DRUG ELIMINATION
RENAL EXCRETION OF DRUGS

For Class- B.Pharmacy 6th Semester

Subject- BIOPHARMACEUTICS AND PHARMACOKINETICS (BP604T)

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EXCRETION OF DRUGS

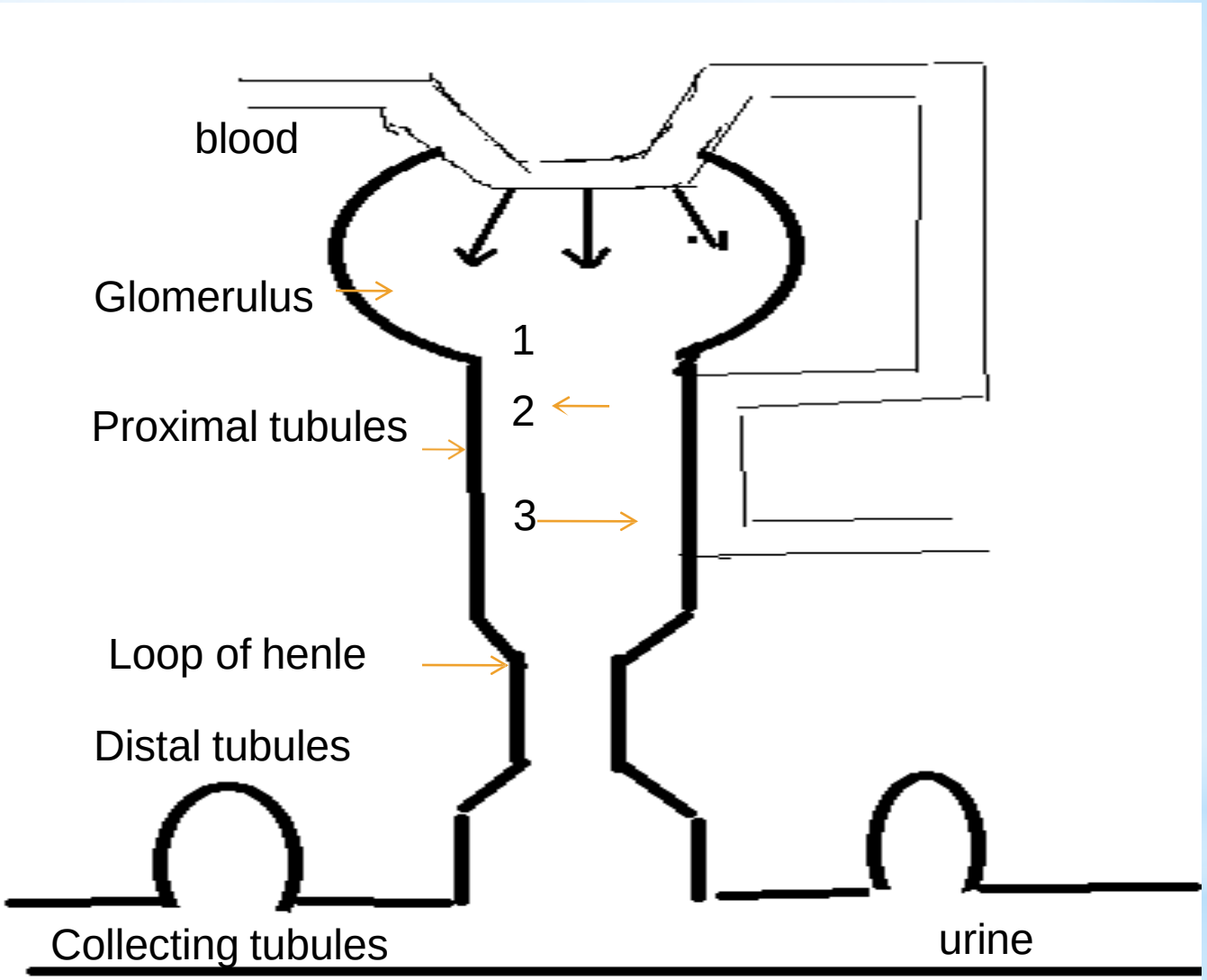
Excretion is defined as the process where by drugs or metabolites are irreversibly transferred from internal to external environment through renal or non renal route.

Excretion of unchanged or intact drug is needed in termination of its pharmacological action.

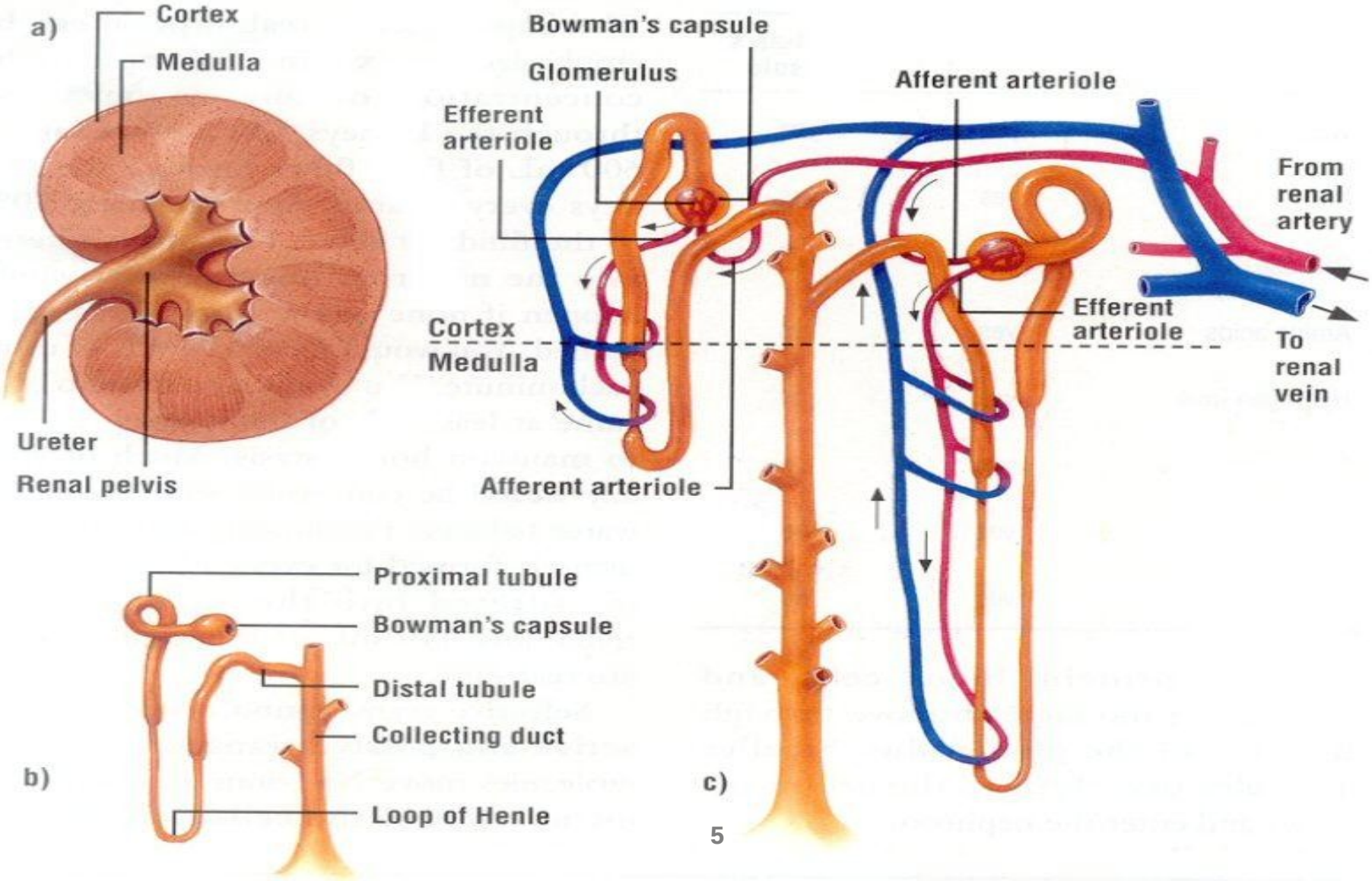
The principal organ of excretion are kidneys.

TYPES OF EXCRETION

1. **RENAL EXCRETION**
2. **NON RENAL EXCRETION**
   - **Biliary excretion.**
   - **Pulmonary excretion.**
   - **Salivary excretion.**
   - **Mammary excretion.**
   - **Skin / Dermal excretion.**
   - **Gastrointestinal excretion.**
   - **Genital excretion.**


blood
Glomerulus
1
2
Proximal tubules
3
Loop of henle
Distal tubules
Collecting tubules
urine

ANATOMY OF NEPHRON



GLOMERULAR FILTRATION

- It Is non selective , unidirectional process
- Ionized or unionized drugs are filtered, except those that are bound to plasma proteins.
- Driving force for GF is hydrostatic pressure of blood flowing in capillaries.
- **GLOMERULAR FILTRATION RATE:**

  Out of 25% of cardiac out put or 1.2 liters of blood/min that goes to the kidney via renal artery only 10% or 120 to 130ml/min is filtered through glomeruli. The rate being called as glomerular filtration rate (GFR).

e.g. creatinine, inulin.

ACTIVE TUBULAR SECRETION

- This mainly occurs in proximal tubule.
- It is carrier mediated process which requires energy for transportation of compounds against conc. gradient Two secretion mechanisms are identified.
- System for secretion of organic acids / anions
  - E.g. Penicillin, salicylates etc uric acid secreted
- System for organic base / cations
  - E.g. morphine, mecamylamine hexamethonium
- Active secretion is Unaffected by change in pH and protein binding.
- Drug undergoes active secretion have excretion rate values
  - greater than normal GFR e.g. Penicillin.

TUBULAR REABSORPTION

- It occurs after the glomerular filtration of drugs. It takes place all along the renal tubules.
- Reabsorption of drugs indicated when the excretion rate value are less than the GFR 130ml/min.e.g. Glucose
- TR can be active or passive processes.
- Reabsorption results in increase in the half life of the drug.

- **Active Tubular Reabsorption:**

  Its commonly seen with endogenous substances or nutrients that the body needs to conserve e.g. electrolytes, glucose, vitamins.

- **Passive Tubular Reabsorption:**

  It is common for many exogenous substances including drugs. The driving force is Conc. Gradient which is due to re-absorption of water, sodium and inorganic ions. If a drug is neither excreted or re-absorbed its conc. In urine will be 100 times that of free drug in plasma.

pH OF THE URINE

- It varies between 4.5 to 7.5
- It depends upon diet, drug intake and pathophysiology of the patient .
- Acetazolamide and antacids produce alkaline urine, while ascorbic acid makes it acidic.
- IV infusion of sodium and ammonium chloride used in treatment of acid base imbalance shows alteration in urine pH.
- Relative amount of ionized ,unionized drug in the urine at particular pH & % drug ionized at this pH can be given by " HENDERSON-HESSELBACH" equation.

HENDERSON-HESSELBACH EQUATION

1)FOR WEAK ACIDS

$$pH = pKa + \log \frac{[\text{ionized}]}{[\text{unionized}]}$$

$$\% \text{ of drug ionized} = \frac{10^{pH - pKa}}{1 + 10^{pH - pKa}} \times 100$$

HENDERSON-HESSELBACH EQUATION

2)FOR WEAK BASE

$$pH = pKa + \log \frac{[\text{unionized}]}{[\text{ionized}]}$$

$$\% \text{ of drug ionized} = \frac{10^{pH - pKa}}{1 + 10^{pH - pKa}} \times 100$$

FACTORS AFFECTING RENAL EXCRETION

- Physicochemical properties of drug
- Plasma concentration of the drug
- Distribution and binding characteristics of the drug
- Urine pH
- Blood flow to the kidney
- Biological factor
- Drug interaction
- Disease state

PHYSICOCHEMICAL PROPERTIES OF DRUG

- **Molecular size**

Drugs with Mol.wt <300, water soluble are excreted in kidney. Mol.wt 300 to 500 Dalton are excreted both through urine and bile.

PLASMA CONCENTRATION OF THEDRUG

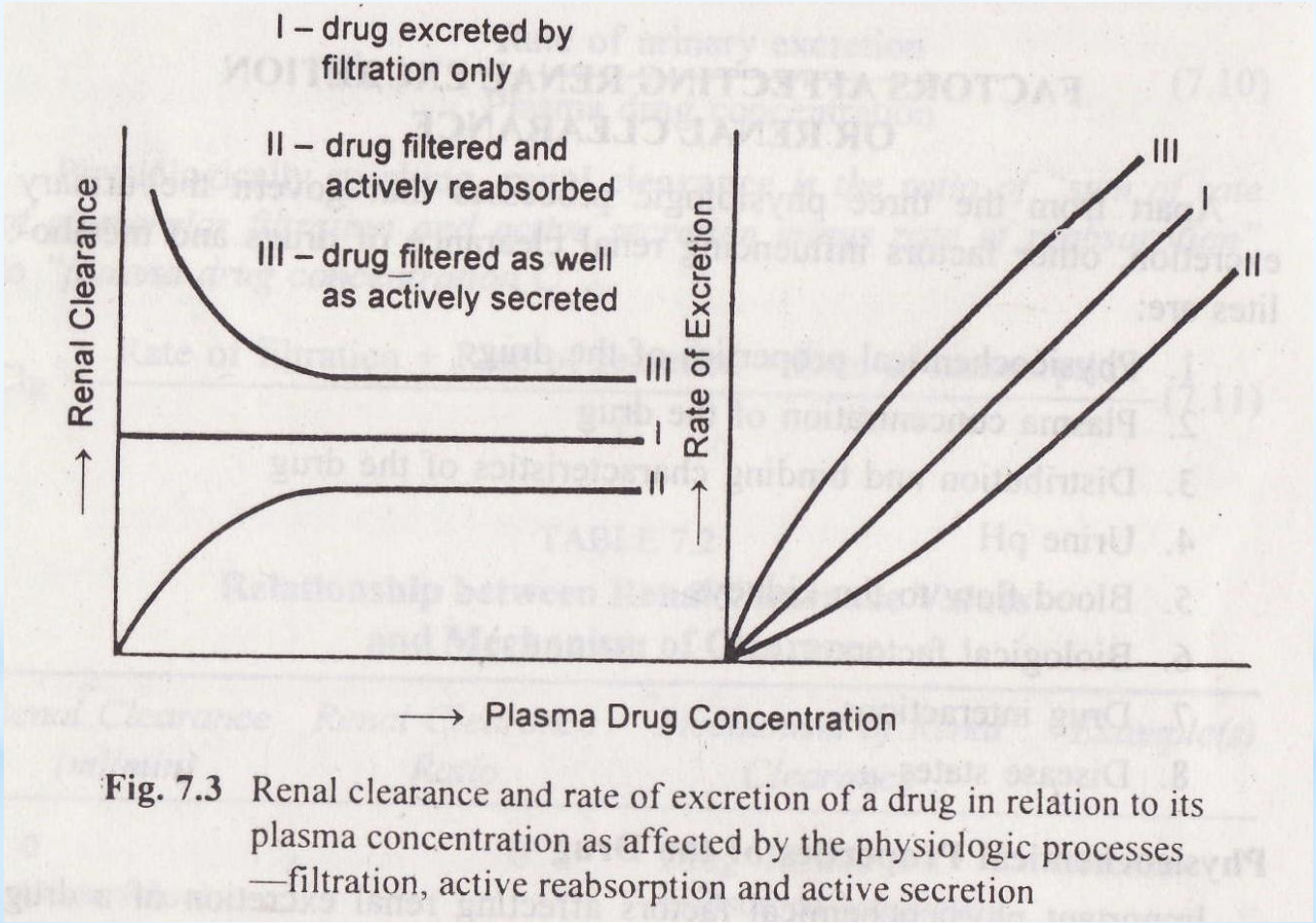


Fig. 7.3 Renal clearance and rate of excretion of a drug in relation to its plasma concentration as affected by the physiologic processes —filtration, active reabsorption and active secretion

DISTRIBUTION AND BINDING CHARACTERISTICS OF THE DRUG

Drugs that are bound to plasma proteins behave as macromolecules and cannot be filtered through glomerulus. Only unbound or free drug appear in glomerular filtrate. Protein bound drug has long halflives.

BIOLOGICAL FACTORS

- Age, sex, species, strain difference etc alter the excretion of the drug.
- **Sex -** Renal excretion is 10% lower in female than in males.
- **Age** – The renal excretion in newborn is 30-40 % less in comparison to adults.
- **Old age** – The GFR is reduced and tubular function is altered which results in slow excretion of drugs and prolonged half lives.

DRUG INTERACTION

Any drug interaction that result in alteration of binding characteristics, renal blood flow, active secretion, urine pH, intrinsic clearance and forced diuresis would alter renal clearance of drug.

Renal clearance of a drug highly bound to plasma proteins is increased after it is displaced with other drug e.g. Gentamicin induced nephrotoxicity by furosemide.

Alkalinization of urine with citrates and bicarbonates promote excretion of acidic drugs.

DISEASE STATE

- **RENAL DYSFUNCTION**

Greatly impairs the elimination of drugs especially those that are primarily excreted by kidney. Some of the causes of renal failure are B.P, Diabetes, Pyelonephritis.

- **UREMIA**

Characterized by Impaired GFR , accumulation of fluids & protein metabolites, also impairs the excretion of the drugs. Half life is increased resulting in drug accumulation and increased toxicity.