Ch. 10: Kidney 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 Urinary System

Regulates:

1. Blood volume - by filtering blood, excreting or reabsorbing water from body as needed (influenced by hormones **ADH**, **ANP**, & **Aldosterone**

2. Blood pressure – by regulating blood volume.

3. Blood osmolarity – by controlling reabsorption/excretion of salts (Na^+, Cl^-, K^+, Ca^{+2}).

4. Blood pH – by controlling reabsorption/excretion of H^+ & HCO_3^- in urine.

5. Endocrine functions:

- ***>Calcitrol*** = increases Ca^{+2} absorbed from proximal convol. tubule
- ***>Erythropoietin*** = stimulates RBC production
- ***>Renin*** = secreted by JGA causes

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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)** = 0.7 – 2.0 L/day (30 – 80 ml/hr)
  - *Oliguria = smaller than normal urine output*
  - *Polyuria = higher than normal urine output*
  - *Anuria = no urine production (BAD)*
- **Obligatory water loss** = **400 ml** (must pee out to rid body of wastes)
  - "*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

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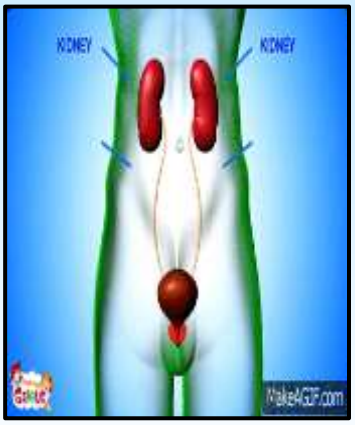
2. REVIEW anatomy of Urinary System

Kidneys = paired organs, posterior abdominal cavity
- 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.

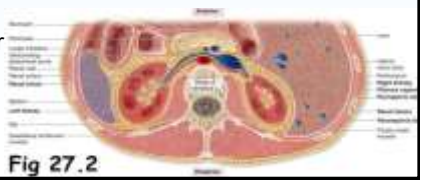


Fig 27.2

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2. REVIEW Anatomy of Urinary Bladder

- Below uterus in females, above prostate in males

- Stores 400 – 600 ml urine for ~5 hrs

- Urinate (**micturate**) ~ 6 – 8 times / day

Has "**detrusor muscle**" = smooth muscle, which

> Under parasympathetic stim. & neurotransmitter ACh and muscarinic cholinergic receptors to allow urine into urethra (bladder contracts/ empties).

> Under sympathetic stimulation and neurotransmitter Epinephrine and β2 and β3-adrenergic receptors to allow bladder filling.

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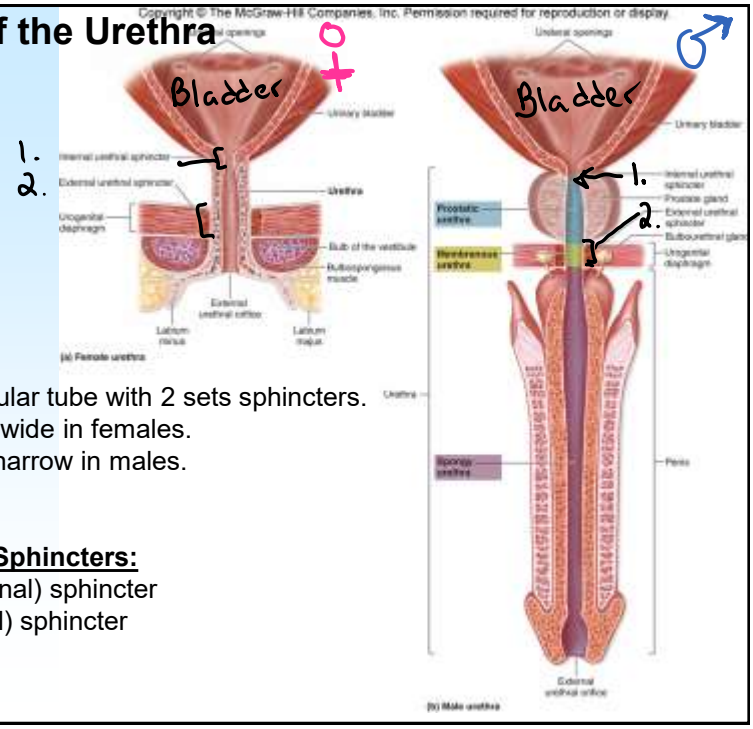
Anatomy of the Urethra



Urethra = muscular tube with 2 sets sphincters.
- short & wide in females.
- long & narrow in males.

2 Sets Urethral Sphincters:
1. Proximal (internal) sphincter
2. Distal (external) sphincter

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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
- contracts detrusor muscle (urine enters urethra)
- relaxes proximal urethral sphincter (urine passes through)

> Sympathetic w/ Epinephrine neurotransmitter & α & β 3 adrenergic receptors
- relaxes detrusor muscle (bladder fills)
- contracts proximal urethral sphincter (sphincter closed – no urine passes!)

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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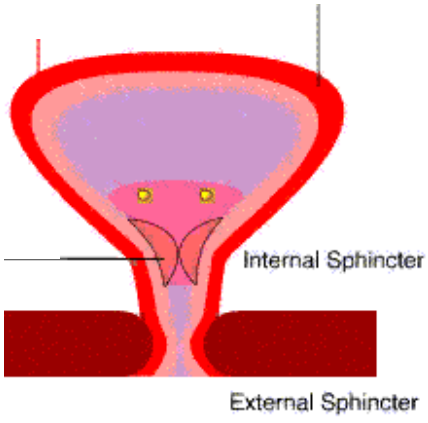
Sympathetic regulation makes detrusor relax (urine fills bladder, but doesn't leave. Contracts the internal urethral sphincter **(to keep urine in).**

Parasympathetic regulation allows detrusor to contract, allows internal urethral sphincter to relax, **to let urine out.**



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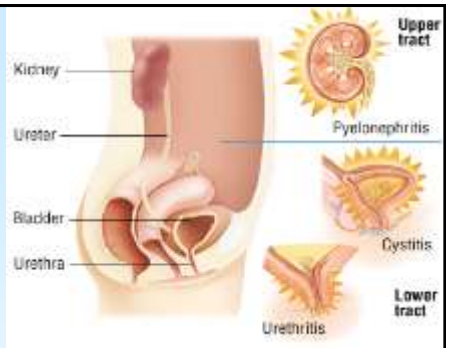
Bladder Problems

1. Urinary tract infections (UTI's) –
Bacteria enter urethra, cause inflammation & infection. More common in females.

"urethritis" = inflamed urethra

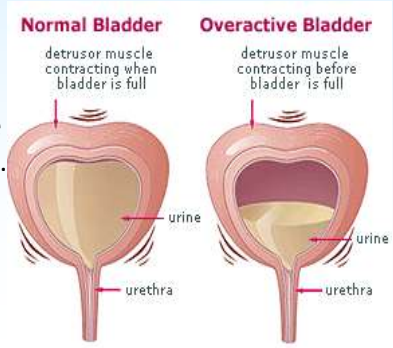
"cystitis" = inflamed bladder

"pylenonephritis" = inflamed kidney(s)
Untreated, can lead to kidney failure.
> Symptoms – severe back pain.



2. Overactive bladder = disorder of overactive detrusor muscle. Contracts before bladder full. Feel frequent urge to urinate.
> 8 times / night.

1 / 11 people, mostly over 65
More common in females.



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Overactive bladder treatments

Tx =

Oxybutynin *= anticholinergic (ACh blocker)*
Keeps detrusor smooth muscle relaxed by blocking ACh receptor.

Mirabegron *= B3 adrenergic agonist*
Keeps detrusor smooth muscle relaxed by stimulating B3 adrenergic receptor

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Bladder Problems contin…

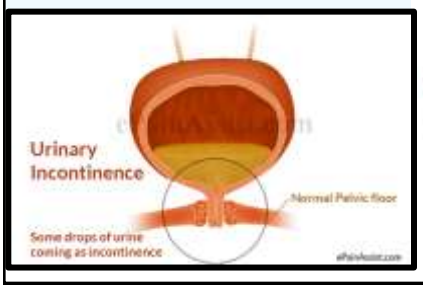
3. Urinary Incontinence – why you can't hold your pee.

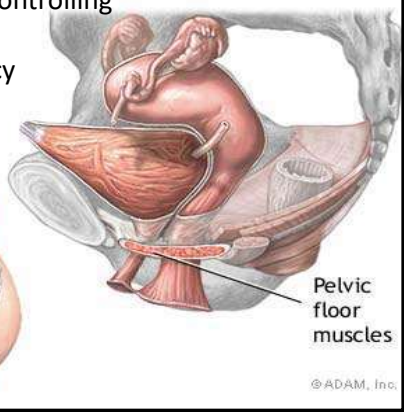
A) Urge incontinence = after strong urge to urinate have complete loss control of urination.

B) Stress incontinence = leakage of urine when laugh, sneeze, cough, or exercise.

> gradual weakening of pelvic floor muscles controlling distal urethral sphincter.

> common in women w/age & after pregnancy





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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.

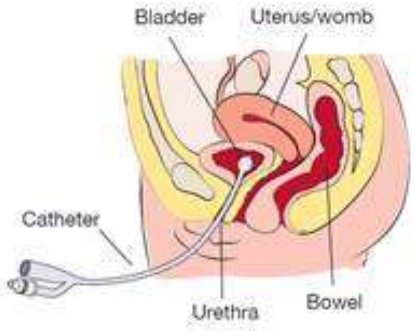

Figure 1 – Female catheter

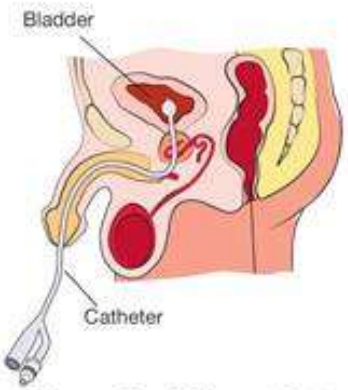

Figure 2 – Male catheter

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Why catheterize the bladder?

Catheterization

- 3 reasons for catheterization:
- 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

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REVIEW Anatomy of the Kidney

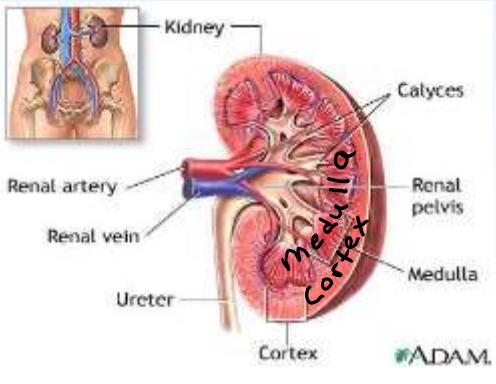
Renal cortex = outer margin of kidney.

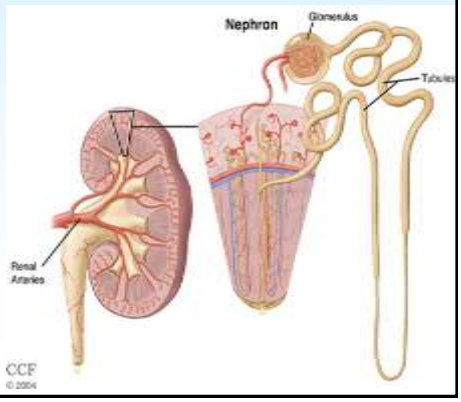
Renal medulla = inner part of kidney with "renal pyramids"

Nephron = functional unit of kidney filtration.

Minor calyx = where urine collected from nephrons

Major calyx = collects urine from minor calyxes.





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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.

Efferent arteriole = **arterial blood leaves the glomerulus of the nephrons**
(RBCs, WBCs, platelets, and large molecules do not make it through glomerular pores.)

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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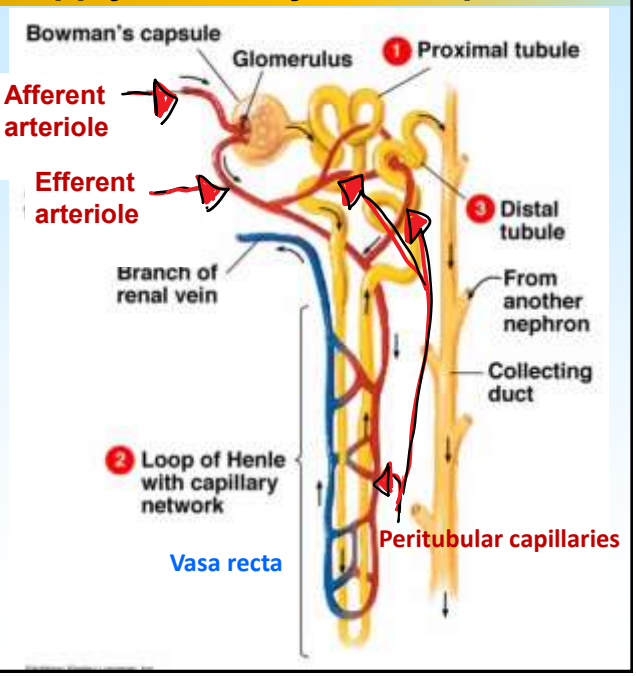
3. REVIEW Blood Supply of Kidneys and nephrons:



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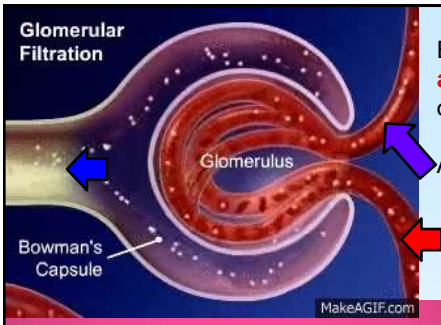
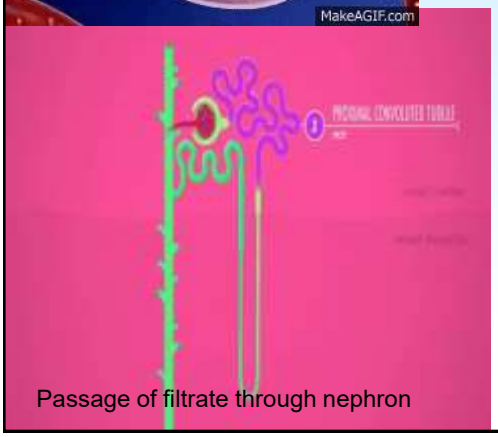


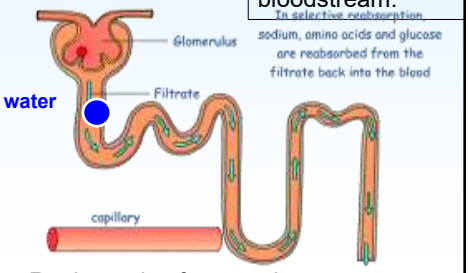
Entry of arterial blood to renal nephron through **afferent arteriole** into **glomerulus**, and creation of **filtrate**

And exit of blood through **efferent arteriole**



Passage of filtrate through nephron

In reabsorption, water, salts, and other substances leave tubule and are returned to the bloodstream.



Reabsorption from nephron

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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**
  - **blood supply (renal artery, afferent & efferent arteriole, peritubular capillaries.**

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4. Physiology of the Nephron

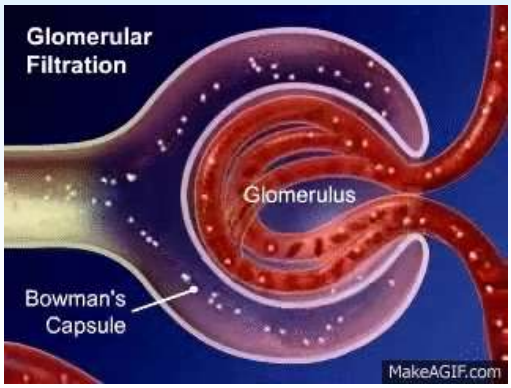
Renal Corpuscle = Glomerulus + Bowman's capsule:

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

****GFR is constant for systolic arterial blood pressure (SBP) 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.

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Regulation of GFR:

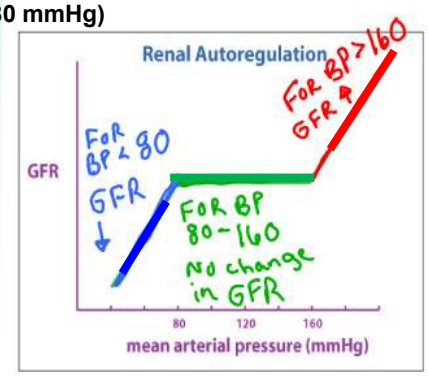
1. Intrinsic regulation – for systolic BP between 80 – 160 mmHg no change in GFR needed.

2. Extrinsic (emergency) regulation – for BP < 80 or > 160 mmHg

A) IF blood volume & pressure too high: (> 160 mmHg)
(overhydrated)
GFR increases, less water retained, urine output ↑, blood volume and BP ↓.

B) IF blood volume & pressure too low: (< 80 mmHg)
(dehydrated, blood loss, shock)

GFR decreases, more water retained, urine output ↓, blood volume & BP ↑



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GFR measured by **creatine** clearance rate in urine.

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.

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4. Physiology of the Nephron

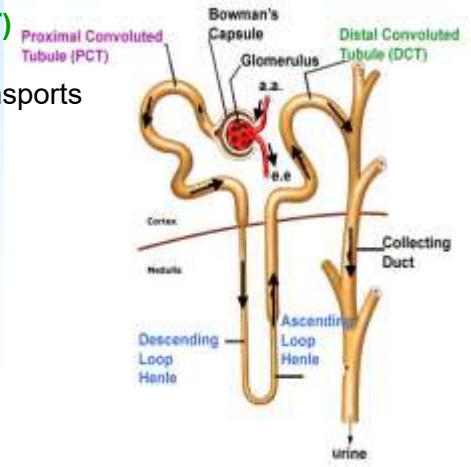
3 Tubules:

1. Proximal convoluted tubule (PCT)

2. Loop of Henle

3. Distal convoluted tubule (DCT)

4. Collecting duct = tube that transports urine from DCT to minor calyx.



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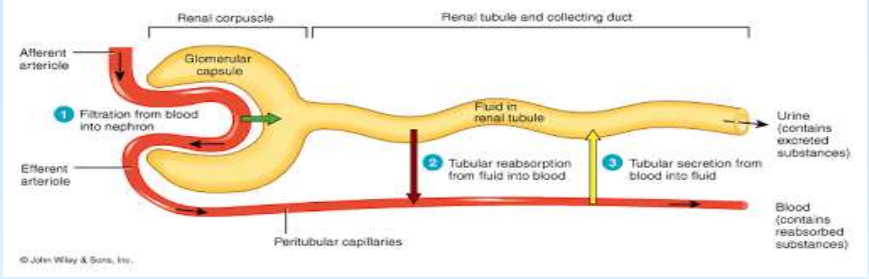
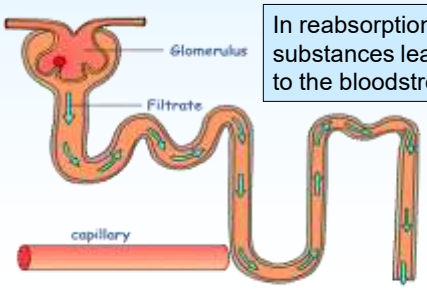


Reabsorption = filtrate within tubule is **re**claimed by the bloodstream.
Secretion = substances from bloodstream are put into filtrate to be removed in urine.
Excretion = removal of filtrate as **urine**, transported out of kidneys by ureter.



In reabsorption, water, salts, and other substances leave tubule and are returned to the bloodstream.

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

1. Proximal convoluted tubule
> 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
> last tubule
> where aldosterone has effect on salt

4. **Collecting duct** – what leaves here is urine.

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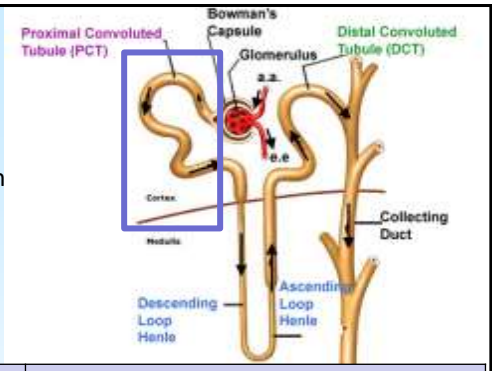
Proximal Convoluted Tubule

> First tubule after glomerulus

> Reabsorbs majority of substances from filtrate automatically, regardless of hydration or hormones.



Things reabsorbed from filtrate:	Things secreted into filtrate
Water! (~65% of filtrate entering!)	Antibiotics, pharmaceuticals
Ions (Na+, Cl-, K+, Ca+2, HCO3-)	H+
Glucose! (only place where reabsorbed)	Some diuretics
Small amino acids	Creatine
	urea

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Loop of Henle :

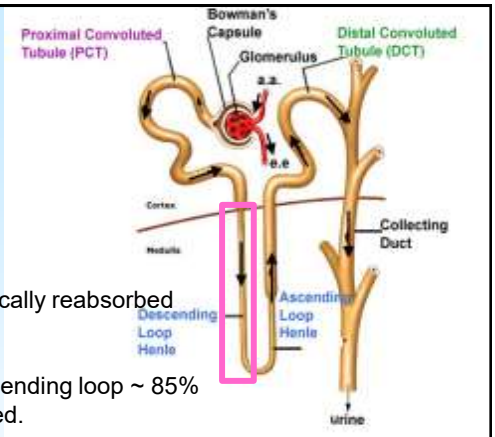
Descending Loop

> From PCT down to bend

> Permeable to water but not salt!

> Where additional 20% of filtrate automatically reabsorbed into bloodstream.

> At bend in loop – between PCT and descending loop ~ 85% of filtrate has been automatically reabsorbed.



Things reabsorbed from filtrate:	Things secreted into filtrate
WATER	

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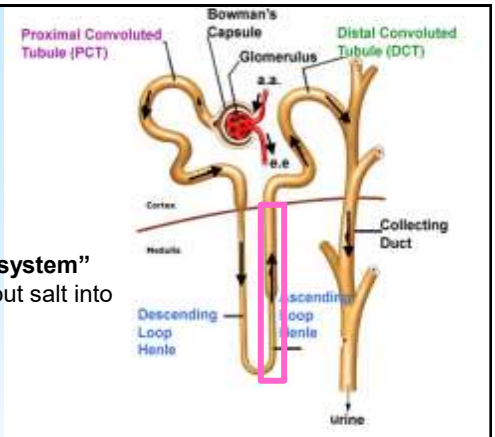
Loop of Henle

Ascending Loop

> From bend in loop to DCT

> Is permeable to salt but not water

> Where "**counter-current multiplication system**" functions to concentration urine by pulling out salt into interstitial space around loop.



Things reabsorbed from filtrate:	Things secreted into filtrate
Na+, Cl-	H+, K+
	urea

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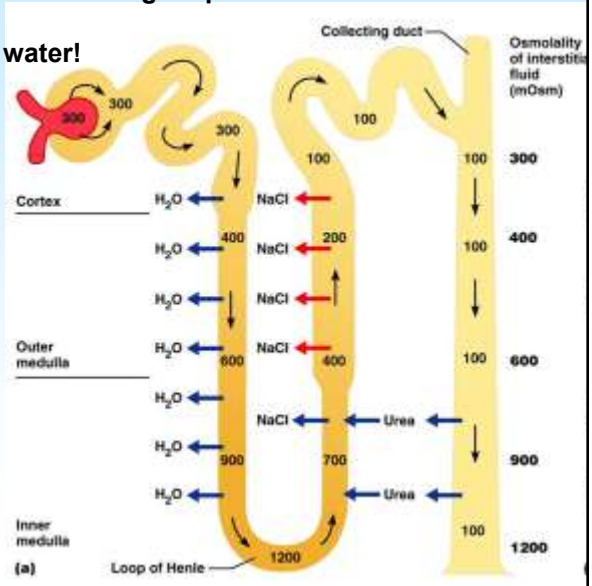
Counter-current multiplication system at loops:

The more salt that is reabsorbed from the ascending loop causes more water to be reabsorbed from descending loop.

- **How our bodies conserve water!**



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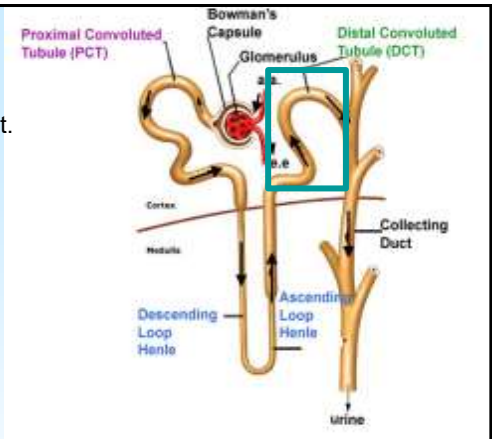
Distal Convoluted Tubule

> Permeable to salt IF **aldosterone** present.



Things reabsorbed from filtrate:	Things secreted into filtrate
Na+, Cl-	H+, K+
	urea

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- **Addison's Disease –** Insufficient Aldosterone

- **Conn's Syndrome** (Hyper-aldosteronism)

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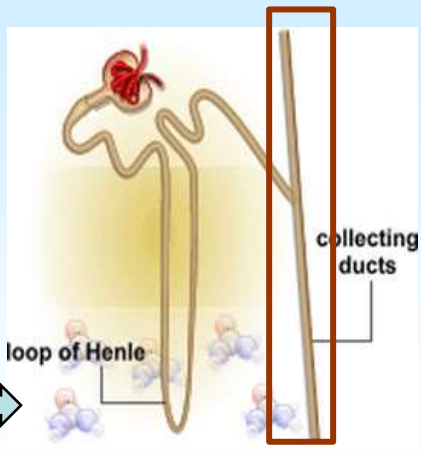
Collecting Duct

Where **ADH** has effect = anti-diuretic hormone

> Released when blood osmolarity rises above 295 mOsm.

> Has effect at collecting duct – increases water reabsorbed from filtrate before it enters minor calyx as urine.

> Last place where filtrate can be modified.



IF blood osmolarity ↑ above normal:
Hypothalamus secretes ADH
ADH ↑ water retention at the collecting duct
Urine output ↓
Blood volume & BP will increase, AND
Blood osmolarity will ↓

IF blood osmolarity ↓ below normal:
No ADH secretion, ↓ water retention, urine output ↑,
Blood volume & BP will ↓, AND
Blood osmolarity will ↑

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Click HERE 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?)**

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5. Regulation of Filtration to Control Blood Volume, Blood Pressure, & Osmolarity

STOP, THINK!

What can happen if BP is too low?

> **What does medulla do?** Increase HR and cause arterial vasoconstriction

> **What do kidneys do?** JGA secretes renin, to start renin-angiotensin-aldosterone system

> ↓ GFR

What can happen if BP is too high?

> **What does medulla do?** Decrease HR and cause arterial vasodilation

> **What does heart do?** Secretes ANP, which

> ↑ GFR

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6. Kidney Disorders

Urinary Stones ("urolithiasis")

= Small salt crystals (Calcium, phosphate, or uric acid) precipitate out of urine and stick together (stones).

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

Result

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

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

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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*.

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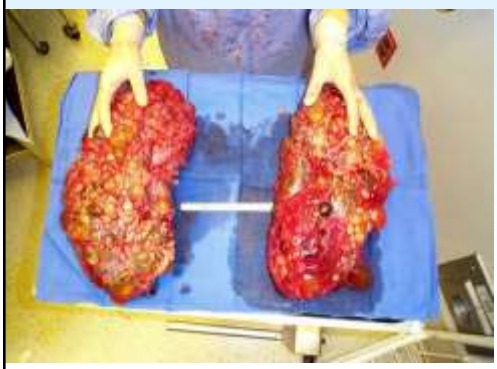
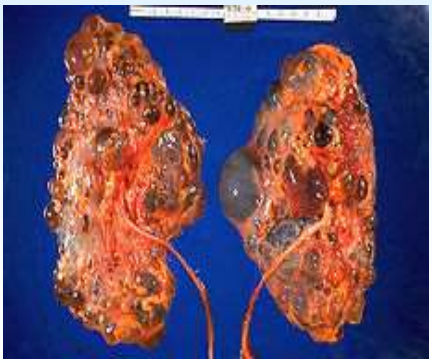
Polycystic kidney disease

= autosomal dominant inherited disorder in which fluid-filled cysts form within kidneys.

Result:

> Similar to kidney stones. Cysts cause pressure within kidneys. Kidneys become enlarged and pressure causes damage.





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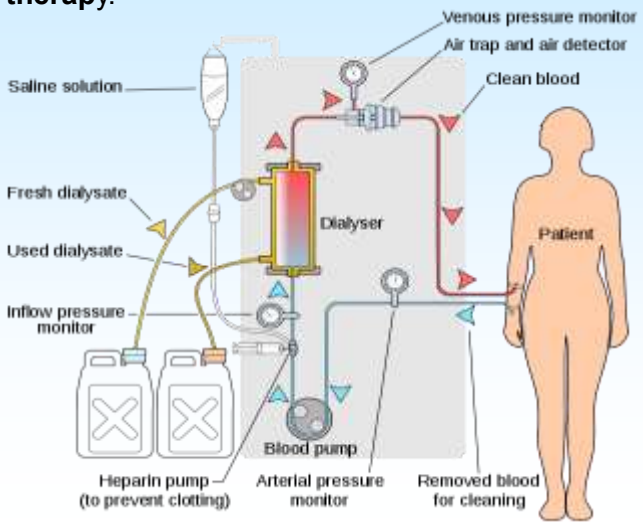
Dialysis

= 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**.



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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**.

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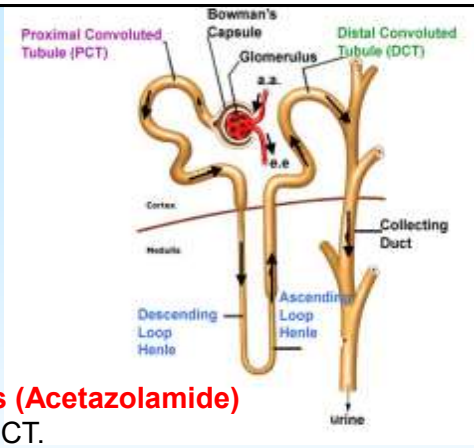
Diuretics



1. Carbonic anhydrase inhibitors (Acetazolamide)
> Decreases salt reabsorption at PCT.

2. Loop diuretics (e.g. furosemide or "Lasix")
> Decreases salt reabsorption at ascending loop of Henle.
(which will decrease water reabsorption at descending loop!)

3. Thiazides (hydrochlorothiazide)
> decreases salt reabsorption at DCT

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PHYSIOLOGY IN HEALTH AND DISEASE

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

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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 diuretics are the **loop diuretics**, 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).

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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 diuretics**. *Spironolactone* (such as *Aldactone*) diuretics block aldosterone action by competing for the aldosterone receptor proteins in the cells of the cortical collecting ducts. *Triamterene* (*Dyrenium*) is a potassium-sparing diuretic that acts more directly to block Na^+ reabsorption and K^+ secretion in the cortical collecting ducts. The diuretic actions of hydrochlorothiazide combined with the weaker diuretic but potassium-sparing actions of these drugs lower the blood volume, and thus the blood pressure, of people with hypertension.

[Interesting, but too much info (too complex) for this course]

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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**

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