Topics to Review

- Epithelial transport
- Transport across cell membranes
- Osmolarity and tonicity
- Capillary filtration
- pH and buffers
Functions of the Urinary System

• Regulation of extracellular fluid volume and BP
  – the kidneys regulate body water content
• Regulation of blood osmolarity
• Maintenance of ion balance
  – the kidneys regulate body Na\(^+\), K\(^+\) and Ca\(^{2+}\) levels
• Homeostatic regulation of pH
  – the kidneys regulate body H\(^+\) and HCO\(_3\)^{-}\) levels
• Excretion of wastes
  – the kidneys remove metabolic wastes and foreign substances
• Production of hormones
  – the kidneys secrete erythropoietin
  – enzymes that the kidneys produce regulate the production of hormones involved in blood pressure regulation and Ca\(^{2+}\) balance
Anatomy of the Urinary System

• Blood flows into the 2 kidneys by the renal arteries at the medially facing concave surface of the kidney called the hilus
  – some of the plasma is filtered into tubes of simple epithelium called renal tubules (the lumen of the renal tubules is outside the body) which removes metabolic wastes, toxins, drugs and substances in excess from the body
• Blood that has been filtered, leaves the 2 kidneys by the renal veins at the hilus
• The urine created by the renal tubules leaves each kidney via a hollow tube called the ureter which pass the urine to the urinary bladder
• As the bladder fills and stretches, reflexes coordinated by the parasympathetic NS cause the bladder to contract which voids the urine through the urethra
Renal Anatomy

• A coronal section shows 2 distinct layers: an outer (superficial) cortex and an inner (deep) medulla
  – these layers are formed by the organized arrangement of nephrons which combine the renal tubules and renal capillaries
  – 80% of the 1 million nephrons found in each kidney are called cortical nephrons since they are almost completely contained within the cortex
  – 20% of the nephrons dip down into the medulla are called juxtamedullary nephrons
Tubular Elements of the Kidney

• Each nephron begins in the cortex with a hollow bowl-like structure of simple squamous epithelial tissue called **Bowman’s capsule** that surrounds the a small ball shaped capillary bed called the **glomerulus**
  – the endothelium of the glomerulus is fused to the epithelium of Bowman’s capsule so that plasma filtering out of the capillaries passes directly into he lumen of the tubule
  – combination of the glomerulus and Bowman’s capsule is called the **renal corpuscle**

• After the plasma has been filtered into Bowman’s capsule it will flow through the remaining segments of the renal tubule where the composition of the tubular fluid will change into urine
Tubular Elements of the Kidney

- From Bowman’s capsule, the filtered fluid (filtrate) flows into the **proximal convoluted tubule**, also located in the cortex and then into the **loop of Henle**, a hairpin shaped segment that dips down (descending limb) into the medulla and then back up (ascending limb) into the cortex.
- Fluid from the ascending limb of the loop of Henle passes into the **distal tubule**.
- The distal tubule of up to 8 nephrons drains into a single larger tube called the **collecting duct**.
- Collecting ducts pass from the cortex through the medulla and drain urine into the **renal pelvis**.
- From the pelvis, the filtered and modified fluid (urine) flows into the **ureter**.
Vascular Elements of the Kidney

• The renal artery divides into smaller arteries and then into arterioles as they branch from the hilus to cortex

• From the arterioles the arrangement of blood vessels turns into a portal system
  – blood flows from the afferent arteriole into a ball-like network of capillaries called the glomerulus
  – blood flowing out of the glomerulus flows into the efferent arteriole and then into a second set of capillaries called the peritubular capillaries which surround the tubule segments of the nephron located in the cortex

• the peritubular capillaries of juxtamedullary nephrons surrounding the loop of Henle and collecting duct (medulla) are called vasa recta

• Finally the peritubular capillaries and vasa recta join to form venules and small veins conducting blood out of the kidney through the renal vein
Unique Features of the Nephron

• An advantage of having 2 separate capillaries allows one capillary to perform the process of filtration while the other capillary to performs absorption
  – the filtration of fluid and solutes out of the blood and into the lumen of the renal tubule occurs at the renal corpuscle
  – the (re)absorption of fluid and solutes from the tubule back into the blood occurs at the peritubular capillaries

• Notice how the nephron twists and folds back on itself so that the final part of the ascending limb of Henle passes between the afferent and efferent arteriole
  – this region is called the juxtaglomerular apparatus
  – the proximity of the ascending limb and the arterioles allows for paracrine communication which is a key feature of renal function
3 Basic Renal Functions

• **Glomerular filtration**
  – the movement of fluid from blood into the lumen of the nephron (takes place at the renal corpuscle)

• **Tubular reabsorption**
  – moving substances in the filtrate from the lumen of the tubule back into the blood flowing through peritubular capillaries

• **Tubular secretion**
  – selectively removes molecules from the blood flowing through the peritubular capillaries and adds them to the filtrate in the tubule lumen

• The amount of solutes and water excreted in urine is determined by the amount that is filtered + the amount that is secreted – the amount that is reabsorbed
Glomerular Filtration

- In the glomerular capillaries, the hydrostatic pressure **NEVER** falls below the osmotic pressure therefore fluid **ONLY** moves out of the glomerulus into Bowman’s capsule (never the opposite)
  - the rate that plasma exits the glomerulus and enters the Bowman’s capsule is called the glomerular filtration rate (GFR) and determines the rate of urine production by the kidneys
- 20% of the plasma that passes through the glomeruli (180 liters) is filtered into the renal tubules daily
- Once the filtrate passes into the lumen of the nephron it becomes part of the body’s external environment, thus anything that is filtered into the nephron is destined for removal in the urine unless it is reabsorbed back into the body
Over 99% of the water and solutes that are filtered into Bowman’s capsule is reabsorbed before it gets to the bladder. This leaves approximately 1.5 liters of urine to be collected in the bladder per day.
Tubular Reabsorption and Tubular Secretion

• As the filtrate moves through the segments of the renal tubule, the processes of reabsorption and secretion modify not only the composition and volume of the fluid within the tubule lumen converting it from what is essentially plasma into urine, but also modifies the composition and volume of plasma

• The epithelial cells of the renal tubule segments following Bowman’s capsule have transporting proteins (channels, primary and secondary active transporters) which selectively move water and solutes between the blood and the lumen of the tubule
Osmolarity of the Interstitial Fluid of the Kidneys

- The segments of the renal tubule and the renal vasculature is surrounded by interstitial fluid of the kidney which in the cortex has a total osmolarity (solute concentration) of 300 mOsm, which is isosmotic with plasma.
- However, the interstitial fluid of the medulla is hyperosmotic (more solutes) compared to plasma as it increases from 300 mOsm at the boundary between the cortex and medulla to a value of 1200 mOsm at its deepest point.
- The high amount of solutes in the interstitial fluid establish both solute diffusion and osmotic gradients between the interstitial fluid and the tubular fluid promoting tubular reabsorption.
Osmolarity of the Interstitial Fluid of the Kidneys
Proximal tubule (PT) (cortex)

- **Very** permeable to many **solutesc** AND **water** due to the presence of **solute transporting proteins** and **aquaporins** in the membranes of the epithelial cells
  - 70% of the glomerular filtrate is reabsorbed out of the renal tubule into the interstitial fluid and then into the **peritubular capillaries**
  - The reabsorption of solutes occurs mainly by primary and secondary active transport processes
    - All of the amino acids and glucose are reabsorbed
    - Most of the ions (Na⁺, K⁺, Cl⁻, HCO₃⁻, Ca²⁺...) are reabsorbed
  - The reabsorption of water follows the reabsorption of the solutes via **solvent drag** which keeps the solute concentration of the filtrate at 300 mOsm as it enters the descending limb of Henle (DLH)
Proximal Tubule

peritubular capillary

amino acids, glucose, lactate, Pi

K⁺, Na⁺

H₂O

Cl⁻

K⁺, H₂O

tubular fluid

glucose, amino acids, lactate, P_i, Cl⁻

K⁺, Na⁺

H₂O
Descending Limb of Henle (cortex → medulla)

- Permeable **ONLY** to water due to the presence of aquaporins and the absence of solute transporters in the membranes of the epithelial cells
- As the filtrate flows through the DLH, the higher solute concentration of the surrounding interstitial fluid creates an osmotic gradient that favors the diffusion of water out of the DLH into the interstitial fluid and then into the vasa recta
  - reabsorbs 15% of the water in the glomerular filtrate
  - the solute concentration of the filtrate increases to 1200 mOsm as it equilibrates with the surrounding interstitial fluid and enters the ascending limb of Henle (ALH)
Ascending Limb of Henle (medulla → cortex)

• Permeable **ONLY to solutes** (mainly $\text{Na}^+$, $\text{K}^+$ and $\text{Cl}^-$) due to the presence of **solute transporters** and the **absence** of aquaporins

• The osmolarity of the filtrate as it enters the ALH is 1200 mOsm
  – As the filtrate flows through the ALH, the lower solute concentration of the surrounding interstitial fluid creates a diffusion gradient that favors the diffusion of solutes out of the ALH into the interstitial fluid and then into the **vasa recta**
    • reabsorbs 25% of the $\text{Na}^+$, $\text{K}^+$ and $\text{Cl}^-$ in the glomerular filtrate
    • the solute concentration of the filtrate decreases as it equilibrates with the surrounding interstitial fluid
Ascending Limb of Henle

• In the thin portion of the ascending limb, the reabsorption of Na\(^+\), K\(^+\) and Cl\(^-\) is passive where solutes leave the filtrate by diffusion and enter the surrounding interstitial fluid.

• In the thick portion of the ascending limb, there is an aggressive reabsorption of Na\(^+\), K\(^+\) and Cl\(^-\) by active transport processes:
  – causes the filtrate to become dilute (hypotonic) compared to the surrounding interstitial fluid.
  • at the end of the ALH (cortex) the filtrate osmolarity is 100 mOsm.
Thick ALH

peritubular capillary

solutes

solutes

solutes

solutes

tubular fluid

Cl⁻
K⁺
Na⁺
K⁺

2 Cl⁻
K⁺
Na⁺
K⁺

solutes

solutes

solutes

solutes
Distal Tubule (DT) and Collecting Duct (CD)

- Permeable to **BOTH** solutes **AND** water due to the presence of solute transporting proteins and aquaporins in the membranes of the epithelial cells – the permeabilities can vary depending upon the levels of certain hormones in circulation that bind to receptors on/in the epithelial cells of the renal tubule
  - change the number and/or activity of the membrane transporting proteins
- As the filtrate flows through the DT and CD, the solute concentrations of the surrounding interstitial fluid creates osmotic and diffusion gradients that favors the diffusion of solutes and water out of these segments into the interstitial fluid and then into the peritubular capillaries and vasa recta
DT and CD

interstitial fluid

peritubular capillary/vasa recta

solutes

solutes

solutes

solutes

Na^+

K^+

H_2O

Na^+

K^+

H_2O

tubular fluid

solutes

solutes

solutes

solutes
Water, Sodium and Potassium Balance

- The kidneys function to regulate the water, Na\(^+\) and K\(^+\) amounts in the body
  - imbalances in these substances will impact blood pressure, membrane potentials, and cell volume
- The reabsorption of water and Na\(^+\) and the secretion of K\(^+\) at the DT and CD can be changed by certain hormones such as Antidiuretic Hormone (ADH), aldosterone, and Atrial Natriuretic Hormone (ANH)
  - the secretion rates of these hormones can either increase or decrease in response to an imbalance in the water, Na\(^+\) and K\(^+\) amounts in the body in order to reestablish homeostasis
Water Balance

- Water balance is achieved when input equals output.
- Changes in water input and output force the kidneys to alter urine volume in order to maintain water balance.
  - controlled by ADH
ADH Secretion

- Chemoreceptors in the hypothalamus monitor the ECF solute ($\text{Na}^+$) concentration
  - an increase in ECF osmolarity (negative water balance) stimulates ADH secretion from the posterior pituitary gland
    - caused by either an increase in solutes or a decrease in water in the ECF
  - a decrease in ECF osmolarity (positive water balance) inhibits ADH secretion from the posterior pituitary gland
    - caused by either a decrease in solutes or an increase in water in the ECF
- A decrease in blood pressure can also stimulate the secretion of ADH through a mechanism discussed later
ADH Action

- ADH targets the cells of the DT/CD
  - binding of ADH to its receptor in tubular cells stimulates the fusion of vesicles containing aquaporins with the apical membrane, increasing the water permeability and thus water reabsorption
  - decreases the ECF osmolarity

- ADH stimulates the thirst center in the brain
  - consumption of fluids decreases the ECF osmolarity
ADH

peritubular capillary/vasa recta

interstitial fluid

H₂O

ADH

H₂O

cAMP

H₂O

with ADH

H₂O

without ADH

H₂O

H₂O
Aldosterone Secretion

• Chemoreceptors in the adrenal cortex (zona glomerulosa) monitor the ECF solute ($\text{Na}^+$) concentration

• Is secreted from the cortex of the adrenal gland in response to any of the following stimuli:
  – *an increase in blood $K^+$*
  – a *decrease* in blood $\text{Na}^+$

• A decrease in blood pressure can also stimulate the secretion of aldosterone through a mechanism discussed later
Effects of K+ Imbalance

(a) Normokalemia
K+ concentrations in equilibrium
Equal diffusion into and out of cell
Normal resting membrane potential (RMP)

(b) Hyperkalemia
Elevated extracellular K+ concentration
Less diffusion of K+ out of cell
Elevated RMP (cells partially depolarized)
Cells more excitable

(c) Hypokalemia
Reduced extracellular K+ concentration
Greater diffusion of K+ out of cell
Reduced RMP (cells hyperpolarized)
Cells less excitable
Aldosterone Action

- Aldosterone targets the cells of the DT/CD
  - binding of aldosterone to its receptor in tubular cells stimulates the transcription and translation of:
    - the Na\(^+\), K\(^+\)-ATPase which is inserted into the basal membrane
    - Na\(^+\) channels which are inserted into the apical membrane
    - K\(^+\) channels which are inserted into the apical membrane
  - the simultaneous functioning of these 3 proteins:
    - increase Na\(^+\) reabsorption
    - increase K\(^+\) secretion
Atrial Natriuretic Hormone (ANH)

• An elevated blood pressure **increases** venous return which excessively **stretches** the wall of the right atrium – causes the secretion of Atrial Natriuretic Hormone from the cardiac myocytes of the right atrium

• ANH targets the cells of the CD – binding of ANH to its receptor in tubular cells inhibits Na\(^+\) channels responsible for Na\(^+\) reabsorption
  - **decreases** the reabsorption of H\(_2\)O as it follows the Na\(^+\) to the bladder – decreases blood volume and blood pressure

• ANH also causes **vasodilation** of arteries further decreasing blood pressure
ANH

interstitial fluid  vasa recta  tubular fluid

**without ANH**

**with ANH**
- The JGA provides a way for the kidneys to monitor and regulate blood pressure
Renal Control of Hypotension

• A decrease in systemic blood pressure will decrease the glomerular hydrostatic pressure which will decrease GFR
  – a decrease in GFR decreases the volume of filtrate in the renal tubule
    • decreases (slows down) the flow rate of the tubular fluid through the renal tubule
• The slow moving tubular fluid is in the thick ALH longer than normal resulting in an increased amount of Na\(^+\) that is actively transported out of the ALH
  – the reduced amount of Na\(^+\) remaining in the tubular fluid as it flows out of the ALH, stimulates the macula densa cells of the DT (chemoreception)
Renal Control of Hypotension

• The stimulated macula densa cells secrete a signaling molecule that diffuses to the afferent arteriole and stimulates the juxtaglomerular (JG) or granular cells of the afferent arteriole to secrete an enzyme called renin into circulation
  – renin catalyzes the conversion of a plasma protein called Angiotensinogen (inactive) to Angiotensin I (active)
    • Angiotensin I circulates through the capillaries of the lungs where the enzyme Angiotensin Converting Enzyme (ACE) converts it to Angiotensin II (more potent form)
Angiotensin II

- **Angiotensin II increases BP by stimulating:**
  - vasoconstriction of arterioles
  - thirst
    - consumption of water
      - increases plasma volume
    - the secretion of **aldosterone** from the adrenal cortex
      - increases Na\(^+\) retention at the kidneys
  - the secretion of **ADH** from the posterior pituitary
    - stimulates **vasoconstriction** of arteries
    - increases water retention at the kidneys

- **“ACE inhibitors”** are a class of drugs prescribed to individuals with hypertension
  - decrease Angiotensin II levels
    - decrease blood pressure
Renal Regulation of pH (acid/base balance)

• The kidneys respond to **acidosis** by:
  – *secreting* excess $H^+$ into the CD
    • decreases $H^+$ in the body
  – *reabsorbing* $HCO_3^-$ out of the CD into the *vasa recta*
    • increases $HCO_3^-$ in the body
  – *synthesizing* “new” $HCO_3^-$ which enters circulation
    • increasing $HCO_3^-$ in the body

• The kidneys respond to **alkalosis** by:
  – *reabsorbing* $H^+$
    • increases $H^+$ in the body
  – *decreasing* the reabsorption of $HCO_3^-$
    • decreases $HCO_3^-$ in the body
Control of Body Ca\(^{2+}\) and PO\(_4\(^{2-}\)\) Levels

• Parathyroid glands are 4 tiny glands embedded in the posterior aspect of the thyroid
• Functional cells are called chief (or principal) cells
  – synthesizes and secretes the hormone parathyroid hormone (PTH) following a decrease in plasma Ca\(^{2+}\) levels
• Thyroid gland (parafollicular cells) secrete calcitonin following an increase in plasma Ca\(^{2+}\) levels in children
  – targets the osteoblasts in bone and stimulates the synthesis of bone matrix
Parathyroid Glands

- Pharynx (posterior view)
- Thyroid gland
- Parathyroid glands
- Esophagus
- Trachea
PTH

• Targets:
  – **osteoclasts** in bone to
    • break down bone matrix
      – $\text{Ca}^{2+}$ and $\text{PO}_4^{2-}$ moves into plasma (increasing levels of both)
  – the **small intestine**
    • increase the absorption of calcium from the diet into plasma
  – **kidneys** to:
    • *increase* the $\text{Ca}^{2+}$ permeability in the DT/CD
      – increase $\text{Ca}^{2+}$ reabsorption
        • increase plasma $\text{Ca}^{2+}$ levels
    • *decrease* $\text{PO}_4^{2-}$ permeability in the DT/CD
      – decrease $\text{PO}_4^{2-}$ reabsorption
        • maintain plasma $\text{PO}_4^{2-}$ levels