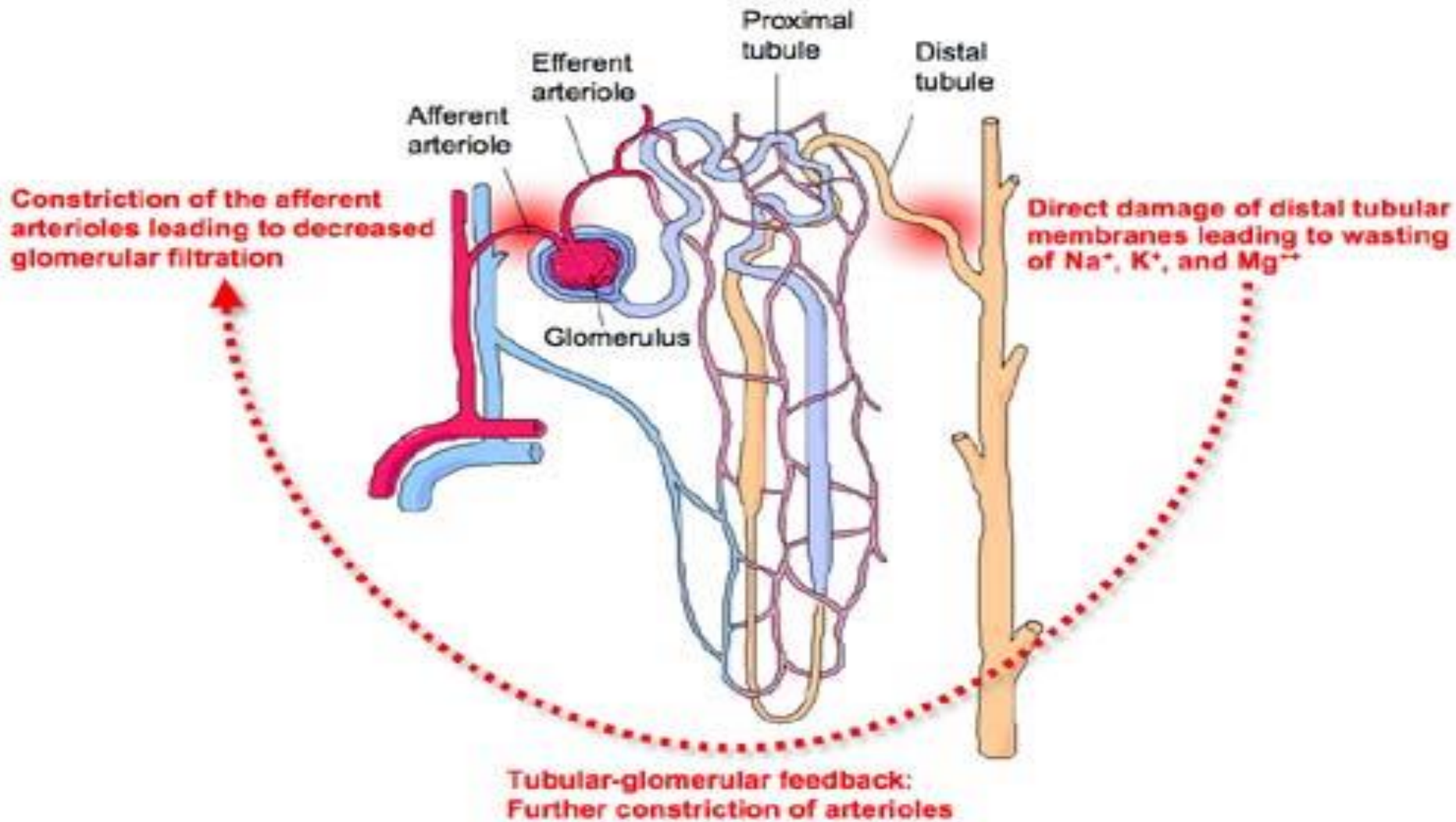
- It is the loss of unchanged drug & its metabolites by secretory organs which eliminate polar compounds more efficiently than lipid soluble ones.
- Lipid soluble compound → metabolized into more polar compound → eliminated.
Routes of drug excretion:
 1. Renal excretion
 2. Biliary & fecal excretion
 3. Pulmonary elimination: for gases & vapor e.g. halothane & alcohol.
 4. Excretion via other routes (breast milk, saliva, sweat, tears, hair & skin).

1. Renal drug excretion:

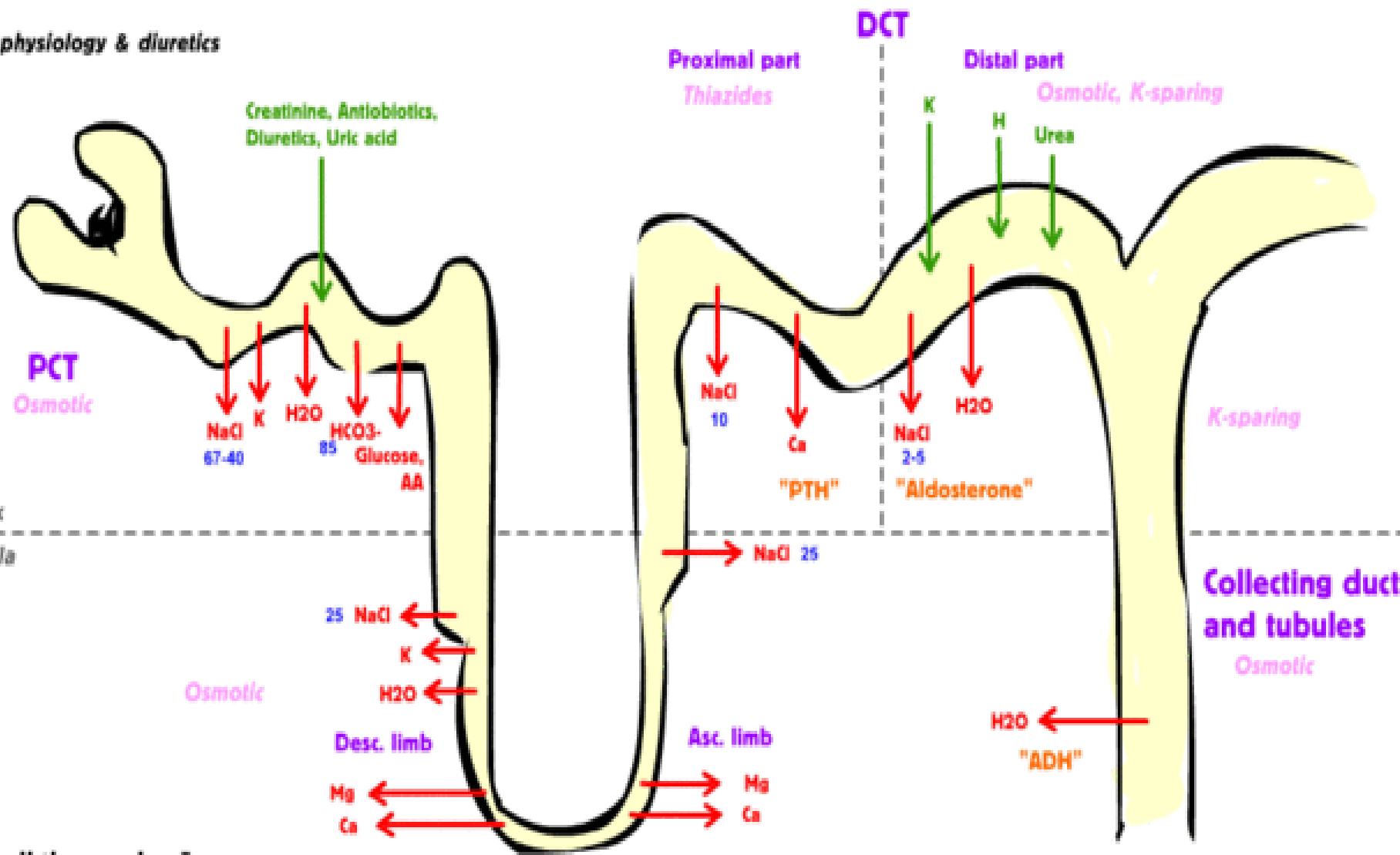
Kidney is the most important excretory organ for drugs & their metabolites.

- A. Glomerular filtration
- B. Active tubular secretion
- C. Tubular reabsorption:
Passive or active.





Renal physiology & diuretics



Why all these colors?

- Segment name in violet
- Diuretic name in pink
- Reabsorption in red
- Secretion in green
- Percentage in blue
- Hormone in orange

Loop of Henle
Loop diuretics

A. Glomerular filtration: It is a passive process.

- It depends on:
 - a. Glomerular filtration rate (GFR): is the volume of fluid filtered from the renal capillaries into the Bowman's capsule per unit time
 - b. Creatinine & inulin excretion rates are used to measure the GFR (completely removed by GF & are neither actively secreted nor reabsorbed) → as diagnostic indicators for kidney function.
 - b. Protein binding of the drug:
Protein binding limits GF but doesn't limit active tubular secretion.
 - c. Molecular weight of the drug (M.W):
↓ M.W drugs (below 20000)

B. Active tubular secretion (ATS):

80% of the drug delivered to the kidney is excreted by active tubular secretion.

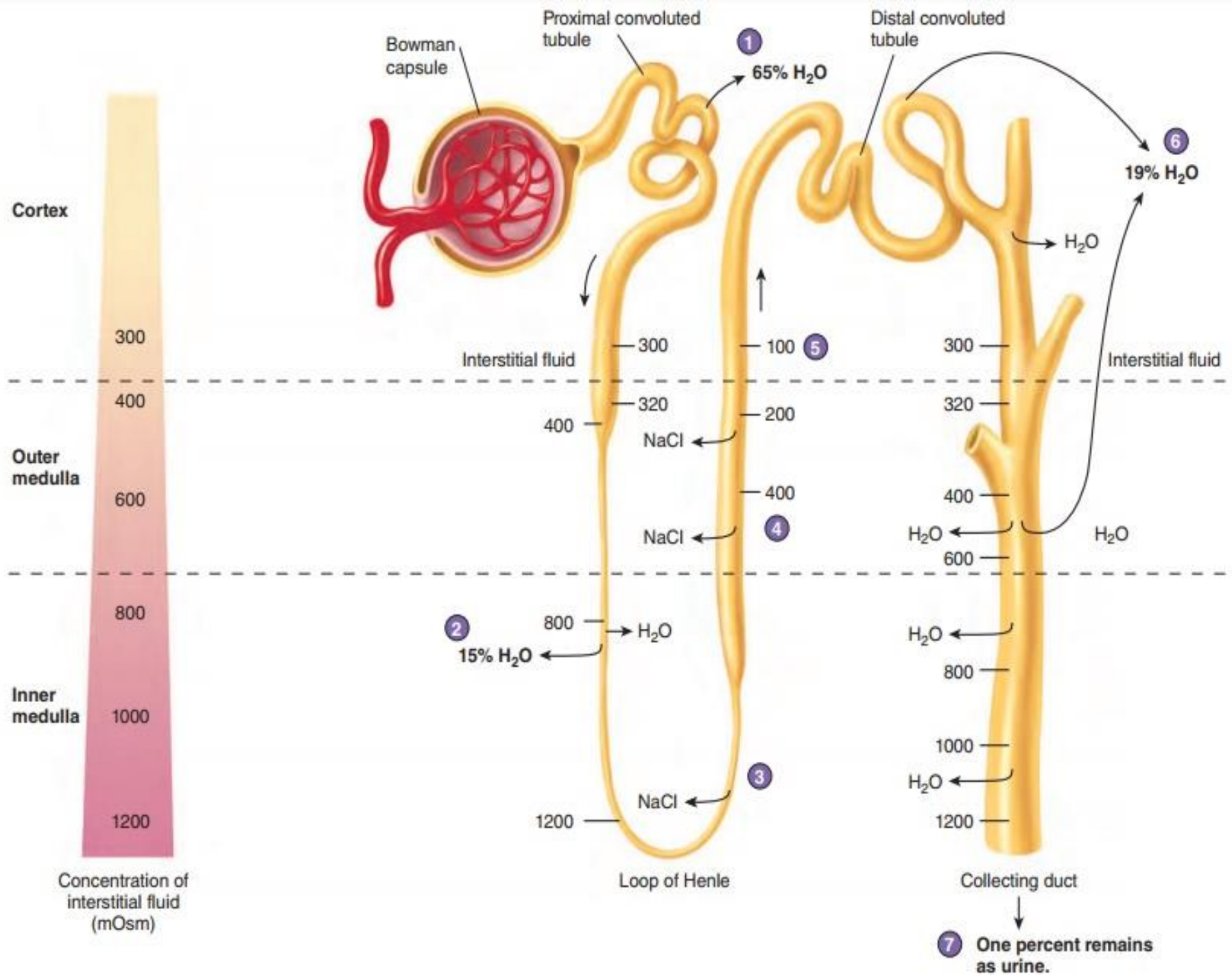
- a. Acid carrier system: Transports acidic drugs & endogenous compounds (penicillins, probenecid, salicylic acid, phenobarbitone, frusemide, indomethacin & uric acid)
 - b. Base carrier system: Transports basic drugs & endogenous compounds (amphetamine, chloroquine, quinine, morphine, histamine, serotonin & dopamine).
- ATS may act as a site for drug-drug interactions:
 - Probenecid inhibits active tubular secretion of penicillins.
 - Probenecid also inhibits active secretion of methotrexate → toxicity.
 - Aspirin (analgesic dose) inhibits uric acid excretion.

C. Tubular reabsorption:

a. Passive tubular reabsorption:

lipid soluble drugs are rapidly and extensively reabsorbed.

- Polar compounds have low tubular permeability, mainly excreted in urine (digoxin and aminoglycosides).
- It is pH dependent (urinary acidification & alkalinization).
- Active tubular reabsorption: e.g.
lithium, fluoride & uric acid
- Uricosuric drugs [probenicid, sulfinpyrazone and aspirin (high dose)] inhibit the active tubular reabsorption of uric acid.
- Some drugs concentrate in urine & precipitate in renal tubules (low urine solubility) → crystalluria e.g. sulfonamides.



- **Factors affecting renal excretion of drugs:**
 1. Alteration of urine pH & diuresis (alkaline diuresis for treating salicylates and phenobarbital intoxication).
 2. Protein binding of the drug:
Limits GF but doesn't limit active tubular secretion
 3. Age:
↓GFR & tubular functions in newborn.
GFR declines slowly with age

2. Biliary & fecal excretion:

A. Orally unabsorbed drugs

B. Metabolites excreted in the bile (active transport or P-glycoprotein) → GIT e.g. rifampicin.

- Molecular weight and polarity are the primary determinants of biliary excretion.
- conjugation enhances biliary excretion.
- Enterohepatic circulation of the drugs (E.H.C): The glucuronide conjugate of some drugs are excreted in bile → intestine (hydrolysis) → releasing the parent drug → reabsorbed to the blood.
- It prolongs the half-life of the drug & permits conservation of endogenous comp. such as bile acid, vit D & B₁₂, folic acid & estrogens.

- e.g. Ivermectin, morphine & ethinyl estradiol.
 - Interruption of the cycle → traps drugs in GIT
 - Treatment of drug intoxication (cholestyramine with digoxin)
 - Treatment failure (tetracycline with oral contraceptive)
3. Excretion of drugs by other routes:
Quantitatively unimportant and mainly dependent on simple diffusion of unionized drug.
- A. Excretion in breast milk:
almost any drug present in the mother's blood may be detected in her milk, but since milk is more acidic than plasma (6.6), basic drugs may be trapped in breast milk.

- Drugs should be avoided as much as possible during lactation.
- If the drug is relatively safe, the nursing mother should take it 30-60 min. after nursing or 3-4 hrs before the next feeding.
- Drugs for which no data are available on safety during lactation should be avoided or breast feeding discontinued while they are being given.
- Examples of drugs that are contraindicated during lactation:
 - Tetracyclines
→ permanent tooth staining in infant
 - INH → pyridoxine deficiency
 - Chloramphenicol → bone marrow suppression
 - Diazepam → sedation
 - Opiates "morphine" → neonatal narcotic dependence.
(if mother stop morphine or breast feeding)

B. Salivary excretion:

The concentration of some drugs in saliva parallels that in plasma (bioavailability determination). e.g. phenytoin (gingival hyperplasia), acetaminophen, theophylline, lithium, tolbutamide & digoxin.

- Saliva is more acidic than plasma, so basic drugs are trapped in saliva e.g. . Lithium concentrations in saliva is 2-3 times higher than in plasma.

C. Excretion into hair and skin:

- Although excretion of drugs into hair and skin is quantitatively unimportant, sensitive methods for detection of toxic metals in these tissues have forensic significance .