

Unit-II

PHARMACOLOGY OF DRUGS ACTING ON RENAL SYSTEM AND CARDIOVASCULAR SYSTEM

By : Dr. Mayur Savaliya,
Lecturer, Clinical Research,
Indus University.

Key Contents

- Outline of renal function
- Nephron
- Diuretics, Antidiuretics
- Drugs which alter the pH of kidney
- Drugs acting on cardiovascular system

Outline of Renal Function

- Excretory system also known as renal system consists of 2 kidneys which are bean shaped organs, 2 ureters, bladder, urethra.
- Kidneys are located on each sides of lower back. Each are about the size of fist. Inside kidneys are nephrons.
- These are tiny units where the filtering of excess fluids and dissolved particles occurs. There are between 1 and 1.3 million nephrons in each kidneys.

- Kidneys are responsible in many ways –
 - Removing extra fluid
 - Wastes
 - Filter the blood
 - Fluid and mineral balance
 - Controlling BP
 - Activation of Vit D
 - Production of hormones for RBC formation

Nephron

- Nephron is the functional unit of kidney. It's main functions are ultrafiltration, selective reabsorption, osmoregulation.
- Nephrons filter blood and then reabsorb useful materials from the filtrate before eliminating the remaining as urine.
- When blood enters a nephron, it goes into renal corpuscle which contains glomerulus and Bowman's capsule.
- **Glomerulus** is a cluster of capillaries that absorb protein from blood travelling through renal corpuscle.
- **Bowman's capsule** first part of nephron where blood is initially filtered at a capillary tuft called glomerulus. Here, remaining fluid called capsular urine passes into renal tubules.

- **Renal tubules**
- These are a series of tubes that begin after the Bowman's capsule and end at collecting duct. Each tubules has several parts such as-
- **Proximal convoluted tubule** connected to Bowman's capsule where selective reabsorption occurs. This section absorbs water, sodium, and glucose back into the blood.
- **Loop of Henle** a selectively permeable loop that descends into the medulla and establishes a salt gradient. In this, further absorption of potassium, chloride, and sodium takes place into the blood.
- **Distal convoluted tubule** is connected to loop of Henle where further selective reabsorption occurs where more absorption of sodium into blood and takes potassium and acid.

- The blood to be filtered enters the Bowman's capsule via an afferent arteriole and leaves the capsule via efferent arteriole, which forms a blood network called vasa recta that reabsorbs the components of the filtrate from the nephron.
- By the time fluid reaches the end of the tubule, it's diluted and filled with urea.
- Urea is the by-product of protein metabolism that gets released in urine.
- **Renal Cortex**
- It's an outer part of kidney containing glomerulus and convoluted tubules.
- **Renal Medulla**
- It is smooth, inner tissue of kidney containing loops of Henle as well as pyramids.

- **Renal Pyramids**

- They are small structures that contains nephrons and tubules. Tubules transport fluid into the kidney which then moves away from nephrons towards inner structures that collect and transport urine out of the kidney.

- **Collecting Duct**

- It is present at the end of each nephron in renal medulla from where filtered fluid exit the nephrons.

- **Ureter**

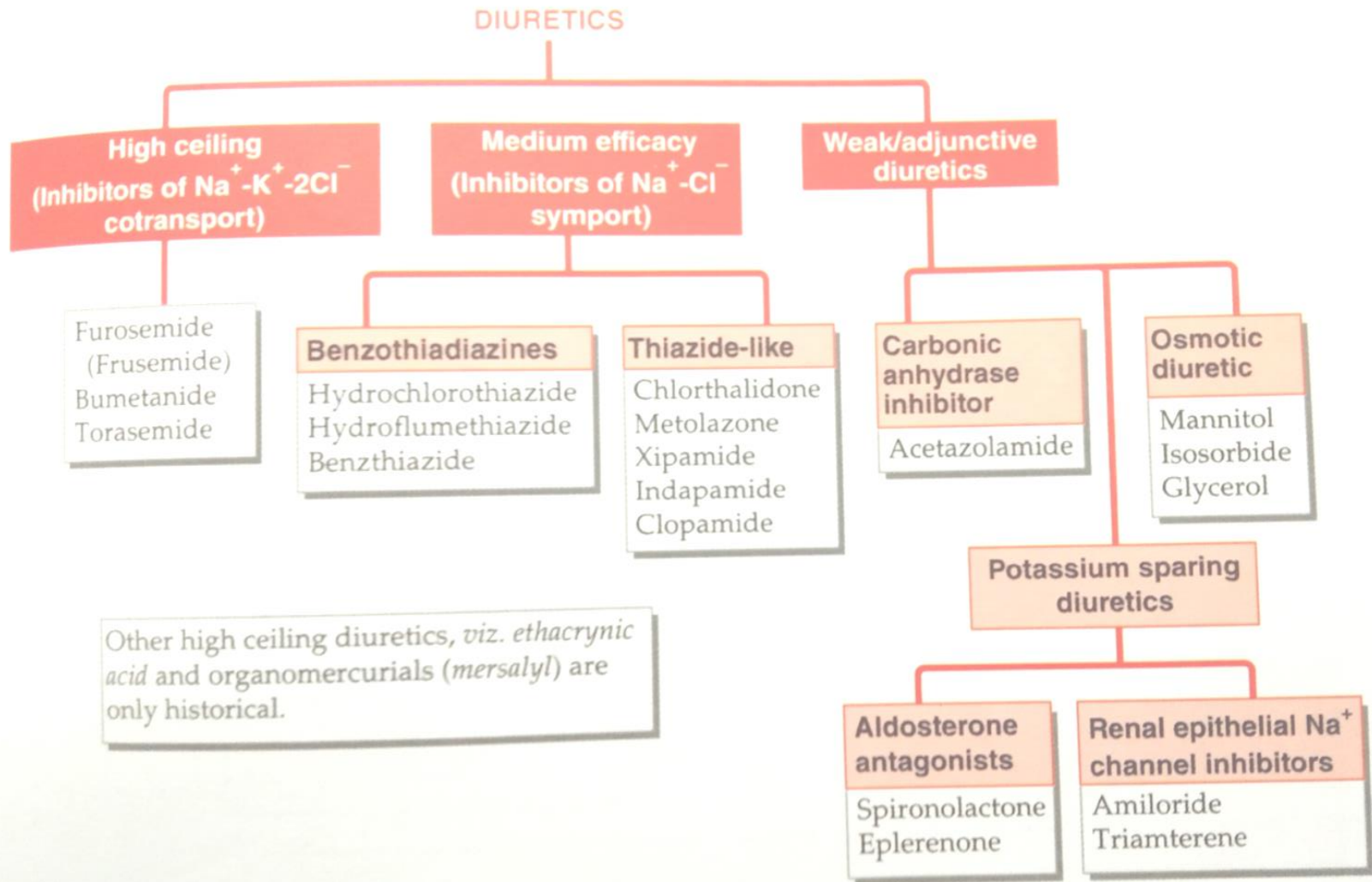
- It is a tube that pushes urine into the bladder where it gets collected and flushes followed by urethra out of the body.

Diuretics

- Diuretics (natriuretics) are drugs which cause a net loss of Na^+ and water in urine. When it is given regularly, Na^+ balance is soon restored by compensatory homeostatic mechanism of the body.
- Diuretics are among the most wisely prescribed drugs. These drugs increase the urine output or urine volume.

According to Efficacy:

1. High efficacy diuretics: Loop Diuretics.
2. Medium efficacy diuretics: Thiazide Diuretics
3. Weak diuretics:
 - *Carbonic Anhydrase inhibitors
 - *Osmotic Diuretics.
 - *Potassium sparing Diuretics.

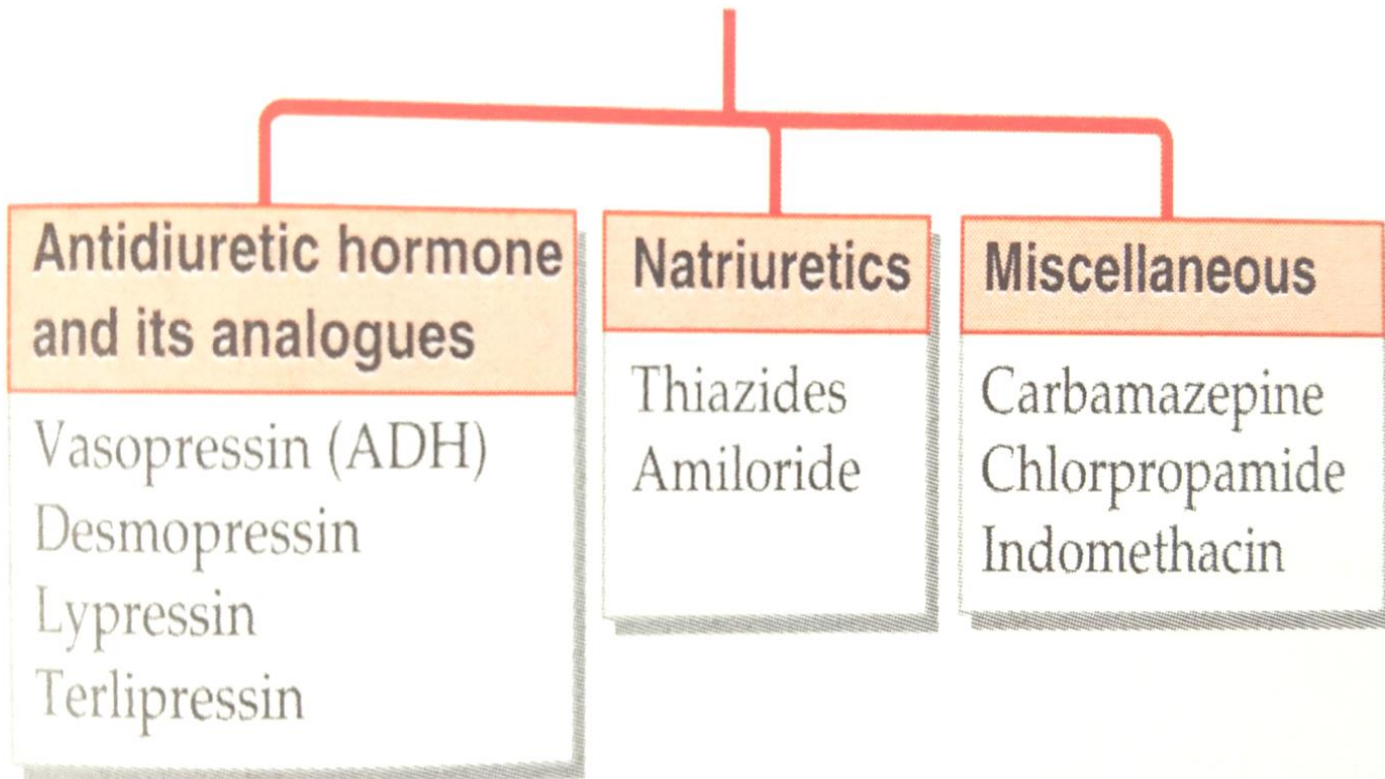


Reference: Textbook of K D Tripathi

Antidiuretics

- Antidiuretics (anti- aquaretics) inhibit water excretion without affecting salt excretion. They are the drugs that reduce urine volume, particularly in diabetes insipidus (DI) which is primary indication.
- Its mechanism of action is by reducing urine flow by acting reabsorption of water by kidney tubules.
- It is also used in treating primary nocturnal enuresis (bed wetting), nocturia associated with multiple sclerosis.

ANTIDIURETICS



Reference: Textbook of K D Tripathi

Drugs altering pH of Kidney

- Urine pH has a great influence on whether a drug is excreted quickly or slowly.
- It has been manifested to control the excretion of certain drugs from the body in clinical situations.
- Most of the drugs are either weak acids or weak bases.
- In acidic urine, alkaline drugs are more readily ionised which are more soluble in water and hence gets dissolved in body fluids readily for excretion.

- In a situation like blood poisoning drug must be excreted rapidly from body, so it can be done by altering the urine pH to increase excretion.
- Eg. In the case of **aspirin** poisoning, if making urine more alkaline with sodium bicarbonate will increase ionisation of salicylic acid leading to increase in excretion.
- In alkaline urine, weak acids are excreted faster that is due to causing greater fraction of drug to be in a charged form which can't be reabsorbed.
- Eg. In case of **amphetamine**, if making urine acidic with aluminium chloride will increase the renal elimination of weak base by keeping them in charged form.

Now, if urine pH is lower than neutral pH 7 it could indicate for kidney stones. Also other conditions may be –

- Acidosis
- Dehydration
- Diabetes ketoacidosis
- Diarrhoea
- Starvation

If urine pH is higher than neutral pH 7 then indications may be as follows-

- Kidney failure
- Kidney tubular acidosis
- Pyloric obstruction
- Respiratory alkalosis
- UTIs

Cardiotonic Drugs

- Drugs acting on cardiovascular system are also known as cardiotonic drugs.
- These drugs increase the force of contraction of the heart.

Classification:

1. Cardiac glycosides

- Digoxin
- Digitoxin

3. Anticholinergic drugs

- Atropine
- Scopolamine

2. Sympathetic drug

- Adrenaline
- Dopamine
- Isoprenaline

4. Xanthines

- Theophylline
- Theobromine

Angina pectoris

- It is a clinical syndrome characterized by pre-cardiac pain or discomfort due to myocardial ischemia, which is precipitated by exercise and relief by rest or sublingual nitro-glycerine.
- It occurs when coronary blood flow is insufficient to meet the metabolic requirement of the heart muscle.

Myocardial oxygen demand mainly depends on

- • Preload,
- • After load and
- • Heart rate

Anti-anginal drugs

- Calcium channel blockers:
 - Nifedipine
 - Diltiazem
- Beta-adrenergic blockers:
 - Atenolol
 - Propranolol
- Nitrates
 - Nitroglycerine
 - Isosorbide dinitrate
- Others
 - Antiplatelet agents
 - Statins.etc