Ch. 13: 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.

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**, & **Renin**)

2. **Blood pressure** – by regulating blood volume.

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


5. **Endocrine functions**:  
   - **Calcitrol** = increases Ca^{2+} absorbed from proximal convol. tubule  
   - **Erythropoietin** = stimulates RBCs production  
   - **Renin** = secreted by **JGA**, causes
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** = less than normal output
  - **Polyuria** = greater than normal output
  - **Anuria** = no urine produced

- **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.
**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 sympathetic stimulation and neurotransmitter epinephrine and α and β3 adrenergic receptors to allow bladder filling. Detrusor relaxes
  > Under parasympathetic stim. & neurotransmitter Acetylcholine (Ach) and muscarinic cholinergic receptors to allow urine into urethra (bladder empties). Detrusor contracts

**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 - smooth muscle
2. Distal (external) sphincter - skeletal muscle
2 Sets Urethral Sphincters:
1. **Proximal (internal) sphincter** – innervated by sacral & pelvic splanchnic nerves

**Smooth muscle, Autonomic motor control:**
> Parasympathetic w/ \(\text{ACH}\) neurotransmitter & **muscarinic cholinoergic** receptors
- contracts detrusor muscle (urine enters urethra)
- relaxes proximal urethral sphincter (urine passes through)

> Sympathetic w/ \(\text{Epinephrenergic}\) neurotransmitter & \(\alpha\) & \(\beta_3\) 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
- \(\text{ACH}\) neurotrans. & **nicotinic cholinoergic** 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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**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 kidneys**

   Untreated, can lead to kidney failure.
   > Symptoms – severe back pain.

2. **Overactive bladder** = disorder of overactive detrusor muscle. Feel frequent urge to urinate. More common in females. > 8 times / night.

   **Tx** =
   - **Oxybutynin** = **anticholinergic (ACH antagonist)**
   - **Mirabegron** = **B3 adrenergic agonist**
Bladder Problems (Continued)  

3. Urinary Incontinence (Clinical App Online)

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

Kegel exercise: contract pelvic floor muscles to strengthen them.

Friday Nov 8

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 catheter up urethra into bladder.
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

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.
Renal artery – brings arterial blood to kidneys to be filtered.
– BP in renal artery sensed by the ____________________________

**Afferent arteriole** = **takes arterial blood into the glomerulus to be**
Plasma, ions, glucose, small proteins, and other substances get filtered through glomerular pores. “Filtrate” then enters PCT.

**Efferent arteriole** = **is where large substances leave (are rejected by) the glomerulus.**
(RBCs, WBCs, platelets, and large molecules do not make it through glomerular pores.)

Becomes **vasa recta** and reabsorbs substances from loop of Henle.

**Peritubular capillaries** = **surround the nephron and are what receive retained substances from the tubules or excrete substances into the tubules.**

Abbreviations for nephron tubules:
- **PCT** = proximal convoluted tubule
- **Loop** = Loop of Henle
- **DCT** = distal convoluted tubule
Review

- Functions of renal system
  - blood volume, pressure, osmolarity
  - endocrine functions
- Urinary problems
  - infections
  - incontinence
- Anatomy of renal system
  - bladder, urethra, blood supply

4. Anatomy & Physiology of the Nephron

**Afferent arteriole** = brings arterial blood into glomerulus.

**Efferent arteriole** = where unfiltered material exits glomerulus.

Renal corpuscle = glomerulus surrounded by Bowman's capsule.

**3 Tubules:**
1. Proximal convoluted tubule (PCT)
2. Loop of Henle
3. Distal convoluted tubule (DCT)

**Collecting duct** = tube that transports urine from DCT to minor calyx.
Renal Corpuscle = Glomerulus + Bowman’s capsule:

A) Glomerulus = _______ receives and filters arterial blood _______.
> 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.

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.
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)
     - $\uparrow$ GFR, urine output $\uparrow$ (lose body water), blood volume $\downarrow$, BP $\downarrow$
   - B) IF blood volume & pressure too low: (< 80 mmHg) (dehydrated, blood loss, shock)
     - $\downarrow$ GFR $\downarrow$
     - urine output $\downarrow$ (retain water)
     - blood volume $\downarrow$, BP $\uparrow$

GFR measured by **creatinine 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.
Vocabulary

Excretion = removal of filtrate as urine, transported out of kidneys by ureter.

<table>
<thead>
<tr>
<th>Table 17.4</th>
<th>Effects of Filtration, Reabsorption, and Secretion on Renal Plasma Clearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>Filtration</td>
<td>A substance enters the glomerular filtrate.</td>
</tr>
<tr>
<td>Reabsorption</td>
<td>A substance is transported from the filtrate, through tubular cells, and into the blood.</td>
</tr>
<tr>
<td>Secretion</td>
<td>A substance is transported from peritubular blood, through tubular cells, and into the filtrate.</td>
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<tr>
<td>Effect on Renal Clearance</td>
<td>Some or all of a filtered substance may enter the urine and be “cleared” from the blood.</td>
</tr>
<tr>
<td></td>
<td>Reabsorption decreases the rate at which a substance is cleared; clearance rate is less than the glomerular filtration rate (GFR).</td>
</tr>
<tr>
<td></td>
<td>When a substance is secreted by the nephrons, its renal plasma clearance is greater than the GFR.</td>
</tr>
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</table>

After Glomerulus →

3 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
Proximal Convoluted Tubule

> First tubule after glomerulus

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

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<th>Things reabsorbed from filtrate:</th>
<th>Things secreted into filtrate</th>
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<tr>
<td>Water! (~65% of filtrate entering!)</td>
<td>Antibiotics, pharmaceuticals</td>
</tr>
<tr>
<td>Ions (Na⁺, Cl⁻, K⁺, Ca²⁺, HCO₃⁻)</td>
<td>H⁺</td>
</tr>
<tr>
<td>Glucose! (only place where reabsorbed)</td>
<td>Some diuretics</td>
</tr>
<tr>
<td>Small amino acids</td>
<td>Creatine</td>
</tr>
<tr>
<td></td>
<td>urea</td>
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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.
**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.

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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!
Distal Convoluted Tubule

> Permeable to salt IF aldosterone present.

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- **Addison’s Disease** – Insufficient Aldosterone
- **Conn’s Syndrome** (Hyper-aldosteronism)
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:**
- ADH secreted
- Water retained at collecting duct
- Urine output ↓, Blood volume & BP ↑
- Blood osmolarity ↓

**IF blood osmolarity ↓ below normal:**
- NO ADH secreted
- urine output ↑ (lose body water)
- Blood volume & BP ↓
- Blood osmolarity ↑

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?)
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?  
  \[ \uparrow \text{HR}, \text{vasoconstrict arteries} \]
> JGA senses it \( \xi \) secretes Renin
> What do kidneys do?

> \( \downarrow \text{GFR} \)

**What can happen if BP is too high?**

> What does medulla do? \( \downarrow \text{HR}, \text{vasodilate arteries} \)
> heart senses \( \xi \) secretes ANP
> What does heart do?

> \( \uparrow \text{GFR} \)

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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.
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.
**Dialysis**

Dialysis is the 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.
Diuretics

Physiology in Health & Disease Pg 353

Thiazides, loop diuretics, and carbonic anhydrase inhibitors block the receptor which allows reabsorption of 1 sodium and 2 chloride ions, and 1 potassium ion, SO they cause the excretion of both salt and potassium into the urine!

Click HERE for PDF on Effects of 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
   > decreases salt reabsorption at DCT

**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 osmolality 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...
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 ketoadidosis; 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% 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).
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.

**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 osmolality & change water reabsorption)
  - Renin-angiotensin-aldosterone system (influenced by BP and change salt reabsorption)

- **Urinary stones (urolithiasis)**
- **Polycystic kidney disease**
- **Dialysis**
- **Diuretics**