The Urinary System

Waste Elimination
- Management of waste the responsibility of numerous processes and organs
  - Buffers, blood, liver, lungs, sudoriferous glands, GI and kidney
- The kidney primarily for excess water, ammonia, urea, uric acid, bilirubin, creatine, ions, and some toxins

Kidney Function
- Waste removal
- Blood composition (osmolarity) – balance of water and solutes at ~290 mOsm/L
- Blood ionic composition – Na⁺, K⁺, Ca²⁺, Cl⁻, HPO₄²⁻
- Blood volume
- Blood pressure - secretion of renin which interacts with angiotensinogen
  - Increased aldosterone → water reabsorption and blood volume
  - Increased vasoconstriction → increased BP
- Blood pH - H⁺ & HCO₃⁻ ions
- Hormone secretion
  - Parathyroid hormone stimulates calcitriol secretion → increase GI Ca²⁺ & HPO₄²⁻ absorption
  - Erythropoietin → more RBCs
- Manufactures glucose (gluconeogenesis) when fasting - deamination of glutamine

Kidney - External Anatomy
- Recognizable shape
- Retroperitoneal along with adrenal glands and ureters
- Located between T12-L3
- Three exterior layers that serve to protect and anchor kidneys
  - From inside out - renal capsule (dense irregular connective tissue), adipose capsule, and renal fascia
- Renal hilus

Kidney Shaped (graphic)
Location of Kidney - Frontal (graphic)
Location of Kidney – X-section (graphic)

Kidney - Internal Macrostructure
- Renal cortex including extensions (renal columns)
- Renal medulla
  - Renal pyramids alternating with renal columns
  - Papillary ducts & renal papillae
- Functional unit, the nephron, found in cortex and pyramids
• Calyces (major and minor)
• Renal pelvis

**Kidney – Internal Structure (graphic)**

**Nephron Organization**
• Renal corpuscle
• Proximal convoluted tubule
• Descending and ascending loop of Henle
• Distal convoluted tubule
• Collecting duct
• Papillary duct

**Nephron Structure (graphic)**

**Nephron Function**
• Renal corpuscle - glomerular filtration
• Renal tubule - tubular reabsorption and secretion

**Nephron – General Function (graphic)**

**Renal Blood Supply**
• Renal arteries - at rest, receive about 20% of cardiac output (1200 ml/min) - 0.5% of body mass
• Segmental artery → interlobar artery → arcuate artery → interlobular artery → afferent arterioles → glomerulus → efferent arteriole → peritubular capillary and or vasa recta → peritubular venule → interlobular vein → arcuate vein → interlobar vein → segmental vein → renal vein
• Vasodilation/constriction of afferent and efferent arterioles change vascular resistance
• Primary nerve supply from celiac ganglion of sympathetic NS
  – Largely vasomotor for regulating blood flow and vascular resistance

**Kidney Circulation (graphic)**

**Renal Corpuscle**
• Located in renal cortex
• Composed of glomerulus and glomerular (Bowman’s) capsule
• Capillaries surrounded by specialized cell (podocytes) layer (simple squamous)
  – Together - endothelial-capsular membrane (the filter)
• Outer parietal layer of capsule (also simple squamous)
• Membrane has several filtering layers
  – Endothelial fenestrations - blocks cells & platelets only
  – Basal lamina (glycoprotein fibers) - blocks large proteins
  – Slits between pedicels of podocytes - blocks mid-sized proteins (e.g. only 1% of albumin passes)
• Mesangial cells (contractile) among capillaries - regulate filtration surface area

**Renal Corpuscle (graphic)**
Renal Corpuscle - Microscopic (graphic)
Glomerular Structure (graphic)
Podocytes (graphic)
Filtration Membrane (graphic)
Renal Tubule
• Convoluted tubes in cortex
• Loop of Henle and collecting ducts in medulla
• About 80% of nephrons have a short loop of Henle with superficial renal corpuscle - cortical nephrons
• Remaining 20% have long loop of Henle and deep renal corpuscle - juxtamedullary nephrons (have vasa recta)
  – Include both thick and thin ascending limb of tubule
Cortical Nephron (graphic)
Juxtamedullary Nephron (graphic)
Histology of Renal Tubule
• Proximal convoluted tubule - cuboidal epithelium with microvilli
  – Reabsorption of 65% of water, and up to 100% of some solutes
• Descending loop of Henle and thin ascending portion - simple squamous epithelium
• Ascending thick portion of loop of Henle - simple cuboidal to columnar epithelium
• At junction of ascending and distal tubule - juxtaglomerular apparatus including:
  – Macula densa cells of tubule (monitor Na⁺ and Cl⁻)
  – Adjacent afferent arteriole surrounded by modified smooth muscle fibers - juxtaglomerular cells
• Distal tubule - cuboidal with few microvilli
• Collecting ducts (and last portion of DCT) - two cell types
  – Principal cells that respond to ADH and aldosterone
  – Intercalated cells with microvilli that secrete H⁺
• Papillary ducts - with simple columnar
Nephron Cell Types (graphic)
Renal Physiology
• Glomerular filtration
• Tubular reabsorption
• Tubular secretion
Glomerular Filtration
• 16-20% of plasma is filter as it passes through kidney (180 liters/48 gals per day (less for females) - all but a liter or two returned)
• Across endothelial-capsular membrane
• Directly related to state of mesangial cells and hydrostatic & osmotic pressure across membrane
– Glomerular blood hydrostatic pressure (GBHP) - about 55 mm Hg (higher than the usual 35)
– Capsular hydrostatic pressure (CHP) - about 15 mm Hg
– Blood colloid osmotic pressure (BCOP) - largely due to plasma proteins, at inlet: about 25 mm Hg, at outlet: about 35 mm Hg, average: 30 mm Hg
– Net filtration pressure (NFP)
  - NFP = GBHP - CHP – BCOP
– If filtration surface damaged by disease, plasma proteins lost, changes BCOP throughout body and results in edema

Net Filtration Pressure (graphic)

Glomerular Filtration Rate (GFR)
• Filtrate formed by both kidneys per minute
• Directly related to NFP
• Normal about 125 ml/min or 180 liters/day (less for females – 105ml/min)
• If too high, insufficient reabsorption
• If to low, insufficient excretion of wastes (anuria - less than 50 ml of urine/day)

GFR Regulation
• Regulation based on water volume and concentration of Na\(^+\) and Cl\(^-\)
• Autoregulation - maintains GFR through myogenic mechanism and tubuloglomerular feedback
  - Myogenic - as BP rises, smooth muscle stretch in afferent arterioles causes constriction, and vice versa as BP decreases - response in seconds
  - Tubuloglomerular feedback - JGA secretion of vasodilator (nitric oxide) is inhibited causing decreased flow in afferent arterioles in response to high levels of Na\(^+\), Cl\(^-\) and water in thick ascending portion (sensed by macula densa), and vice versa for low levels - slower response
• Hormonal regulation
  – Angiotensin II
    • Juxtaglomerular cells sense decreased stretch of afferent, also sympathetic stimulation
    • Renin secreted by juxtaglomerular cells
    • Initiates angiotensinogen - angiotensin II pathway
    • Causes vasoconstriction of afferent arterioles (dec GFR)
    • Also increases Na\(^+\)/H\(^+\) antiporters in PCT
    • Also increases secretion of aldosterone by adrenal cortex (increases Na\(^+\), Cl\(^-\) and water retention - inc in BP)
  – Atrial natriuretic peptide (ANP)
    • Produced by cells in the heart atria
    • Release stimulated by stretch of atrial walls
    • Increases water loss (diuresis) by relaxation of mesangial cells (inc GFR)
    • Decreases secretion of ADH and aldosterone
    • Decreases reabsorption of Na\(^+\) and water in PCT and CD
• Neural regulation
– Sympathetic innervation (neurotransmitter is norepi) of smooth muscle surrounding afferent and efferent arterioles (with $\alpha_1$ receptors) causing vasoconstriction (dec GFR)
– Enhanced vasoconstriction in afferents by release of epinephrine from adrenal medulla upon strong sympathetic response
– Reduces urine production and redirects blood flow

**Regulation of GFR (graphic)**

**Reabsorption**
- About 99% of filtrate reabsorbed
- Paracellular (about 50%) vs. transcellular reabsorption
- Solute by active (primary or secondary) or passive movement
  - $Na^+$ plays major role - sodium pumps on basolateral membrane, not apical
- Water by osmosis
- Proteins by pinocytosis
- Involves renal tubules and collecting ducts

**PCT Reabsorption**
- Epithelial cells with microvilli - effective transporters
- 100% of glucose & amino acids, 80-90% of $HCO_3^-$, 65% of water, $Na^+$, & $K^+$, 50% of $Cl^-$, varying % of $Ca^{2+}$, $Mg^{2+}$ & $HPO_4^{2-}$
- $Na^+$ reabsorption
  - Based on low concentration and negative charge in epithelial cells - $Na^+$ leakage channels present on apical side
  - Active $Na^+$ transport on opposite side into interstitial fluid (estimated 6% ATP use at rest)
  - Passive diffusion into peritubular capillaries
- Water follows - osmotic gradient created by $Na^+$ transport
- Increased concentration of remaining molecules in filtrate cause them to diffuse or respond to the movement of the positively charged $Na^+$
- $HCO_3^-$ reabsorption related to $H^+$ secretion (later)
- Glucose, amino acids, lactic acid, phosphate & sulfate reabsorbed into epithelial cells by $Na^+$ symporters - transported into interstitial fluid by facilitated diffusion
  - Concept of renal transport maximum (mg/min - normal 300 mg/min for glucose) and renal threshold (mg/ml in plasma - usually 200 mg/100ml for glucose)
  - glucosuria (glycosuria) results from exceeding limits - diabetes mellitus
- $HPO_4^{2-}$, $SO_4^{2-}$, amino acids and lactic acid reabsorbed much like glucose

**PCT Sodium Reabsorption (graphic)**

**Misc. PCT Reabsorption (graphic)**

**PCT Bicarbonate Reabsorption (graphic)**

**PCT Glucose Reabsorption (graphic)**
Loop of Henle Reabsorption

- Flow rate about 40-45 ml/min (down from 125 ml/min in PCT)
- Ionic reabsorption in thick ascending portion - 20-30% of filtered K⁺, Na⁺, & Ca²⁺, 10-20% HCO₃⁻, 35% Cl⁻
  - Symport with Na⁺ - two Cl⁻ & one K⁺ on apical surface
  - Na⁺ actively transported on basal surface and Cl⁻ follows based on charge via leakage channels
  - K⁺ may flow back into tubule via apical channels causing negative charge - draws cations in from tubule including K⁺, Na⁺, Ca²⁺, & Mg²⁺
- Water (about 15%) osmotically reabsorbed in descending portion (ascending portion impermeable to water)

LOH Sodium Reabsorption (graphic)
LOH Water Reabsorption (graphic)

DCT Reabsorption

- Flow rate about 25 ml/min
- Symport reabsorption of Na⁺ & Cl⁻
- Ca²⁺ reabsorption controlled by parathyroid hormone
- Little permeability to water but still 10-15% of H₂O reabsorbed
- By the end of DCT, less than 10% of filtrate remains (18 liters/day)

Collecting Duct Reabsorption

- Primarily Na⁺ and water (includes the last part of DCT)
- Na⁺ active transport on basolateral side of principal cells causing leakage on apical side (unlike previous regions with symporters)
  - Aldosterone contributes by stimulating Na⁺/K⁺ pump activity and number → increased Na⁺ & water reabsorption and K⁺ secretion
- Intercalated cells aid absorption of K⁺ and HCO₃⁻ (secretion of H⁺)
- Obligatory vs. facultative water reabsorption
- Facultative dependent on principal cell response to ADH and aldosterone
  - Osmoreceptors in hypothalamus sense increased osmolarity → posterior pituitary releases ADH → ADH increases insertion of integral protein water channels (aquaporin-2) on apical side → more water is reabsorbed
  - Increased sodium reabsorption → increased water reabsorption

Bicarbonate Absorption (graphic)

Tubular Secretion

- H⁺ for managing blood pH
- Ammonia (NH₃) or ammonium ion (NH₄⁺) for removal after amino acid catabolism
- K⁺ for maintaining appropriate concentration

Tubular Secretion of H⁺

- Secretion process linked with absorption of HCO₃⁻ and its manufacture - also contributes to blood pH
• PCT - CO₂ diffuses into PCT cells which convert it to H⁺ and HCO₃⁻ in presence of CA
  – Cells secrete H⁺ via an antiporter
  – HCO₃⁻ carried across basolateral surface by facilitated diffusion
  – Secreted H⁺ combines with filtered HCO₃⁻ → reverts back to CO₂ and H₂O
  → CO₂ diffuses into cells….thus filtered is reabsorbed along with more Na⁺
• CD - H⁺ secreted by active transport (proton pump) across apical side of intercalated cells
  – Capable of concentrating 1000 higher than blood
  – Excess HCO₃⁻ transported across basolateral surface via Cl⁻/HCO₃⁻ antiporter
  – Other intercalated cells have transport systems in opposite membranes thus secreting HCO₃⁻ and absorbing H⁺
  – H⁺ may be buffered by monohydrogen phosphate or ammonia within tubule

PCT Hydrogen Secretion (graphic)
CD Hydrogen Secretion (graphic)
Tubular Secretion of NH₃
• Ammonia (very poisonous) may be converted to urea (less poisonous) in liver
• PCT cells also produce more NH₃ in conversion to glutamine to glucose
• NH₃ + H⁺ → NH₄⁺ which can be substituted for H⁺ in apical Na⁺/H⁺ antiport in PCT
• Byproduct of glutamine conversion is HCO₃⁻ which enters blood
  – Process can aid in managing blood pH
Tubular Secretion of K⁺
• Nearly 100% of filtered K⁺ reabsorbed
• Homeostasis of K⁺ maintained by secretion in DCT and CD under the control of aldosterone (increases secretion) and high plasma concentration
• Principal cells secrete K⁺ based on Na⁺/K⁺ pump on basolateral side with leakage channels on apical side
  – Increases if Na⁺ high in tubule
CD Potassium Secretion (graphic)
Urine Concentration
• Varies depending on fluid intake while maintaining a constant blood volume
• Largely dependent on water reabsorption controlled by ADH in CD and portion of DCT
• Can be up to 4X more or less concentrated than blood plasma
• Dependent on renal medullary solute concentration gradient (Na⁺, Cl⁻, urea) formed by selective secretion and water permeability, and countercurrent exchange mechanism
Dilute Urine Production (graphic)
Concentrated Urine Production (graphic)
Summary of Kidney Function (graphic)
Hormonal Control

- Low blood volume/BP in afferent arterioles → renin secretion by juxtaglomerular cells → angiotensin II
  - Decreased GFR by vasoconstriction of afferents
  - Increased reabsorption of Na\(^+\), Cl\(^-\) and water due to enhanced activity of Na\(^+\)/H\(^+\) antiporters in PCT
  - Stimulates release of aldosterone → principal cells reabsorb more Na\(^+\) and Cl\(^-\) and thus more water reabsorption
  - Stimulates ADH → increased water permeability of apical membrane of principal cells in CD (facultative reabsorption) - other stimulating factors for ADH in hypothalamus

- Stretch of atrial wall → ANP secretion → reduces Na\(^+\) and water reabsorption in PCT and CD and inhibits secretion of ADH and aldosterone

Urinalysis

- Volume, appearance, odor, density (specific gravity), pH, solutes, abnormal solutes
- On your own

Level of Kidney Function

- Variety of screening tests
  - Blood urea nitrogen (BUN) - level of N as urea
  - Plasma creatinine - from creatine phosphate in skeletal muscle (ATP source)
  - Renal plasma clearance (ml/min) - rate depends on molecule used - UV/P (U=conc in urine in mg/ml, P=conc in plasma in mg/ml, V=urine flow rate in ml/min)
    - Dependent on filtration, absorption & secretion of molecule
    - Creatinine (largely filtered only) - quick GFR measure

Dialysis

- On your own

Ureters

- Kidney to bladder
- Arrangement of openings into bladder prevent backflow
- Three layers - inside to outside
  - Mucosa - transitional epithelium that produces mucous (protective)
  - Muscularis - peristaltic movement of urine along with hydrostatic pressure and gravity
  - Adventitia - areolar connective tissue, blood and nerve supply, also stabilizes position

Urinary Bladder Structure (graphic)

Urinary Bladder

- All three layers
  - Muscularis called detrusor – 3 layers…longitudinal, circular, longitudinal
Adventitia enclosed in visceral peritoneum
- 700-800 ml capacity
- Internal (smooth) and external (skeletal) urethral sphincters
- Voiding of urine - micturition - combined relaxation of internal and external sphincters
- Stretch receptors in wall sense filling causing parasympathetic relaxation of internal sphincter and contraction of bladder wall musculature - input and response called micturition reflex (a spinal reflex)
  - Cortex controls external sphincter

**Urethra**
- Mucosal layer - transition of epithelial type
  - transitional → pseudostratified → nonkeratinized stratified squamous
- Muscularis layer - simplified layering (circular only)

**Effects of Aging and Disorders**
- Kidneys shrinks in size - 260g @ 20yrs, 200 g @80yrs
- Renal blood flow and glomerular filtration drop by 50% between 40 & 70yrs
- Increased variety of dysfunction
  - Nephrogenic, cardiovascular, control or inflammation/infection
  - Affects blood volume/pressure, urine production, various solute concentrations
- Disorders on your own