



## Diuretic Drugs

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# DIURETICS

## DEFINITION :

- These are drugs which cause a net loss of  $\text{Na}^+$  and water in urine
- There are several categories of diuretics.
- All diuretics increases the excretion of water from body.

# Renal Physiology

- **Kidney-**
  - Weight- 0.5% of Body,
  - Receive 25% of cardiac output (50 times)
- **Kidney functions**
  - Balance of electrolytes, Plasma volume, Acid Base
  - Activation of Vitamin D
  - Synthesis of Erythropoietin, Urokinase
  - Excretion of Urea, Uric acid, Creatinine etc.
- **Transport types**
  - **Passive**
    - Simple, channel mediated and facilitated diffusion, solvent drag
  - **Active**
    - Primary and Secondary (Symports and Secondary Counter transport)

Contd....

- **Pressure difference** at Bowman's Capsule- 20mm Hg
- **Filter**= Plasma-Proteins
- **Volume of**
  - Filter- 180 liters
  - Urine- 1.5 liters (1%)
- **Kidneys**
  - Renal Blood Flow- 1200ml/min
  - Renal Plasma Flow- 650 ml/min
  - GFR- 120 ml/min
  - Reabsorb – Sodium, Chloride and Bicarbonates > 99% while Potassium about 85%

- **Natriuresis**- increased sodium excretion
- **Kaliuresis**- Increased Potassium excretion
- **Diuretics**- Drugs which cause a net loss of Na<sup>+</sup> and water.

## Macula Densa and Juxtaglomerular Apparatus

- Contact between Ascending limb with afferent arterioles – by specialized columnar epithelial cells Macula Densa
- Macula Densa sense NaCl conc. in filtrate
- Give signal to J.G. Cells present in afferent arterioles
- J.G. Cells of afferent arterioles secrete Renin

# The relative magnitudes of Na<sup>+</sup> reabsorption at sites

PT - 65%

**Asc LH - 25%**

DT - 9%

CD - 1%.



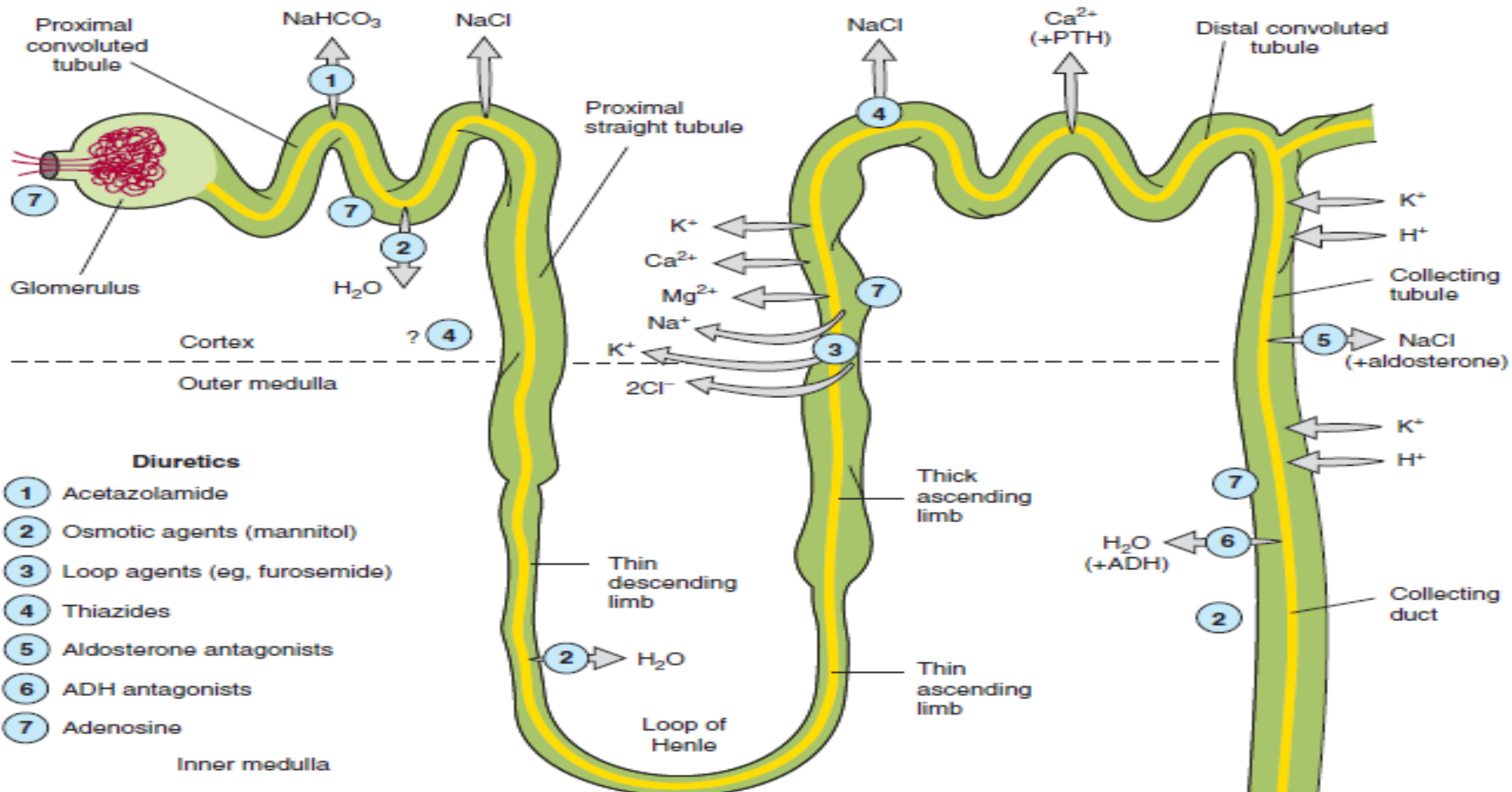
# Renal Function Regulation

- Sympathetic- Increase Na reabsorption, Renin
- RAAS- Renin in response to Low sodium, Low BP
- ADH – Water reabsorption at collecting duct
- Atrial Natriuretic Peptide/Factor- Released when atrial pressure is high and causes solute and water diuresis and reduces blood volume and BP. Inhibits synthesis of Renin, Aldosterone, ADH and overcomes the long term persistent effect of aldosterone (Opposite of RAAS)

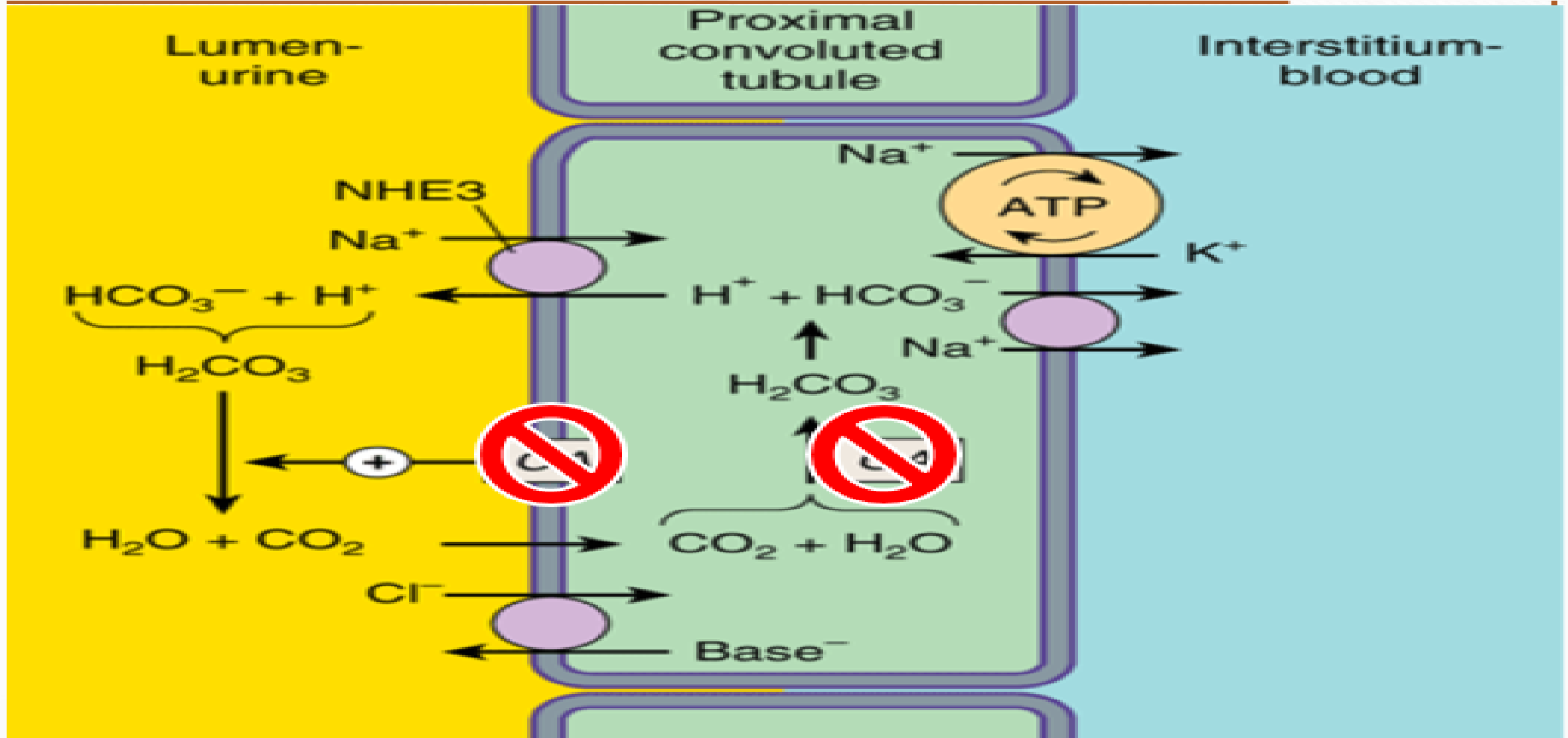
• Prostaglandins maintain renal circulation

# Diuretics

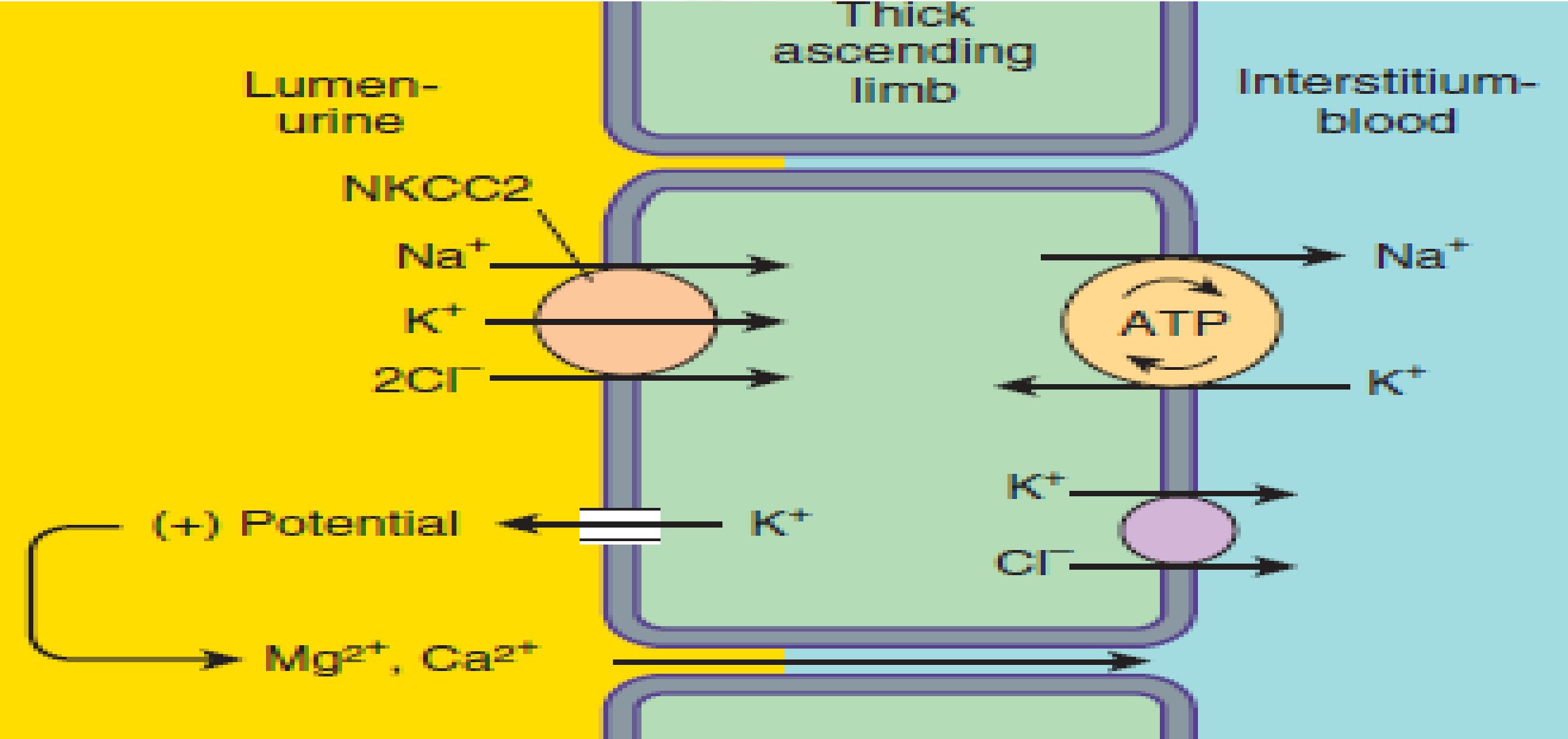
- Carbonic Anhydrase Inhibitors (Site I)
  - Brinzolamide, Acetazolamide, Dorzolamide
- Osmotic Diuretic (Site II)
  - Glycerine, Urea, Mannitol, Isosorbide
- Loop Diuretics (Site III)- TALH
  - Frusemide/ Furosemide, Bumetanide, Torasemide, Ethacrynic acid
- Thiazide Diuretics (Site IV)
  - Hydrochlorothiazide, Clopamide, Benzthiazide, Chlorthalidone, Metolazone, Xipamide, Indapamide
- Potassium Sparing Diuretics (Site V)
  - Aldosterone Antagonist
    - Spironolactone, Canrenone, Eplerone
  - Direct Acting (Inhibition of renal epithelial  $\text{Na}^+$  channel)
    - Triamterene, Amiloride (more potent)



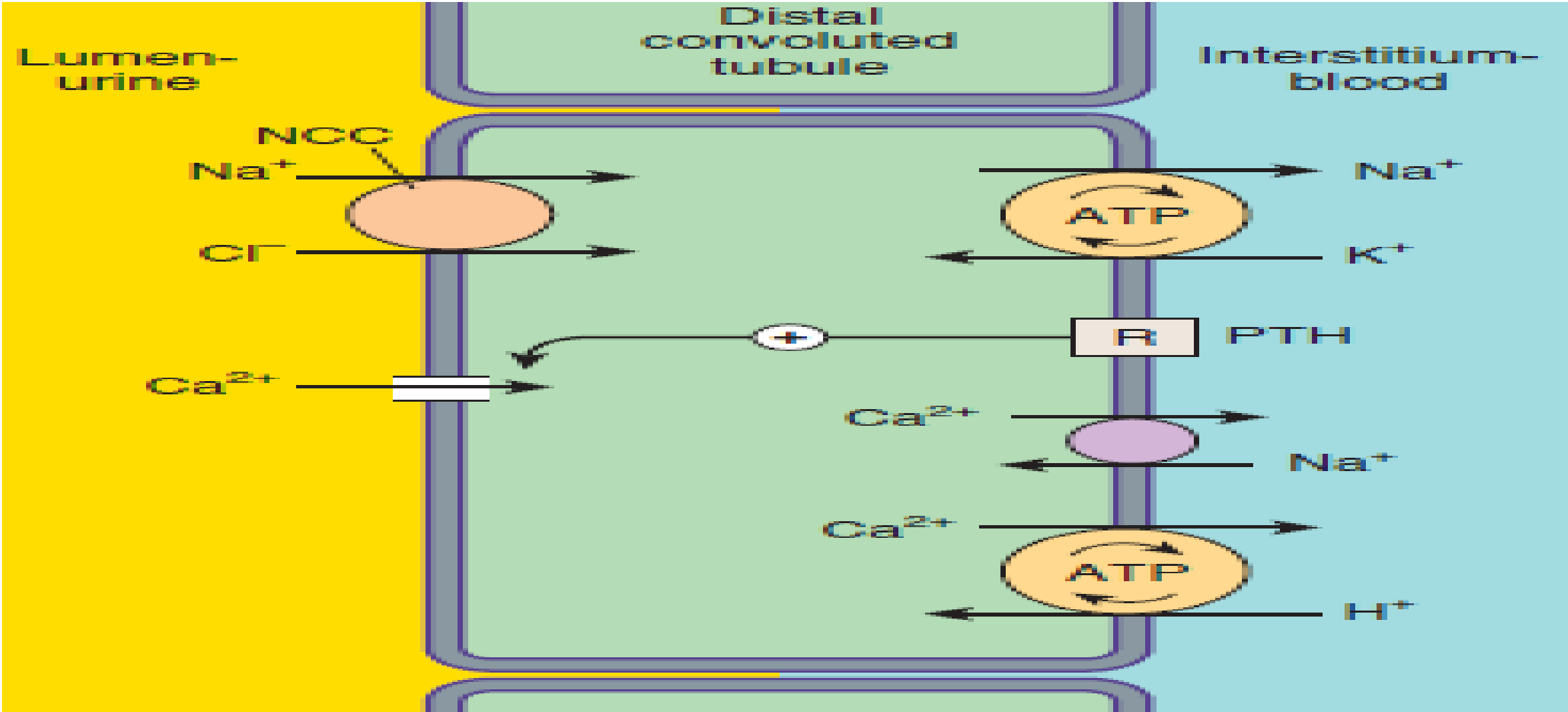
# Carbonic Anhydrase Inhibitors



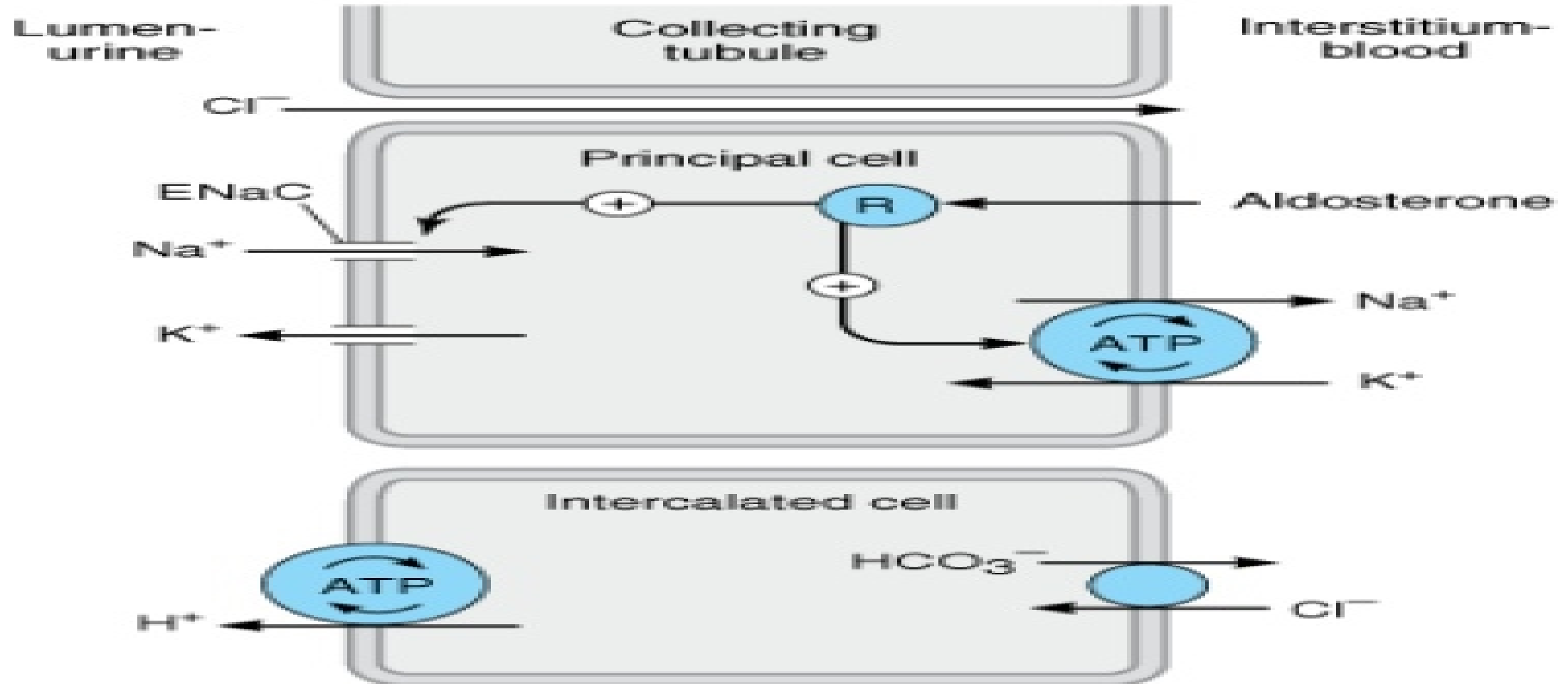
# Loop Diuretics



# Thiazides



# Spironolactone and Amiloride



<b>Diuretic</b>	<b>Site of Action</b>	<b>Adverse Effects</b>	<b>Special points</b>
<b>Carbonic anhydrase inhibitors</b>	<b>PTC</b> (inhibition of CAE)	<b>Metabolic Acidosis</b>	<b>Weak, Used in Glaucoma, Petit mal epilepsy, Acute mountain sickness, to alkaline the urine</b>
<b>Osmotic Diuretics</b>	<b>PTC, LOH, DCT</b> (Osmotic retention of water, Dilates Afferent arterioles, Increased hydrostatic pressure in glomerulus)	<b>Shifting of fluid from intracellular to extracellular, Hyponatremia, Pulmonary edema</b>	<b>Potent</b> <b>Used in Glaucoma, Poisoning, Increased ICT, impending ARF</b>
<b>Loop Diuretics</b>	<b>Thick Ascending Limb of Henle</b> (NaK2Cl inhibition) Weak CAI action	<b>Hyponatremia</b> <b>Hypomagnesaemia</b> <b>Hypocalcaemia</b> <b>Hyperuricemia</b> <b>Hyperglycemia</b> <b>Hyperlipidemia</b> <b>Hyperuricemia</b> <b>Ototoxic (ECA)</b>	<b>Most potent, Most Potent is Bumetanide, Effective even in low GFR, All except Ethacrynic acid are sulphonamide related,</b> <b>Venodilatation, Decrease Left Ventricle Pressure, Used in Acute LVF, Pulmonary Edema, Nephrotic syndrome, ARF, NSAIDS blunt effect, Cerebral edema, short term tt of Hypertension, to reduce volume overload during transfusion,</b>
<b>Thiazide Diuretics</b>	<b>DCT</b> (NaCl)	<b>Hypokalemic</b> <b>metabolic alkalosis</b> (Gitelman's Syndrome) <b>Hypercalcemia</b>	<b>Moderate, Chlorthalidone is Longest acting, Paradoxical effect in Diabetes Insipidus</b> <b>First line in Hypertension,</b>
<b>Potassium Sparing Diuretics</b>	<b>CD</b>	<b>HyperKalemia</b> <b>Antiandrogenic effect</b>	<b>Weak, As supplement to other to counter the hypokalemia, Canrenone is active metabolite, used in Conn's syndrome (Primary Hyperaldosteronism) cirrhotic edema, polycystic ovary</b>



## References

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2. Dale M M, Rang H P, and Dale M M. Rang & Dale's Pharmacology', 7<sup>th</sup> edition. Edinburgh: Churchill Livingstone, 2007.
3. Satoskar RS, Ainapure SS, Bhandarkar SD, Kale AK, 'Pharmacology and pharmacotherapeutics', 14<sup>th</sup> edition, Popular Prakashan, Mumbai, 1995.