

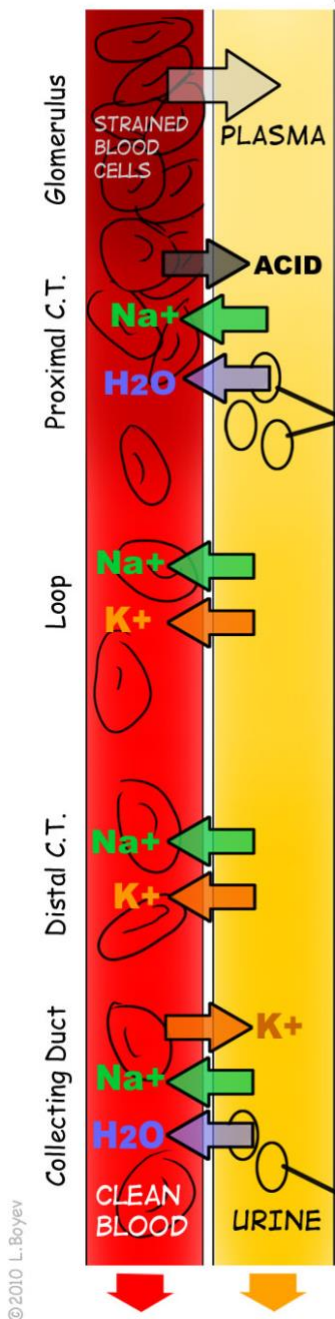
DIURETICS aka "Water Pills"

Na⁺ = sodium, K⁺ = potassium, Cl⁻ = Chloride, Ca⁺⁺=Calcium, Mg⁺⁺=Magnesium

Osmolarity is a term which refers to how concentrated any given solution is. Salt water with a lot of salt in it would be described as having high osmolarity. If you dilute that salt water so you can barely taste the salt, that is low osmolarity. In the body, water will always flow from low osmolarity to high osmolarity. It is almost as if Sodium (Na⁺) is acting like a sponge to draw the water with it. WATER FOLLOWS SODIUM (Na⁺)

THE KIDNEY: NATURE'S BLOOD FILTRATION PLANT

Just think of the nephron as a "blood vessel" running alongside a "urine" vessel and it makes more sense...



STEP 1. JUST LIKE STRAINING SPAGHETTI. EVERYTHING COMES OUT OF THE BLOOD BUT THE CELLS AND BIG PROTEINS. ALMOST IMMEDIATELY ALL THE GOOD STUFF (SUGARS, PROTEINS) GETS BACK INTO BLOOD. LET'S FOCUS ON IONS AND WATER...

STEP 2. THE KIDNEY GETS RID OF ACID USING CARBONIC ANHYDRASE. IT GETS SODIUM BACK INTO BLOOD AS SODIUM BICARBONATE.

Acetazolamide (a Carbonic Anhydrase Inhibitor) blocks this, so the sodium stays in the urine.

THERE ARE HOLES (AQUAPORINS) HERE FOR WATER TO FOLLOW THE SODIUM.

Mannitol (an Osmotic) works against these pores by giving water something more attractive than sodium to follow.

STEP 3. THE NAK2CL PUMPS SPENDS A LOT OF ENERGY SIMULTANEOUSLY PUMPING SODIUM, POTASSIUM (AND CHLORIDE) BACK INTO THE BLOOD.

Furosemide (a Loop Diuretic) blocks this NaK2Cl pump, so the sodium (and potassium) stays in the urine.

Remember, the water will follow the sodium out of the body....

STEP 4. ANOTHER NA PUMP PUMPS MORE SODIUM (AND POTASSIUM) BACK INTO THE BLOOD

HCTZ (a thiazide) blocks this pump, so the sodium and potassium stays in the urine... seeing a trend?

STEP 5. THE HORMONE ALDOSTERONE WORKS TO KICK EXTRA POTASSIUM OUT OF THE BLOOD WHILE PUTTING SODIUM BACK IN.

Potassium-sparing diuretics work here to stop the Na/K exchange. This is why patients taking these get high potassium blood levels!

THERE ARE WATER PORES HERE AS WELL... WATER FOLLOWS SODIUM (BY NOW THERE IS A LOT OF SODIUM BACK IN THE BLOOD!) THE BODY RETAINS ALL THAT WATER AND ONLY A LITTLE BIT LEAVES IN URINE

The kidney is responsible for excreting metabolic waste products, but is also crucial for regulating the blood volume, blood pH (acidity), electrolyte balance & blood pressure.
-It is so important that 25% of the cardiac output is to the kidneys.

Diuretic: a drug that increases the volume of urine produced and excreted

Diuretics are extremely useful to reduce blood volume a small amount (hypertension patients) or large amount (acute CHF patients) and to reduce edema.

All diuretics can cause orthostatic hypotension, some worse than others!

On a practical note, **don't forget to reduce salt intake** and that patients should take diuretics **in the morning** so they aren't up all night urinating.

MAJOR GROUPS of DIURETICS:

1) OSMOTIC DRUGS (as DIURETICS)

Big molecules that are filtered by glomerulus and can't be reabsorbed into the blood
Work by osmosis to suck water out of your blood vessels and into your urine, because water is more strongly attracted to osmotics than it is to sodium!

Mannitol: extremely large molecule that does not easily get absorbed into the GI system

Only given IV (*What would happen if you gave it orally?*)

Indications: -Acute Renal Failure, Acute Glaucoma, Brain Swelling

Can worsen HF and pulmonary edema!

Because first all the fluid will get sucked into the blood stream before it gets sucked into the nephron, and that huge increase in preload could send your patient into acute deadly heart failure!!

Other osmotics: glycerol, sugar alcohols, even glucose

Type 2 Diabetics with high glucose levels lose glucose into their urine, which draws water into the urine, causing frequent urination and susceptibility to urinary tract infections.

Remember **osmotics taken orally act like laxatives** (more on this later!)

2) CARBONIC ANHYDRASE INHIBITORS

The body constantly makes acid waste products. Constantly. So to stay in balance it has to constantly get rid of acid, which means getting rid of H⁺ ions.

By blocking Carbonic Anhydrase, H⁺ ions cannot exchange with Na⁺, so Na⁺ (and thus water) is not reabsorbed into the blood stream

acetazolamide (*Diamox*) is used for: emergent diuresis for acute glaucoma and altitude sickness

Use for altitude sickness may be useful if you ever practice outside of flat Illinois!

Used PO or IV, can cause hypokalemia +

3) LOOP DIURETICS

Act at TAL of Loop of Henle to block that NaK2Cl pump.

Used in **moderate to severe edema**

Good for **CHF**, cirrhosis (**liver failure**), *near kidney failure*, or hypertensive crisis

PO or IV, can induce a huge volume loss (“**high ceiling diuretic**”)

IV works fast, in ~10 minutes, and lasts ~2 hours.

Examples: **furosemide** (*Lasix*), bumetanide, ethacrynic acid, torsemide

SIDE EFFECTS: **Can cause big electrolyte imbalances** Na^+ , K^+ , Cl^- , Ca^{++} and Mg^{++})

K^+ loss (hypokalemia)

Ototoxicity (especially if infused IV too fast (deafness can happen up to 6 months later))

Allergy (**furosemide- sulfa**)

Gout

Contraindicated in **anuria** (zero urine output) or **hypokalemia** (*Why?*)

THIAZIDE DIURETICS

Block NaCl reabsorption in DCT, so water stays with the salt and leaves as urine.

Some examples: hydrochlorothiazide (HCTZ, *Hydrodiuril*), chlorothiazide (*Diuril*), indapamide (*Lozol*),

Hydrochlorothiazide (HCTZ): commonly used as first-line drug in mild **hypertension**

Side Effects: **K^+ loss (hypokalemia)**

hypercalcemia

can aggravate **gout**

Sulfa allergies

Aplastic anemia/ blood count changes (usu. reversible)

Can aggravate kidney disease (can slow down the GFR (filtration rate))

Use cautiously in diabetics (it increases blood glucose and lipid levels)

“POTASSIUM- SPARING” DIURETICS

These block K^+ secretion in DCT & CCT and lead to Na^+ loss (and water) in urine

Side effects: **hyperkalemia**, remember, high K^+ levels cause the heart to slow or stop!

Drugs that work at the Na/K pump in the distal tubule:

triamterine (*Dyrenium*): **directly acts** at DCT to block that Na/K pump.

It is marketed in combination with thiazides. Why?

Turns urine blue. Yay?

amiloride (*Midamor*)

Aldosterone antagonists: block aldosterone receptor at that same pump

eplerenone (*Inspira*)

spironolactone (*Aldactone*): cross-reacts with and blocks testosterone receptors

used for acne, but can cause **gynecomastia** (enlarged breasts also in men!)

ADH Antagonists: Same pump, **blocks ADH receptor**. Example: conivaptan (*Vaprisol*)

OTHER DRUG INTERACTIONS of DIURETICS:

anything to do with **potassium** will interact with digoxin (*why?*)

all diuretics worsen lithium toxicity (& actually most drugs' toxicity) (*why?*)

all diuretics potentially increase chance of a blood clot (*why?*)

all diuretics potentially cause orthostatic hypotension, loop diuretics are the worst (*why?*)