Unit V – Problem 8 – Pharmacology: Diuretic Agents

- **Thiazide diuretics:**
  - **Examples**: hydrochlorothiazide and chlorothalidone.
  - **What are they?**
    - ✓ Sulfonamide derivatives.
  - **Where do they work and how?**
    - ✓ All thiazides work in the early segment of the distal convoluted tubule (DCT).
    - ✓ They block Na^+/Cl cotransport on the luminal side of the distal convoluted tubule.
  - **Used for:**
    - ✓ Hypertension (drug of choice).
    - ✓ Heart failure (2^{nd} line drug).
    - ✓ Renal failure (2^{nd} line drug).
  - **How do thiazides affect plasma Ca^{2+} levels?**
    - ✓ Unlike loop diuretics, they decrease Ca^{2+} levels in the urine.
  - **Adverse reactions:**
    - ✓ Hypokalemia.
    - ✓ Hyponatermia.
    - ✓ Hypercalcemia.
    - ✓ Gout.
    - ✓ Hyperglycemia.
    - ✓ Hyperlipidemia.
- **Loop diuretics:**
  - **Examples**: furoseamide and bumetanide
  - **Mechanism of action**: blocking the Na^+/ K^+/ $2Cl^-$ cotransport system in the thick ascending limb of the loop of Henle.
  - **Used for:**
    - ✓ Heart failure (drug of choice).
    - ✓ Pulmonary edema (drug of choice).
    - ✓ Renal failure (drug of choice).
  - **Adverse reactions:**
    - ✓ Hypokalemia.
    - ✓ Hyponatermia.
    - ✓ Hypocalcemia.
    - ✓ Gout.
    - ✓ Hyperglycemia.
    - ✓ Hyperlipidemia.
    - ✓ Dehydration and hypovolemia.
- **Potassium-sparing diuretics:**
  - **Examples**: spironolactone, amiloride and triamterene.
  - **Mechanism of action**: they are aldosterone antagonists preventing reabsorption of sodium from collecting tubules and inhibiting secretion of potassium.
  - **Used for:**
    - ✓ Ascites (drug of choice).
    - ✓ Otherwise, they are added to other diuretics to prevent hypokalemia.
  - **What is the clinical indication for the use of spironolactone?**
    - ✓ Primary hyperaldosteronism (Conn's syndrome).
  - **Are there problems associated with administration of spironolactone?**
    - ✓ Gynecomastia and impotance in males owing to spironolactone's structural similarity to progesterone.
    - ✓ Irregular menstrual cycle in females.

- **Adverse reactions of potassium-sparing diuretics:**
  - ✓ Hyperkalemia (most serious).
  - ✓ Skin reaction.

- **Carbonic anhydrase inhibitors:**
  - **Example**: acetazolamide.
  - **Mechanism of action**: inhibition of carbonic anhydrase in proximal convoluted tubule. This inhibits diuresis.
  - **Used for**: glaucoma.
  - **Adverse reactions:**
    - ✓ Hypokalemia.
    - ✓ Metabolic acidosis.
- **Osmotic diuretics:**
  - **Example**: mannitol.
  - **Mechanism of action**: mannitol is filtered but not reabsorbed. Therefore, attracting water to the lumen of renal tubules.
  - **Used for**: head injury and glaucoma.
  - **Adverse reaction:**
    - ✓ Tissue edema.
    - ✓ Hyperkalemia.
    - ✓ Hypernatremia.