Urinary Physiology
Urinary Section pages 9-17

Urine Formation

• Filtrate
  – Blood plasma minus most proteins
• Urine
  – <1% of total filtrate
  – Contains metabolic wastes and unneeded substances

Urine Formation
1. Glomerular filtration
2. Tubular reabsorption
   • Returns components to blood
   • Glucose, amino acids, water and salt
3. Tubular secretion
   • Reverse of reabsorption
   • Selective addition to urine
4. Water conservation

Glomerular Filtration
• Occurs at renal corpuscle
• Passive process driven by hydrostatic pressure
• Glomerulus is a very efficient filter
  • Permeable membrane
  • Water and small solutes pushed through filter
  • Large surface area
  • Higher blood pressure
Glomerular Filtration

• Filtration membrane
  – 3 components
    • Fenestrated capillary endothelium
    • Basement membrane
    • Podocytes
  – Allows passage of water and small solutes
    • Fenestrations prevent filtration of blood cells
    • Negatively charged basement membrane repels large anions

• Net Filtration Pressure (NFP)
  – The pressure responsible for filtrate formation
  \[ NFP = HP_g - (OP_g + HP_c) \]
Net Filtration Pressure

\[ \text{NFP} = \text{HP}_G - (\text{OP}_G + \text{HP}_C) \]

\[ = 55 \text{ mm Hg} - (30 \text{ mmHg} + 15 \text{ mmHg}) \]

\[ = 10 \text{ mmHg} \]

Glomerular Filtration

- Glomerular Filtration Rate (GFR)
  \[ = 125 \text{ ml/min} \]
  1800 liters of blood through kidneys/day

  \[ = 1200 \text{ ml/min} \approx 180 \text{ liters filtrate/day} \]

Glomerular Filtration

- Factors affecting GFR
  - Kidney disease
    - \( \downarrow \) blood osmotic pressure, \( \uparrow \) capsular osmotic pressure
  - Hemorrhage
    - \( \downarrow \) glomerular blood hydrostatic pressure
  - Hypotension
    - Glomerular blood hydrostatic pressure = capsule hydrostatic and blood osmotic pressure = filtration stops!
      - Termed renal suppression

- GFR is tightly controlled by two types of mechanisms

  - Intrinsic control (renal autoregulation)
    - Act locally within the kidney
  - Extrinsic controls
    - Nervous and endocrine mechanisms that maintain blood pressure and affect kidneys

Intrinsic Control

- Goal = Maintain a nearly constant GFR when MAP is in the range of 80–180 mm Hg
  - Renal autoregulation
    - Mechanisms that cause vasoconstriction of afferent arterioles in response to increased BP
    - Reduces glomerular flow to keep GFR the same

Extrinsic Controls

- Sympathetic nervous system
  - At rest
    - Renal blood vessels are dilated
    - Renal autoregulation mechanisms prevail
    - GFR maintained
  - Extreme stress
    - Norepinephrine and epinephrine released
    - Both cause constriction of afferent arterioles
      - Inhibits filtration
      - Shunts blood to other vital organs
Tubular Reabsorption

- 125 ml/min of filtrate produced
- Most of this fluid is reabsorbed
- A selective transepithelial process
- Includes active and passive process
- Most occurs in PCT

Tubular Reabsorption

- PCT
  - Site of most reabsorption
  - 65% of Na\(^+\) and water
  - All nutrients
  - Ions
  - Small proteins

Tubular Reabsorption

- Transcellular route
  - Luminal membranes of tubule cells
  - Cytosol of tubule cells
  - Basolateral membranes of tubule cells
  - Endothelium of peritubular capillaries

Tubular Reabsorption

- Paracellular route
  - Between cells
  - Limited to water movement and reabsorption of Ca\(^{2+}\), Mg\(^{2+}\), K\(^+\), and some Na\(^+\) in the PCT where tight junctions are leaky

Tubular Reabsorption

- Sodium
  - Most abundant cation in filtrate
  - Primary active transport out of the tubule cell by Na\(^+\)-K\(^+\) ATPase in the basolateral membrane
  - Na\(^+\) passes in through the luminal membrane by secondary active transport or facilitated diffusion mechanisms
At the basolateral membrane, $\text{Na}^+$ is pumped into the interstitial space by the $\text{Na}^+\text{-K}^+$ ATPase. Active $\text{Na}^+$ transport creates concentration gradients that drive:

1. "Downhill" $\text{Na}^+$ entry at the luminal membrane.
2. Reabsorption of water by osmosis. Water reabsorption increases the concentration of the solutes that are left behind. These solutes can then be reabsorbed as they move down their concentration gradients.
3. Reabsorption of organic nutrients and certain ions by cotransport at the luminal membrane.
4. Lipid-soluble substances diffuse by the transcellular route.
5. $\text{Cl}^-$ (and other anions), $\text{K}^+$, and urea diffuse by the paracellular route.

Tubular Reabsorption

- **Sodium**
  - Low hydrostatic pressure and high osmotic pressure in the peritubular capillaries
  - Promotes bulk flow of water and solutes (including $\text{Na}^+$)

Tubular Maximum

- Transport maximum ($T_m$) reflects the number of carriers in the renal tubules available.
- When the carriers are saturated, excess of that substance is excreted.
- Example: too much glucose in the blood entering glomerulus will cause glucosuria.

Tubular Reabsorption

- Reabsorption of nutrients, water and ions
  - Blood becomes hypertonic to filtrate
  - Water is reabsorbed by osmosis
  - Cations and fat-soluble substances follow by diffusion.

Tubular Secretion

- Reabsorption in reverse
  - $\text{K}^+$, $\text{H}^+$, $\text{NH}_4^+$, creatinine and organic acids move from peritubular capillaries or tubule cells into filtrate.
  - Involves active transport since no concentration gradients in this case.
**Tubular Secretion**

- **Principle effects**
  - Rids body of:
    - Foreign substances (penicillin and other drugs)
    - Nitrogenous wastes
    - Excess K⁺
  - Controls blood pH:
    - Altering amounts of $\text{H}^+$ or $\text{HCO}_3^-$ in urine

**Variations in Urine Formation**

- Composition varies
  - Fluid volume
  - Solute concentration

**Variations in Urine Formation**

- Water intake must equal water loss
  - Kidney regulates water loss by producing:
    - Hypotonic urine (dilute)
    - Hypertonic urine (concentrated)

**Countercurrent Mechanism**

- Role of countercurrent mechanisms
  - Establish and maintain an osmotic gradient
  - Creates hypertonic interstitial fluid within kidney medulla
  - Hypertonic interstitial fluid allows the kidneys to vary urine concentration
Formation of Concentrated Urine

- Depends on the medullary osmotic gradient and the ability to alter permeability of the collecting tubules
  - ↑ osmolality of extracellular fluid (also ↓ plasma volume)
  - ↑ ADH release
  - ↑ aquaporins in collecting duct
  - ↑ H₂O reabsorption in collecting duct
  - Small volume of concentrated urine

Formation of Dilute Urine

- Filtrate is diluted in the ascending Loop of Henle
- In the absence of ADH, dilute filtrate continues into the renal pelvis as dilute urine
  - ↓ osmolality of extracellular fluid
  - ↓ ADH release
  - ↓ aquaporins in collecting duct
  - ↓ H₂O reabsorption in collecting duct
  - Large volume of dilute urine

Acid-Base Balance

- pH affects all functional proteins and biochemical reactions in the body
  - Regulation prevents changes in body’s internal environment
- Alkalosis or alkalemia: arterial blood pH > 7.45
- Acidosis or acidemia: arterial pH < 7.35

Acid-Base Balance

- Concentration of hydrogen ions is regulated by
  1. Chemical buffer systems in blood
     - Rapid, first line of defense
  2. Brainstem respiratory centers
     - Acts within 1–3 minutes
  3. Renal mechanisms
     - Most potent
     - Requires hours to days to affect pH changes
Acid-Base Balance

- **Blood**
  - $\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \text{H}^+$

- **Lungs**
  - Regulate carbonic acid levels by $\text{CO}_2$ manipulation

- **Kidneys**
  - Selectively secrete and reabsorb to maintain pH

Acid-Base Balance

- **Most important renal mechanisms:**
  - Conserving (reabsorbing) $\text{HCO}_3^-$
  - Excreting $\text{HCO}_3^-$
  - Secretion of $\text{H}^+$
    - $\text{H}^+$ secretion occurs in the PCT and in collecting tubules

Acid-Base Balance

- **Examples**
  - **Respiratory Acidosis**
    - Lungs are unable to eliminate $\text{CO}_2$ adequately
    - Kidneys reabsorb $\text{HCO}_3^-$, secrete $\text{H}^+$ (and $\text{NH}_4^+$)
  - **Respiratory Alkalosis**
    - $\text{CO}_2$ levels are low
    - Kidneys secrete $\text{HCO}_3^-$, retain $\text{H}^+$ (and $\text{NH}_4^+$)

Variations in Blood Pressure

- **Activity of kidney related to variations in blood pressure**
  - Blood pressure and blood volume are related
  - Blood volume is controlled by
    - Solute concentration
    - Water regulation

Variations in Blood Pressure

- **Renal mechanisms influencing blood pressure**
  - ADH
    - Water
  - Renin-angiotensin mechanism
    - Sodium
    - Potassium
Antidiuretic Hormone (ADH)

- Plasma osmolarity
  - Increases (what could cause this?)
    - Osmoreceptors stimulated
    - Thirst & ADH secretion
    - Water reabsorption (decreased urine output)
    - Increased blood volume
    - Increased blood pressure

Aldosterone

- Produced in adrenal cortex in response to...
  - Low blood volume
  - Low blood pressure
  - Low plasma Na⁺
  - High plasma K⁺
  - Stimulates K⁺ secretion and Na⁺ reabsorption
  - Changes in plasma sodium levels affect...
    - Plasma volume
    - Blood pressure

Aldosterone

- Regulation of sodium balance
  - Na⁺ reabsorption
    - 65% is reabsorbed in the proximal tubules
    - 25% is reclaimed in the Loops of Henle
  - Aldosterone causes active reabsorption of remaining Na⁺ in DCT and collecting ducts
  - Water follows Na⁺
  - How would this affect blood volume and blood pressure?

Aldosterone

- Renin-angiotensin mechanism is the main trigger for aldosterone release
  - Granular cells of JGA secrete renin in response to
    - Sympathetic nervous system stimulation
    - ↓ Filtrate osmolality (decreased sodium)
    - ↓ Stretch (due to ↓ blood pressure)

Aldosterone

- Renin catalyzes the production of angiotensin II
  - Prompts aldosterone release from the adrenal cortex
    - Targets cells of DCT and collecting ducts
    - Initiates sodium reabsorption
  - Causes systemic vasoconstriction
  - Effect on BP?
Blood Pressure Control

- 3 main mechanisms
  - Renin-angiotensin system
  - Neural regulation (sympathetic control)
  - ADH release

Factors Affecting Urine Volume

- Increased temperature
  - Increases vasodilation and perspiration
  - Decreases blood flow to kidneys
- Decreased temperature
  - Increases blood flow to kidneys

Diuretics

- Chemicals that increase urine output
  - Osmotic diuretics
    - Substances not reabsorbed
      - Glucose in a diabetic patient
  - ADH inhibitors
    - Alcohol and water
  - Substances that inhibit Na⁺ reabsorption
    - Caffeine, thiazides (class of medications), loop diuretics (inhibit Na⁺-K⁺-Cl⁻ symport proteins)
  - Potassium levels are affected by some diuretics
    - Can be extremely dangerous

Factors Affecting Urine Output

- ↑ blood pressure
- ↑ blood solute concentration
- ↓ plasma proteins
- Psychological factors