Ch. 10: Kidney (Renal) Physiology

Objectives:

- 1. Understand renal functions.
- 2. Review anatomy of the urinary system & kidneys.
- 3. Understand blood flow to kidneys.
- 4. Anatomy & physiology of the nephron.
- 5. Regulation of nephron filtration.
- 6. Kidney disorders.

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1. Functions of Renal System

Regulates:

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1. Removes metabolic wastes from bloodstream.

Can live only few weeks (may month) with kidney failure. Patients on kidney dialysis 10 -20 years.

- 2. Blood volume by filtering blood, excreting or reabsorbing water from body as needed (influenced by hormones ADD & ANP)
- **3. Blood pressure** by regulating blood volume.
- 4. Blood osmolarity by controlling reabsorption/excretion of salts (Na+, Cl-, X+, Ca⁺²). Influenced by hormone Aldosterone
- 5. Blood pH by controlling reabsorption/excretion of H+ & HCO_3 in urine.
- 6. Endocrine functions:
 - >Calcitrol = increases Ca⁺² absorbed from proximal convol. tubule
 - > Erythropoietin = stimulates RBC production
 - *> Renin = secreted by JGA causes Renin Angiotensin Aldosterore

Urinary Facts:

- Kidneys CAN filter 5.5L/40min OR 180 L/day!
- 99% of filtrate is automatically reabsorbed,, regardless of hydration state
- 1% might/might not be reabsorbed depends on hormones.

Avg urine output (pee) = 0.5 - 1.5 ml/kg/hr (or about 0.8 - 2 Liters/day)

- · Oliguria = lower than normal urine output.
- · Polyuria = higher than normal urine output
- · Anuria = no urine output.
- Obligatory water loss = minimum ucine output to remove

 400 ml (must pee out to rid body of wastes) toxins from blood.
- "osmolality" = osmoles (Osm) of solute per kg of solvent (Osm/kg)
- "osmolarity" = osmoles (Osm) of solute per liter of solution (Osm/L)
 More accurate for understanding osmotic effects than mass of solute in solution

Different kinds of solute can have different sizes

Some solutions may have multiple kinds of solute https://www.ncbi.nlm.nih.gov/books/NBK606132/

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2. REVIEW anatomy of Renal System

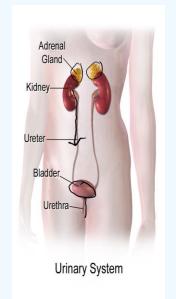
Kidneys = paired organs, posterior abdominal cavity

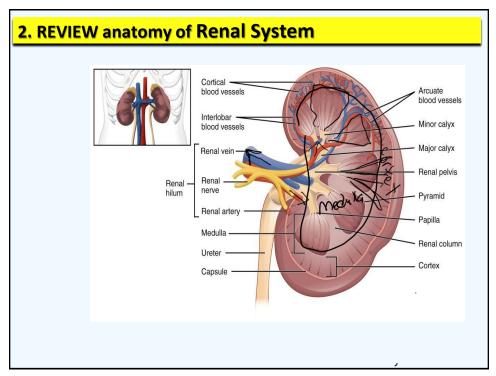
- filter arterial blood continuously.
- 8 12 renal lobes per kidney
- lobes contain millions of nephrons
- adrenal glands on top of kidneys.

Ureters = paired tubes transport urine from kidneys to bladder

Urinary bladder = muscular sac for temp. storage of urine.

Urethra = tube that transports urine from bladder to exterior of body.





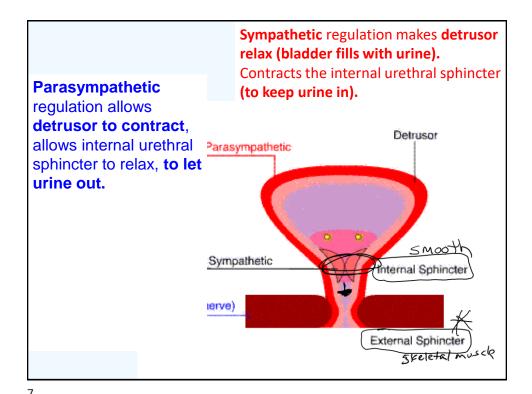
2. REVIEW Anatomy of Urinary Bladder

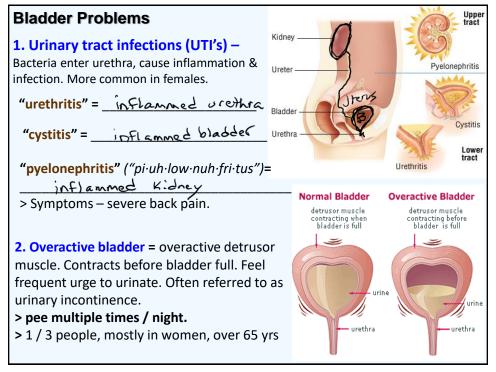
- Below uterus in females, above prostate in males
- Stores 400 600 ml unine for ~5 hrs
- Urinate ($\underline{\text{micturate}}$) ~ 6 8 times / day

Has "detrusor muscle" = smooth muscle, which

- > Under <u>parasympathetic stim</u>. & neurotransmitter <u>ACh</u> and <u>muscarinic</u> cholinergic receptors <u>contracts</u> to push using into wrether.
- > Under <u>sympathetic stimulation</u> and neurotransmitter <u>Epinephri</u>ne and β2 and β3-adrenergic receptors <u>Γελαχ Δελκυ Σος (Κεφς υπίπε ίπ</u>)

 B2 & B3 think "It's <u>De</u> <u>B</u>est 2 hold pee with 3"









Oxybutynin = anticholinergic (ACh blocker)

Keeps detrusor smooth muscle relaxed
by blocking ACh receptor.

Botox injection – stops ACh release from neurons to muscles.



Mirabegron = B3 adrenergic agonist

Keeps detrusor smooth muscle relaxed by stimulating B3 adrenergic receptor

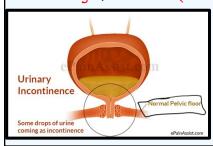
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Bladder Problems contin...

- 3. Urinary Incontinence why you can't hold your pee.
- A) <u>Urge incontinence</u> = bladder dysfunction. After strong urge to urinate might leak a little (or a lot) urine.
- B) Stress incontinence = Small seakage of orine with sneezing

Coughing, laughing exercise.

- > 1 / 3 people more often in women
- > common in women w/age & after pregnancy
- > Tx Kegel exercise





Kegel Exercises (to strengthen pelvic floor muscles within 4-6 wks)

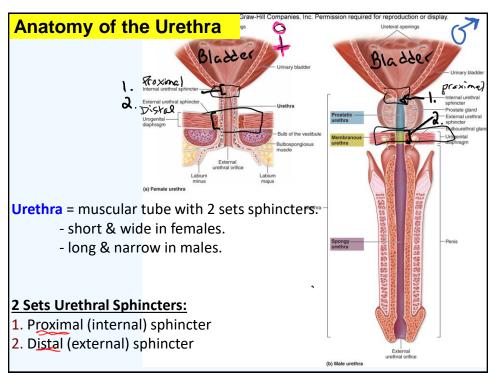
- **1.** Make sure your bladder is empty, then sit or lie down.
- 2. Tighten pelvic floor muscles. Hold tight & count 3 to 5 sec.
- 3. Relax muscles & count 3 to 5 sec.
- 4.Repeat 10 times, 2 or 3 times a day (morning, afternoon, and night).

Good for urinary incontinence, or fecal incontinence.

Source

Steps for Doing Kegels. First, locate your pelvic floor muscles. Start by tightening your pelvic floor muscles for 3 seconds, then relaxing for 3 seconds. This is one Kegel. Try to repeat this 10 times. **10** × **10** This is called a set. Do one set in the morning and one set at night. As you gain strength, try increasing these numbers .. for example, hold and relax for 5 seconds each. Cleveland Clinic

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2 Sets Urethral Sphincters: Proximal & Distal

1. Proximal (internal) sphincter – innervated by **sacral** & pelvic splanchic nerves.

Smooth muscle, Autonomic motor control:

- > Parasympathetic with ACh neurotransmitter & muscarinic cholinergic receptors
 - detrusor muscle Contract
 - proximal urethral sphincter 50/axes

Think "UR" ABout to hold the pee in 3 sec).

- > Sympathetic w/ Epinephrine neurotransmitter & α & β3 adrenergic receptors
 - proximal urethral sphincter _____ Contract

Detrusor w/sympathetic stimulation will __relax Which adrenergic receptors for detrusor??____

2. Distal (external) sphincter

- skeletal muscle, somatic (voluntary) motor control.
- ACh neurotrans. & nicotinic cholinergic receptors
- pelvic floor muscles (pubococcygeus) and pudendal nerve, we learn to control with "guarding reflex".



"Guarding reflex" = voluntary control of distal urethral sphincter.

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Getting a urine sample:

Voided sample = collected from normal urination (through urethra) in sample cup. - Can contain sloughed urethral cells and possible bacteria from lower urinary tract.

Catheterization = insert (Foley) catheter up urethra into bladder.

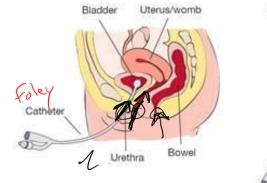


Figure 1 - Female catheter

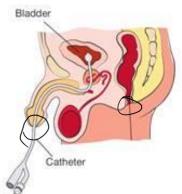


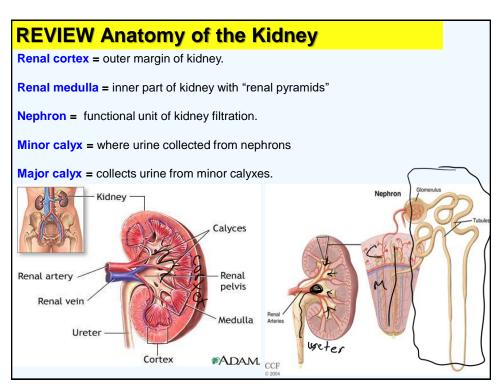
Figure 2 - Male catheter

Why catheterize the bladder?

Catheterization

- 3 reasons for catheterization: bladde (
- To obtain a sterile urine sample for analysis
- To relieve urinary retention
- To instill medicine into the bladder, after the bladder is emptied
- For urine sample: Quick Cath, In & Out Cath
- For incontinence: Foley Catheter
 - · For long (>3 hrs) surgery

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3. REVIEW Blood Supply of Kidneys and nephrons:

Renal artery – brings arterial blood to kidneys to be filtered.

– BP in renal artery sensed by the JGA

Afferent arteriole = arterial blood enters the glomerulus of the nephrons

Plasma, ions, glucose, small proteins, and other substances get filtered through glomerular pores. "Filtrate" then enters PCT.

Exits nephron

Efferent arteriole = arterial blood leaves the glomerulus of the nephrons

(RBCs, WBCs, platelets, and large molecules do not make it through glomerular pores.)

around _nephron-tube

Peritubular capillaries = capillaries that surround nephron and receive reabsorbed substances, from filtrate, which return to the bloodstream. OR secrete substances into the filtrate to be removed in the urine.

Abbreviations for nephron tubules:

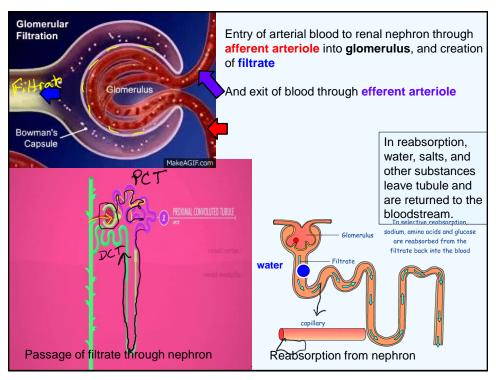
PCT = proximal convoluted tubule

Loop = Loop of Henle

DCT = distal convoluted tubule

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3. REVIEW Blood Supply of Kidneys and nephrons: Bowman's capsule Proximal tubule Glomerulus Afferent arteriole **Efferent** Distal arteriole tubule Branch of From renal vein another nephron Collecting Loop of Henle with capillary network Peritubular capillaries Vasa recta



Review

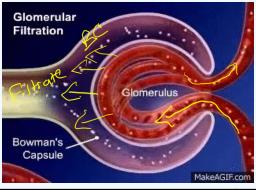
- Functions of renal system
 - blood volume, pressure, osmolarity
 - endocrine functions
- Urinary problems
 - infections
 - incontinence
- Anatomy of renal system
 - Bladder detrusor muscle
 - Urethra and sphincters
 - Kidney anatomy
 - blood supply (renal artery, afferent & efferent arteriole, peritubular capillaries.

4. Physiology of the Nephron & Blood Filtration

Renal Corpuscle = Glomerulus + Bowman's capsule:

- A) Glomerulus = receives arterial blood from afferent arteriole, and filters it.
- > has small pores (slits) to allow fluids, ions, glucose, small proteins through.
- > do not allow large molecules or cells (RBCs, WBCs, platelets) through.
- **B)** Bowman's capsule = capsule surrounding the glomerulus. Receive the filtrate into the nephron tubule.





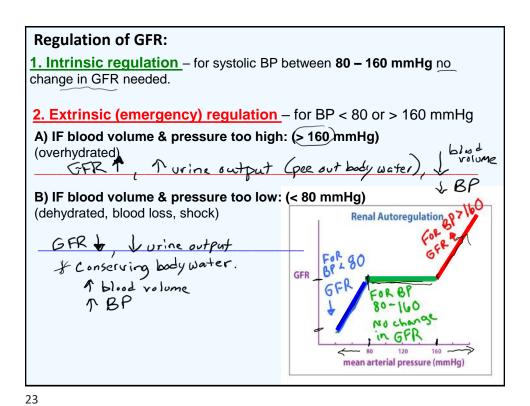
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Glomerular Filtration Rate (GFR) = volume of filtrate produced by both kidneys per minute. (ml/min)

- Kidneys Filter: > average of 5.5 L blood every 40 min (entire blood volume!)
- Females = ~ 115 ml/min
- Males = ~ 125 ml/min

***<u>GFR is constant for systolic arterial blood pressure (SBP)</u> between 80 – 160 mmHg due to "intrinsic regulation".

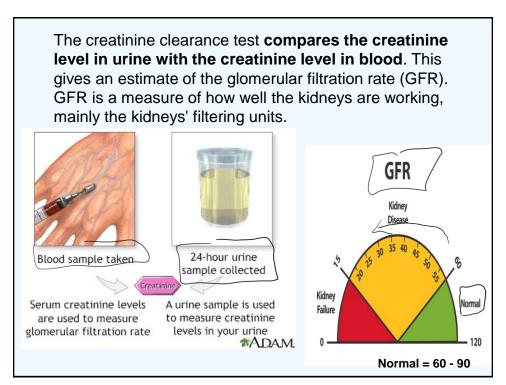
The only time GFR changes is when SBP drops below 80 mmHg or goes above 160 mmHg—then it's an "emergency" or extrinsic regulation.



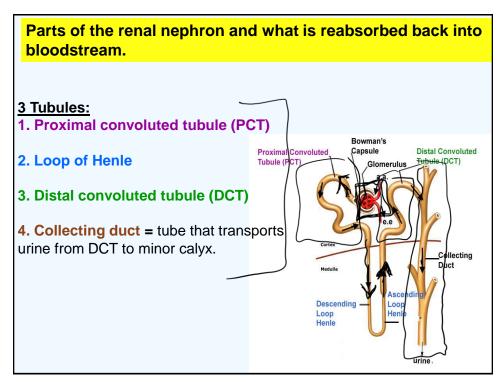
GFR measured by blood and urine creatine.

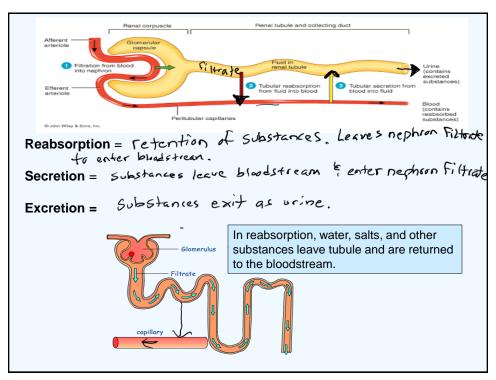
CLINICAL APPLICATIONS

Measurements of the GFR are used clinically to assess kidney health. Most often, this involves measurements of the creatinine concentration in the blood and urine. Creatinine, a waste product derived from muscle creatine, enters the blood at a constant rate and is normally eliminated by the kidneys at a constant rate. The renal plasma clearance of creatinine is only slightly higher than the GFR, indicating that it is slightly secreted by the nephron tubules. Thus, the GFR can be measured to an approximate degree by the renal plasma clearance of creatinine. More often, a simple measurement of the plasma creatinine concentration can provide an index of the GFR and thus the health of kidney function.



| 5 Stages of Kidney Disease | | |
|----------------------------|---------------------|--|
| Do NOT memorize! | Kidney Function/GFR | Description |
| Stage 1 | > 90% | Normal or High Function |
| Stage 2 | 60-89% | Mildly Decreased Function |
| Stage 3 | 30-59% | Mild to Moderately Decreased Function |
| Stage 4 | 15-29% | Severely Decreased Function |
| Stage 5 | < 15% | Kidney Failure |





After Glomerulus & Bowman's capsule → 4 Types of Tubules in Nephron:

- 1. Proximal convoluted tubule (PCT) reabsorbs pretty much everything.
- > First tubule after glomerulus
- > Reabsorbs majority of substances from filtrate automatically, regardless of hydration or hormones.

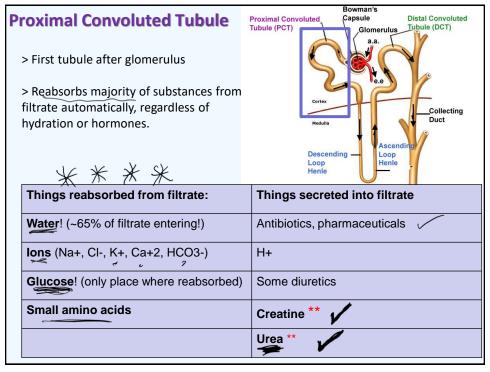
2. Henle's loop

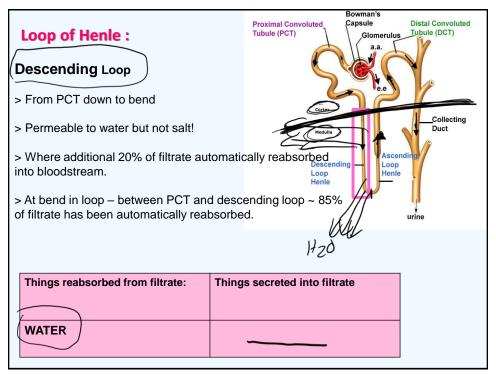
> where urine concentrated by Counter-Current multiplication system

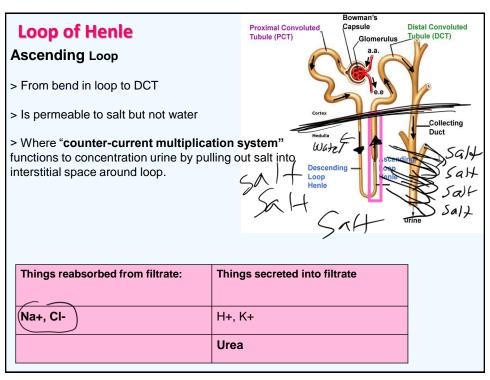
3. Distal convoluted tubule DCT

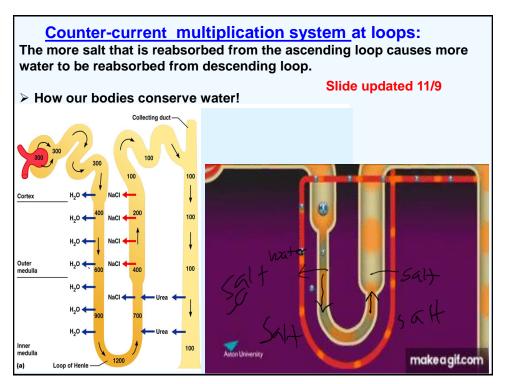
- > last tubule
- > where aldosterone has effect on salt reals orphion
- 4. Collecting duct what leaves here is urine.

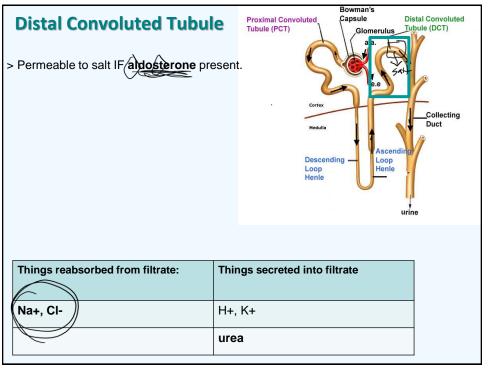
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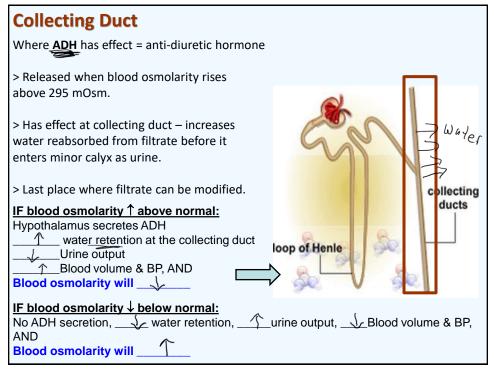








- Addison's Disease Insufficient Aldosterone
- Conn's Syndrome (Hyper-aldosteronism)



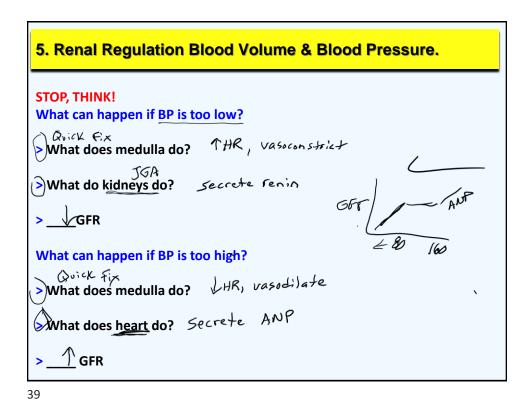
Click <u>HERE</u> for a YouTube video showing reabsorption versus secretion from nephron tubules, and how the counter current multiplier system works for concentration urine (conserving body water).

3 min 30 sec

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Review

- · Intrinsic regulation of GFR
 - GFR steady with minor BP fluctuations by afferent arteriole vasodilation / vasoconstriction
 - endocrine functions
- · Extrinsic regulation (medulla) of GFR
 - If BP ↓ sympathetic stim ↓ GFR causing ↓ urine output and ↑ blood volume and BP.
 - If BP ↑ parasympath. stim ↑ GFR causing ↑ urine output and ↓ blood volume and BP.
- · Structure of nephron
 - Glomerulus
 - PCT (what is reabsorbed & secreted?)
 - Loop of Henle : descending (what is reabsorbed & secreted?)
 ascending (what is reabsorbed & secreted?)
 - DCT (what is reabsorbed & secreted? What hormone influences?)
 - CD (what is reabsorbed? What hormone influences?)



Urinary Stones ("urolithiasis") - frequency 1 / 10 people

= when salt crystals precipitate (come out of solution)

Out of ucine.

Calculi can block renal calyx, ureter, and in males even urethra).

Shore?

Result

> is buildup of fluid pressure (hydronephrosis) within kidneys, causes pressure necrosis.

- > buildup of toxinas in bloodstream, causes organs to shut down.

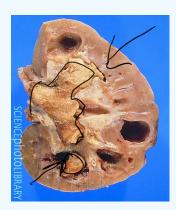
(a) An x-ray showing several kidney stones (b) This kidney stone, 8 mm in length, was removed through surgery.

Added picture 4/1

Urinary Stones ("urolithiasis")

Hydronephrosis = urine backed up in Kidney.

- > can cause pressure necrosis.
- > buildup of toxins in bloodstream, causes organs to shut down.
- > Can also be caused by infection, enlarged prostate (males).



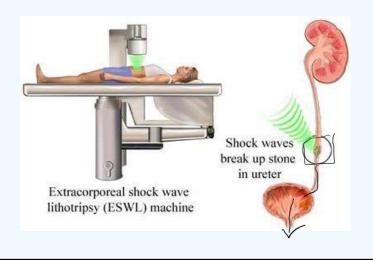


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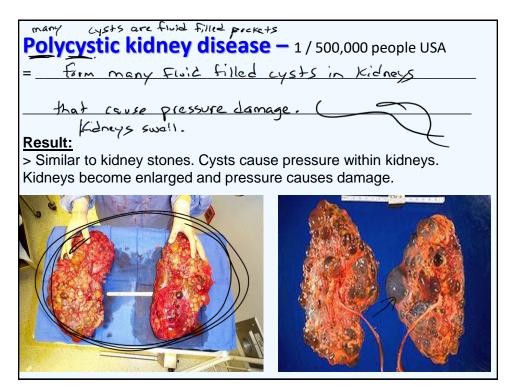
CLINICAL APPLICATIONS

Kidney stones are composed of crystals (of calcium oxalate, calcium phosphate, and other substances) and proteins that grow until they break loose and pass into the urine collection system. When a stone breaks loose and passes into a ureter, it produces steadily increasing pain, which can become so intense that the patient requires narcotic drugs. The calcium and other substances in kidney stones are normally present in urine, but they become supersaturated and crystalize to form stones for reasons not currently understood. The stones may be removed surgically or broken up by a noninvasive procedure called *shock-wave lithotripsy*.

A machine called a **lithotripter** generates shock waves that are focused on a stone (or stones) using X-ray or ultrasound imaging. The shock waves break the stone into smaller pieces that can pass through urinary system.



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Chronic Kidney Disease (CKD)

- > 1 / 7 people, USA
- > Majority (9/10 people) of those with CKD don't even know they have it.

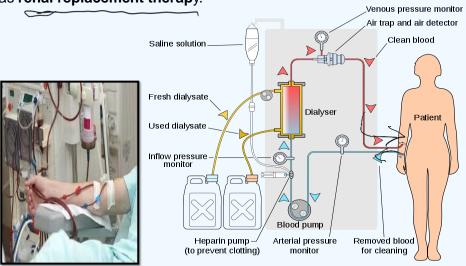
Kidney Failure

- ★ GFR < 15%
- > Life expectancy without treatment range from 3 days to 3 weeks.
- **>** Life expectancy with dialysis -5 10 years.

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Dialysis

= process of removing excess water, solutes and toxins from the blood in those whose kidneys can't perform anymore. This is also referred to as **renal replacement therapy**.



CLINICAL APPLICATIONS

The term *dialysis* refers to the separation of molecules using their ability to diffuse across an artificial semipermeable membrane (chapter 3). This principle is used in the "artificial kidney" machine for **hemodialysis**. Like the walls of the glomerular capillaries, the artificial semipermeable membrane allows water and dissolved waste molecules (such as urea) to easily diffuse through the membrane pores, whereas plasma proteins are excluded by their larger size. However, unlike the tubules, the artificial membrane can't reabsorb Na⁺, K⁺, glucose, and other molecules needed in the blood. These substances are therefore included in the fluid around the dialysis membrane, so that there is no concentration gradient to cause their net diffusion out of the blood. Sometimes a patient's own peritoneal membranes (which line the abdominal cavity) are used as the dialysis membrane, in a technique called **continuous ambulatory peritoneal dialysis**.

Click <u>HERE</u> for YouTube video explaining dialysis methods 3 min 30 sec

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Diuretics - prescribed to treat high BP or edema

1) Carbonic anhydrase inhibitors (Acetazolamide)

> Decreases salt reabsorption at PCT. I water absorption in tissue.

BUT prescribed more for glaucoma patients than patients with hypertension.

2 Loop diuretics (e.g. furosemide or "Lasix")

> Decreases salt reabsorption at ascending loop of Henle L (resorp.)

(which will decrease water reabsorption at descending loop!)

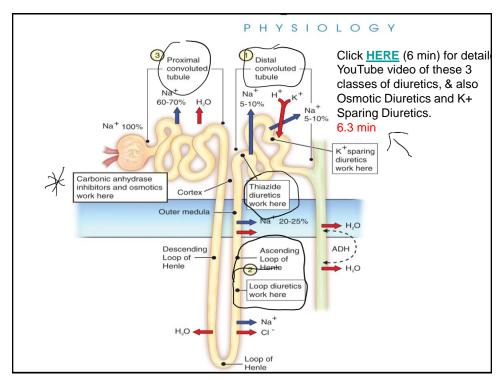
High BP.

Most powerful diuretic, BUT use can lead to loss of other ions (K+, Ca+2, Cl-, and Mg)

3. Thiazides (hydrochlorothiazide)

> decreases salt reabsorption at DCT (BUT can also lead to K+ loss)

Salt reabsorption



PHYSIOLOGY IN HEALTH AND DISEASE

Not required reading

A diuretic is a substance that increases urine volume. Water is the most common diuretic, acting to dilute the plasma (lower its osmolarity) and thereby reduce the stimulation of osmoreceptors in the hypothalamus. This lowers the secretion of ADH from the posterior pituitary, which reduces the permeability of the collecting ducts to water and causes diuresis (increased water excretion in the urine).

Osmotic diuretics are extra solutes in the tubular fluid. These increase the osmolarity of the fluid within the collecting ducts, so that the osmotic gradient (difference in concentration) between the tubular fluid and the interstitial fluid of the renal medulla is reduced. As a result, less water can be drawn out of the collecting ducts by osmosis, leaving more to

ibea, painba, to

be excreted in the urine. Glucose is an example of an endogenous molecule that can become an osmotic diuretic, if a person is hyperglycemic and the renal plasma threshold for glucose is exceeded. Because of this, a person with uncontrolled diabetes mellitus who "spills glucose" in the urine has polyuria (literally, "many urines") and can become dehydrated. Similarly, excessive production of ketone bodies (which can cause ketoacidosis; chapter 12) in uncontrolled type 1 diabetes mellitus results in ketonuria, and the extra ketone bodies in the tubular filtrate have an osmotic diuretic effect. A person on a strict weight-reducing diet, who has a rapid breakdown of fat and thus a high plasma level of ketone bodies (ketosis), can also have ketonuria. The resulting osmotic diuresis promotes dehydration, which is part of the reason dieters are advised to drink lots of water. Mannitol is an exogenous substance sometimes used clinically as an osmotic diuretic.

The most powerful clinical diurctics are the **loop diurctics**, including *furosemide* (*Lasix*). These inhibit as much as 25%

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of the salt transport out of the ascending limbs of the loops of Henle. Because of this, the interstitial fluid of the renal medulla is less concentrated (hypertonic), producing less of an osmotic gradient to draw water out of the collecting ducts. The thiazide **diuretics** (such as *hydrochlorothiazide*) inhibit up to 8% of the salt and water reabsorption by inhibiting Na⁺ transport in the last part of the ascending limb and first part of the distal tubule, thereby reducing the osmotic gradient for water reabsorption. Although these are effective and commonly used diuretics, Lasix and hydrochlorothiazide have an undesirable side effect: they promote the excretion of K⁺ in the urine, which lowers the plasma K⁺ concentration (hypokalemia). Hypokalemia can cause neuromuscular disorders and ECG abnormalities. Because of this, people taking Lasix and hydrochlorothiazide should get their blood K⁺ concentrations measured periodically, and must often take potassium supplements (in the form of KCl).

Not required reading

The hypokalemia in people taking Lasix or hydrochlorothiazide is caused by an increase in aldosterone-stimulated secretion of K⁺ into the cortical collecting ducts. Because of this, some medications for the treatment of hypertension (high blood pressure; chapter 10) combine hydrochlorothiazide with one of the potassium-sparing diurctics. Spironolactone (such as Aldactone) diurctics block aldosterone action by competing for the aldosterone receptor proteins in the cells of the cortical collecting ducts. Triamterene (Dyrenium) is a potassium-sparing diurctic that acts more directly to block Na⁺ reabsorption and K⁺ secretion in the cortical collecting ducts. The diurctic actions of hydrochlorothiazide combined with the weaker diurctic but potassium-sparing actions of these drugs lower the blood volume, and thus the blood pressure, of people with hypertension. The esting that too

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Review

- 3 ways the body regulates blood volume & BP (all involve kidney function!)
- Baroreceptors in heart and medulla influenced by BP and change GFR.
- Hypothalamic ADH (influence by blood osmolarity & change water reabsorption)
- Renin-angiotensin-aldosterone system (influenced by BP and change salt reabsorption)
- Urinary stones (urolithiasis)
- Polycystic kidney disease
- Dialysis
- Diuretics