Diuretics overview (first 14 slides)

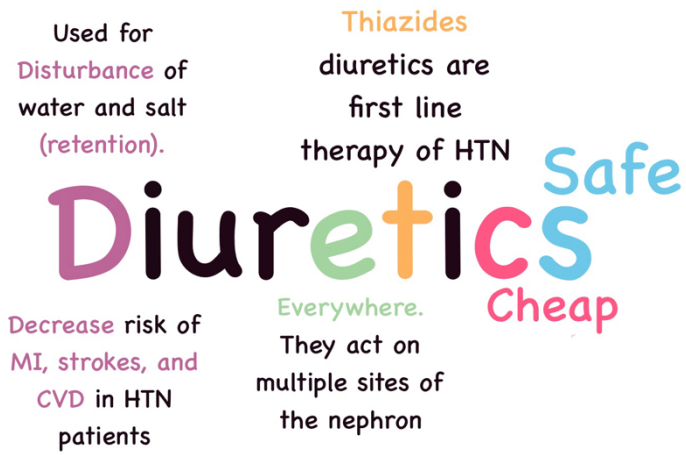
Diuretics increase excretion of fluid from inside (interstitium & plasma) to outside (urine).

- A Natri-uretic increases excretion of Na^+ and water.

Where do they work?

At the reabsorption stage, by blocking reabsorption of water and salts (mainly by blocking ion transporters)

- They often change urine pH and the ionic composition of urine and blood.
- Water, digitalis, caffeine and theophylline have diuretic activity, but are **not diuretics.**



Mechanism of Diuretics Antihypertensive action

Decrease diastolic by: decreaseing plasma volume and thus the cardiac output and eventually the BP

- Can cause reactive peripheral resistance that goes away with chronic use.

Decrease diastolic by:
secretion of PGs, causing vasodialation

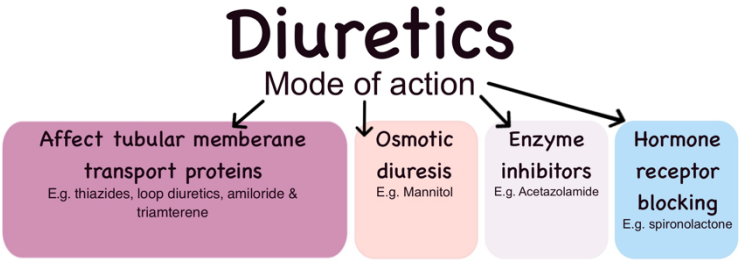
Diuretic therapy cautions

Excessive diuretic usage may lead to a decrease in the blood volume which could cause:

1. **Reduction in the perfusion of vital organs.** [using diuretics to treat edema requires careful monitoring of the patient's hemodynamic status and an understanding of the pathophysiology of the underlying condition]
2. Hypotension and collapse
3. Increased blood viscosity due to an increase in erythro- and thrombocyte concentration, which could lead to an increased risk of intravascular coagulation or thrombosis

Classification:

By: Site of action, mechanism of action or potency

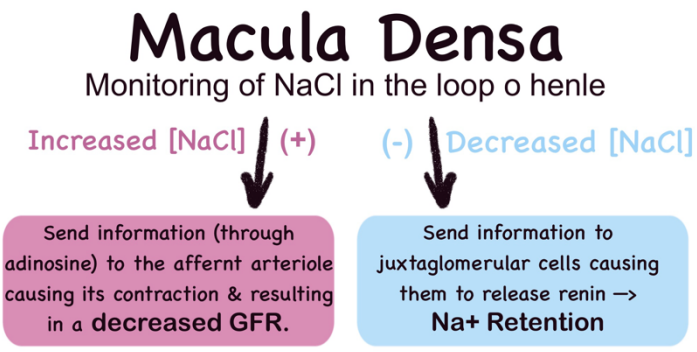


Diuretic resistance causes (Therapeutic Failure)

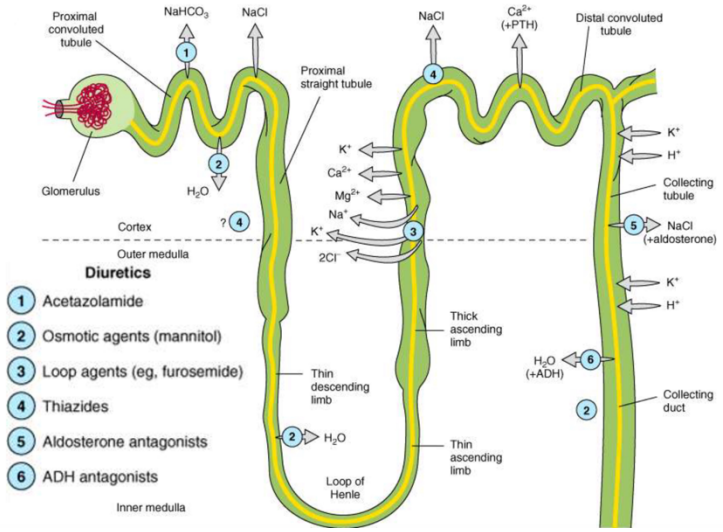
1. Continued ingestion of salt
2. Impairment of organic acid secretion mechanisms in the proximal tubules
3. Secondary hyperaldosteronism
4. Lowered renal blood flow causing increased Na^+ reabsorption (post-diuretic salt retention).
5. Lowered bioavailability of the drug.

Management of diuretic resistance
Restriction of sodium intake, changes in dose, changes in timing, and combination of diuretic therapy.

Macula densa cells work in the nephron:



This photo shows site of action of each diuretic class:



Other agents of diuretic activity:
Caffeine: weak diuretic, it weakly blocks adenosine receptors that participate in the control of proximal tubule Na^+ reabsorption.

Rolofylline: an adenosine A1 receptor antagonist (A new class), it has a potent vasomotor effects (dilation) in the nephron and blunts proximal tubule and collecting duct NaCl reabsorption.

Prostaglandins

- Five subtypes (PGE, PGI, PGD, PGF, and thromboxanes) are synthesized in the kidney.
- The PGE participate in the regulation of salt reabsorption and play a role in the activity of certain diuretics.
- PGE2 decreases both Na+ reabsorption in the Thick ascending limb of Henle's loop and ADH-mediated water transport in collecting tubules.