Urinary System - Overview:

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 25.1

Kidney
Ureter
Urinary bladder
Urethra

• Regulation of blood volume / blood pressure (e.g., renin)
• Regulation of red blood cell formation (i.e., erythropoietin)
• Metabolization of vitamin D to active form (Ca++ uptake)
• Glomerulogenesis during prolonged fasting

Removal of organic waste products from fluids (excretion)

• Discharge of waste products into the environment (elimination)

• Regulation of the volume / solute / pH of blood plasma

HOWEVER, THE KIDNEY AIN'T JUST FOR PEE'IN…

1) Gluconeogenesis during prolonged fasting

Functional Anatomy - Kidney:

Located in the superior lumbar region

"Bar of soap" 12 cm x 6 cm x 3 cm 150 g / kidney

Kidneys are located retroperitoneal

Layers of Supportive Tissue:

Renal fascia: Outer layer of dense fibrous connective tissue; anchors kidney in place

Perirenal fat capsule: Fatty mass surrounding kidney; cushions kidney against blows

Fibrous capsule: Transparent capsule on kidney; prevents infection of kidney from local tissues

Renal ptosis: Kidneys drop to lower position due to loss of perirenal fat

Blood Supply to Kidney:

• 1/4 of cardiac output delivered to kidneys
• 0.25 x 5 L / min = 1.25 L / min

Aorta
Renal artery
Segmental artery
Interlobar artery
Arcuate artery
Cortical radiate artery
Inferior vena cava
Portal vein
Ganuliferous capillaries
Proximal convoluted tube
Distal convoluted tubule
Coil of Henle
Renal pelvis
Major calyx
Minor calyx
Nerve supply to the kidney provided via the renal plexus (primarily sympathetic)

Pyelonephritis:
Inflammation of the kidney

Pyonephrosis:
Infection of the kidney

Polysplenic kidney disease (autosomal dominant condition)

Nephron:
Functional unit of the kidney (~ 1 million / kidney, active filtration)

• Filter ~ 150 L of blood plasma / day
• Produce ~ 1 – 1.5 L of urine / day
• 99% of filtrate returned to blood

Nephron Anatomy:

1) Glomerulus
• Networks of capillaries
• Tightly wound coil (7 surface area)

2) Renal tubule
• Location of filtrate (plasma-derived fluid)

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.5 / 25.7
Urinary System

**Functional Anatomy - Kidney:**

- **Renal Corpuscle** (site of filtration)
  - Glomerulus + Glomerular capsule
  - Different arterioles
  - Simple squamous epithelium
  - Podocyte (foot cell)
  - Fenestrated capillaries

**Renal Corpuscle** (site of filtration)

- **Afferent arteriole**
- **Efferent arteriole**
- **Fenestrated capillaries**
- **Glomerulus**
  - **Glomerular capsule**
- **Simple squamous epithelium**
- **Podocyte**
- **Foot processes**
- **Podocyte cell body**

**Filtration Membrane:**

- **Size selectivity (fenestrations / slits)**
- **Charge selectivity (basement membrane)**
  - **Glomerular mesangial cells**: Degrade macromolecules “hung up” in filtration membrane

**Proximal Convoluted Tubule (PCT):**

- **Similar in structure to the PCT**
  - **Thick Segment**
    - Simple cuboidal epithelium
    - Dense microvilli (↑ surface area)
    - Mitochondria, ↑ energy demands
    - Infolded basal membrane (↑ surface area)
  - **Thin Segment**
    - Simple squamous epithelium
    - Freely permeable to water

**Distal Convoluted Tubule (DCT) & Collecting Ducts:**

- **Similar in structure to the PCT**
  - **Principal cell**
  - **Intercalated cells** (acid-base balance)
  - **Collecting duct** (site of secretion / selective reabsorption)
  - **Smaller lumen, ↑ number of cells (compared to PCT)**
  - **Interlobular vein**
Glomerular Filtration:

Changes in the GFR can be brought about by changes in any of the Starling pressures:

\[
GFR = K_f [P_{GC} - P_{BS}] - n_{GC}
\]

- Produced by changes in the resistance of the afferent and efferent arterioles.

For ease of measure, creatinine (endogenous product) also commonly utilized.

Glomerular filtration rate is measured by the clearance of a glomerular marker.

What makes a good marker?

1. It must be freely filtered across the glomerular capillaries (no size / charge restrictions).
2. It cannot be reabsorbed or secreted by the renal tubules.
3. When infused, it cannot alter the GFR.

Clinical Application:

\[
GFR = \frac{[U]_{\text{Marker}} \times V}{[P]_{\text{Marker}}}
\]

- \([U]_{\text{Marker}}\) = Glomerular filtration rate (mg / min
- \([P]_{\text{Marker}}\) = urine concentration of marker (mg / mL)
- \(V\) = urine flow rate (ml / min)
**Glomerular Filtration:**

Renal blood flow, and thus glomerular filtration rate, is autoregulated over a wide range of mean arterial pressures.

\[ Q = \frac{\Delta P}{R} \]

Glomerular Filtration Rate (GFR) - the amount of filtrate formed per unit time

- Filtered load = Plasma concentration of X \( \times \) Plasma flow
- Excretion rate = Urine concentration of X \( \times \) Urine flow
- Reabsorption rate = Filtered load - Excretion rate

**Myogenic Hypothesis:**

- Increased arterial pressure triggers constriction of vascular smooth muscle
- \( \uparrow \) renal arterial pressure \( \rightarrow \) walls of afferent arteriole stretch
- \( \uparrow \) stretch-activated Ca\(^{2+}\) gates open
- \( \uparrow \) \( \text{Ca}^{2+} \) enters cell
- \( \text{Ca}^{2+} \) activates \( \alpha \)-adrenoceptors
- \( \uparrow \) afferent arteriole constriction; \( \uparrow \) resistance

**Tubuloglomerular Feedback:**

- Increased [solute] sensed in DCT; triggers constriction of vascular smooth muscle
- \( \uparrow \) renal arterial pressure \( \rightarrow \) \( \text{GFR} \)
- \( \downarrow \) solute / water load in DCT
- \( \text{Macula densa cells detect change; send signal} \)
- \( \uparrow \) sympathetic input to both arterioles
- \( \text{Afferent arteriole more susceptible than efferent arteriole} \)
- \( \downarrow \) GFR

**Sympathetic input = 1**

- Both afferent and efferent arterioles
- Sympathetic nerve fibers innervate both arterioles
- \( \alpha \)-adrenoceptors on afferent arterioles

**Urinary System:**

For renal autoregulation, it is believed that resistance is controlled primarily at the level of the afferent arteriole.

**Tubular Reabsorption:**

- Water and many solutes (e.g., Na\(^{+}\), Ca\(^{2+}\)) are reabsorbed from the filtrate into the peritubular capillaries via membrane transporters

**Glucose**

- Reabsorbed in proximal convoluted tubule
- Two-step process:
  1. \( \text{Na}^{+} \)-glucose co-transport
  2. Facilitated glucose transport

**Excretion of substances**

- Each of the above losses represents more than 10-fold the amount present in the entire extracellular fluid of the body.
**Tubular Reabsorption:**

A glucose titration curve depicts the relationship between plasma glucose concentration and glucose reabsorption.

**Things to Note:**
- As the plasma [glucose] increases, the filtered load increases linearly.
- All glucose can be reabsorbed up to plasma [glucose] of 200 mg/dL.

**Transport Maximum (Tm):** Point at which all transport proteins are fully engaged (saturated).

- Glucose Tm = 350 mg/dL

**Glucosuria:**
- Diabetes mellitus?
- During pregnancy?

**Solute and water reabsorption are coupled and are proportional to each other in the PCT – Isosmotic reabsorption:**

1. Na enters cell; water follows passively
2. Na actively pumped out of basolateral membrane; water follows passively
3. Isosmotic fluids collected in lateral intracellular space; high osmotic pressure in tubular capillary drives reabsorption

67% of solute absorbed in PCT
67% of water absorbed in PCT

**Sodium (Na+) Reabsorption:**

**Early PCT:**
- Active transport of Na+ drives system
- “Highest priority” reabsorptive work

**Late PCT:**
- Lumen-positive potential
- Na follows Cl down its [gradient] leaves (+) charges in filtrate

67% of solute absorbed in PCT
67% of water absorbed in PCT

**Sodium (Na+) Reabsorption:**

**Thick Ascending Limb:**
- Na moves freely in / out of the thin portions of the loop of Henle but there is no net reabsorption

**Isotonic Reabsorption:**

1. Na enters cell; water follows passively
2. Na actively pumped out of basolateral membrane; water follows passively
3. Isotonic fluids collected in lateral intracellular space; high osmotic pressure in tubular capillary drives reabsorption

67% of solute absorbed in PCT
67% of water absorbed in PCT

**Water is NOT reabsorbed with solutes in this region (diluting segment)**
Tubular Reabsorption:

**Sodium (Na+) Reabsorption**
Like the loop of Henle, the DCT and collecting duct exhibit load-dependent Na+ reabsorption.

**Tubular Secretion**

- A few substances (e.g., organic acids/bases) are secreted from peritubular capillary blood into tubular fluid by way of membrane transporters.

**Tubular Reabsorption / Secretion**

- Along with nutrients, the reabsorption / secretion of ions is an important component of nephron physiology.

**Potassium (K+) Reabsorption / Secretion**

- Potassium (K+) is:
  - Balance essential for excitable tissue function
  - Utilizes both reabsorption and secretion mechanisms for regulation

**Figures and Diagrams**

- Early Distal Tubule
- Late distal tubule / Collecting duct
- A PAH titration curve depicts the relationship between plasma PAH concentration and PAH secretion
- Things to Note:
  - As the plasma [PAH] increases, the filtered load increases linearly.
  - As with reabsorption, a transport maximum exists for PAH.
  - At [low] PAH, steep excretion rate; at [high] PAH, rate declines as Tm reached.

**Urinary System**

- Sodium (Na+) Reabsorption
- Potassium (K+) Reabsorption / Secretion

Along with nutrients, the reabsorption / secretion of ions is an important component of nephron physiology.

**Phosphate (HPO\(_4\)\(^{-}\))**:  
- Important ion for bone and as a urinary buffer for H\(^{+}\)  
- Only reabsorbed at PCT  
  
  Parathyroid hormone blocks reabsorption  
  
  \(\text{G-protein coupled system inhibits Na-phosphate co-transport leaving phosphate in tubule lumen}\)

**Psuedohypoparathyroidism**:  
- Although circulating levels of PTH are high, PTH cannot produce its phosphaturic effects due to renal cells being resistant to PTH action

**Calcium (Ca\(^{2+}\))**:  
- Important ion for bone and excitable tissue function  
- Pattern of reabsorption similar to sodium  
- Only 60% available for filtering  
  
\[180 \text{L/day} \times 5 \text{mEq/L} \times 0.6 = 540 \text{mEq/day}\]  

**Tubular Reabsorption / Secretion**: Along with nutrients, the reabsorption / secretion of ions is an important component of nephron physiology.

**Corticopapillary osmotic gradient**:  
- A gradient of osmolarity in the interstitial fluid of the kidney from the cortex to the papilla that allows the kidney to vary urine concentration / volume  
- What solutes contribute to the osmotic gradient?  
- What mechanisms deposit these solutes in the interstitial fluid?  
  
- 1) Countercurrent multiplication  
- 2) Urea recycling

**Regulation of Urine Volume / Concentration**:  
- The kidneys keep the solute load of body fluids constant, at about 300 mOsm

**Countercurrent Multiplication**:  
- A function of the loops of Henle, which deposit NaCl in the deeper regions of the medulla

**Things to Recall**:  
- 1) The thick, ascending limb of the loop of Henle reabsorbs NaCl  
  
\(\text{Na}^+ - \text{K}^+ - 2\text{Cl}^-\) cotransporter

- 2) The thick, ascending limb of the loop of Henle is impermeable to water

**Step 1**: NaCl reabsorbed from ascending loop  
- Descending limb equilibrates with interstitial fluid  

**Step 2**: New fluid (300 mOsm) enters descending limb from PCT  
- Equal volume displaced from ascending limb  
  
  - High-osmolarity fluid "pushed" down  
  - TUBULAR FLOW

**Tubular Reabsorption / Secretion**: Along with nutrients, the reabsorption / secretion of ions is an important component of nephron physiology.
Regulation of Urine Volume / Concentration:

The kidneys keep the solute load of body fluids constant, at about 300 mOsm

2) Urea Recycling

A function of the collecting ducts, which deposit urea in the deeper regions of the medulla

Urea enters the interstitial fluid via diffusion from the inner medullary collecting ducts and moves down gradient into ascending limb of Henlé via facilitated diffusion

~ 60 L

Regulation of Urine Volume / Concentration:

Formation of Concentrated Urine (~ 1200 mOsm)

1) The PCT pulls out solutes and water in equal proportions (~67%)

Remember: isosmotic reabsorption

2) The thick, ascending limb of the loop of Henlé actively reabsorbs NaCl (Na-K-2Cl cotransporter); cells impermeable to water

ADH increases activity of Na-K-2Cl cotransporters leading to enhanced single effect (e.g., steeper gradient)

3) In early DCT, NaCl reabsorbed (Na-K cotransporter); cells impermeable to water

Filtrate osmolarity reduced to ~ 90 mOsm

Regulation of Urine Volume / Concentration:

Dilute or concentration urine can be formed depending on the presence / absence of antidiuretic hormone (ADH)

Formation of Concentrated Urine (~ 1200 mOsm)

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Filtrate osmolarity reduced to ~ 90 mOsm

Regulation of Urine Volume / Concentration:

Dilute or concentration urine can be formed depending on the presence / absence of antidiuretic hormone (ADH)

4) In late DCT, the principle cells are permeable to water in the presence of ADH

Regulation of Urine Volume / Concentration:

Dilute or concentration urine can be formed depending on the presence / absence of antidiuretic hormone (ADH)

Formation of Dilute Urine (~ 75 mOsm)

1) The PCT pulls out solutes and water in equal proportions (~67%)

2) The thick, ascending limb of the loop of Henlé actively reabsorbs NaCl (Na-K-2Cl cotransporter); cells impermeable to water

ADH increases urea recycling in the inner medullary collecting duct via the insertion of urea UT1 transporters

3) In early DCT, NaCl reabsorbed (Na-K cotransporter); cells impermeable to water

4) Late DCT collecting ducts impermeable to water; limited NaCl reabsorbed

Limited urea recycled
Regulation of Urine Volume / Concentration:

**Diuretics** are chemicals that elevate rates of urination.

**Pharmacological Drugs:**
- Treat hypertension, edema

1) **Loop diuretics**
   - Block Na+ reabsorption in thick ascending loop of Henle
   - Most potent diuretic:
     - Furosemide

2) **Thiazide diuretics**
   - Block Na+ reabsorption in early distal convoluted tubule
   - Isoren

3) **K+ sparing diuretics**
   - Block Na+ reabsorption in late DCT / collecting ducts
   - Amiloride
   - Weak diuretic; Targets PCT
   - Weak diuretic; Blocks ADH release

**Costanzo (Physiology, 4th ed.)** – Figure 6.41

Pathophysiology:

**Conditions which affect ADH release / action can lead to abnormal urine flow rates**

**Inappropriate Formation of Dilute Urine**

- **Central Diabetes Insipidus:**
  - Circulating levels of ADH abnormally low
  - Cause:
    - Trauma / tumor
  - Treatment:
    - Drugs which block ADH activity (e.g., demeclocyline)

- **Syndrome of Inappropriate ADH (SIADH):**
  - Circulating levels of ADH abnormally high
  - Cause:
    - Trauma / tumor
  - Treatment:
    - Drugs which act as ADH analogues (e.g., DDAVP)

**Nephrogenic Diabetes Insipidus:**

- Circulating levels of ADH normal; principal cells of kidney unresponsive to hormone
- Cause:
  - Defect in 2nd messenger system (e.g., genetic)
- Treatment:
  - Thiazide diuretics; triggers ▲ water reabsorption in PCT

Physical Characteristics of Urine:

- **Color & Transparency**
  - Dilute = clear / pale yellow
  - Concentrated = deep yellow

- **Odor**
  - Fresh = slight odor
  - Old = ammonia-like odor

- **pH**
  - Acidic (pH ~ 6)

95% water

5% solutes

- Ions (e.g., Na+, K+, phosphates)

Micturition:

**Incontinence:**

The inability to voluntarily control micturition

- Urinary bladder filling stimulates bladder wall
- Different impulses from stretch receptors
- Simple micturition reflex
- Spinal cord
- Parasympathetic activity
- Promotes micturition by exciting all three spinal efferents

- Detrusor muscle contraction, internal urethral sphincter opens
- Bladder usually voided before 400 mL collects
- Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.22