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 ________, ___________, & ___________)

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 __________ production
   - *Renin* = secreted by ______________, causes
Urinary Factoids:

— 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)
  - Less than this = *oliguria*
  - More than this = *polyuria*
  - Absence of urine = *anuria* (bad! ---kidney failure?)

— **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

### 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
  > Relaxes w/sympathetic stimulation to allow filling (but not emptying).

  > Contracts w/parasympathetic stim. to allow urine into urethra.

**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
2 Sets Urethral Sphincters:
1. **Proximal (internal) sphincter** – innervated by sacral & pelvic splanchnic nerves
   
   **Smooth muscle, Autonomic motor control:**
   > Parasympathetic w/ACh and muscarinic cholinergic receptors
     - contracts detrusor muscle (urine enters urethra)
     - relaxes proximal urethral sphincter (urine passes through)
   
   > Sympathetic w/ epinephrine and α-adrenergic receptors
     - relases detrusor muscle (bladder fills)
     - contracts proximal urethral sphincter (sphincter closed – no urine passes!)

2. **Distal (external) sphincter**
   – skeletal muscle, somatic (voluntary) motor control.
   - ACh & 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.

---

**Bladder Problems**

1. **Urinary tract infections (UTI’s)** – Bacteria enter urethra, cause inflammation & infection. More common in females.
   
   “urethritis” = inflamed urethra.
   
   “cystitis” = inflamed bladder.
   
   “pyelonephritis” = inflamed kidneys. BAD! 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** = beta adrenergic agonist
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

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 = where arterial blood enters the glomerulus. Plasma, ions, glucose, small proteins, and other substances get filtered through glomerular pores. “Filtrate” then enters PCT.

Efferent arteriole = receives non-filtered materials from glomerulus (i.e. RBCs, WBCs, platelets, and large molecules.

Becomes vasa recta and reabsorbs substances from loop of Henle.

Peritubular capillaries = surround the nephrons and secrete 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:

A) **Glomerulus** = network of capillaries that receive blood from afferent arteriole.

> 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** = cap around glomerulus, receives “filtrate” from glomerulus and sends it into proximal tubule.

---

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

2. A) IF blood volume & pressure too high: (over-hydrated)

> 

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

> 

<table>
<thead>
<tr>
<th>Regulation</th>
<th>Stimulus</th>
<th>Afferent Arteriole</th>
<th>GFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sympathetic nerves</td>
<td>Activation by baroreceptor reflex or by higher brain centers</td>
<td>Constricts</td>
<td>Decreases</td>
</tr>
<tr>
<td>Autoregulation</td>
<td>Decreased blood pressure</td>
<td>Dilates</td>
<td>No change</td>
</tr>
<tr>
<td>Autoregulation</td>
<td>Increased blood pressure</td>
<td>Constricts</td>
<td>No change</td>
</tr>
</tbody>
</table>

**“Emergency” = Extrinsic regulation (if BP ↓ 80 mmHg)**

**“Steady GFR” = Intrinsic regulation**

---

Autonomic Regulation of GFR:

**Intrinsic regulation**
- for BP between 80 – 160 mmHg

**Extrinsic (emergency) regulation**
- if BP ↓ 80 mmHg or
- ↑160 mmHg
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.

**Vocabulary**

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

<table>
<thead>
<tr>
<th>Things reabsorbed from filtrate:</th>
<th>Things secreted into filtrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water! (~65% of filtrate entering!)</td>
<td>Antibiotics, pharmaceuticals</td>
</tr>
<tr>
<td>Ions (Na+, Cl-, K+, Ca+2, 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>
</tr>
</tbody>
</table>
**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.

<table>
<thead>
<tr>
<th>Things reabsorbed from filtrate:</th>
<th>Things secreted into filtrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>WATER</td>
<td></td>
</tr>
</tbody>
</table>

**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.

<table>
<thead>
<tr>
<th>Things reabsorbed from filtrate:</th>
<th>Things secreted into filtrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na+, Cl-</td>
<td>H+, K+</td>
</tr>
<tr>
<td>urea</td>
<td></td>
</tr>
</tbody>
</table>
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.

<table>
<thead>
<tr>
<th>Things reabsorbed from filtrate:</th>
<th>Things secreted into filtrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na+, Cl-</td>
<td>H+, K+</td>
</tr>
<tr>
<td></td>
<td>urea</td>
</tr>
</tbody>
</table>
• **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:**

**IF blood osmolarity ↓ below normal:**
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

3 Ways: (Review of Ch 14 – Cardiac Output)
1. Baroreceptors
   > in aortic arch & carotid arteries send signal to medulla
   > in heart atria – respond to high BP by secreting _______________.

2. Hypothalamic ADH release – depends on blood osmolarity

3. Renin-Angiotensin-Aldosterone system – depends on low arterial blood pressure (at renal artery)
6. Kidney Disorders

Kidney Stones (“renal calculi”) – Clinical App Pg 337

= 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
(Clinical App Pg 566)

= 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.
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

---

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

• Polycystic kidney disease

• Diuretics