Physiology 12

Kidney and Fluid regulation

Guyton Ch 20, 21, 22, 23

Roles of the Kidney

- Regulation of body fluid osmolarity and electrolytes
- Regulation of acid-base balance (pH)
- Excretion of natural wastes and foreign chemicals
- Regulation of arterial pressure
- Secretion of hormones (Epo)
- Gluconeogenesis

Renal Physiology

The Nephron and GFR

- Kidney Gross Anatomy
- The Nephron
- Glomerular Filtration Rate (GFR)
- Regulation of GFR
TABLE 21.1 Filterability of Substances by Glomerular Capillaries
Decreases with Increasing Molecular Weight

<table>
<thead>
<tr>
<th>Substance</th>
<th>Molecular Weight</th>
<th>Filterability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>18</td>
<td>1.0</td>
</tr>
<tr>
<td>Sodium</td>
<td>23</td>
<td>1.0</td>
</tr>
<tr>
<td>Glucose</td>
<td>180</td>
<td>1.0</td>
</tr>
<tr>
<td>Inulin</td>
<td>5,500</td>
<td>1.0</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>17,000</td>
<td>0.75</td>
</tr>
<tr>
<td>Albumin</td>
<td>69,000</td>
<td>0.005</td>
</tr>
</tbody>
</table>
Glomerular Filtration Rate (GFR)

- Glomerular capillaries have higher filter rate than other capillaries
  - Due to higher hydrostatic pressure and leakier capillaries
- GFR = 125 ml/min = 180 L/day
- Filtered fraction = GFR/Renal plasma flow = 20%

Glomerular filtration

Favoring filtration:
- Glomerular capillary blood pressure ($P_{GC}$): 60 mmHg
- Fluid pressure in Bowman's space ($P_{B}$): 15 mmHg
- Osmotic force due to protein in plasma ($π_{GC}$): 20 mmHg
- Net glomerular filtration pressure = $P_{GC} - P_{B} - π_{GC}$: 16 mmHg

Figure 21-7:

$P_{Net}$ = $P_{G}$ - $P_{B}$ - $π_{G}$

Net filtration pressure (10 mmHg)

Gluomeral Hydrostatic Pressure (60 mm Hg)

Gluomeral Colloid Osmotic Pressure (32 mm Hg)

Bowman's Capillary Pressure (18 mm Hg)
Influences on GFR

\[ GFR = K_f \times P_{Net} \]

- \( K_f \) = leakiness of capillaries
- \( P_{Net} \) = net hydrostatic pressure = \( P_G - P_B - \pi_G \)
- \( K_f \) of glomerulus is 400-fold higher than \( K_f \) of any other capillaries

Capillary Pressure (out) = 60 mmHg
Bowmans Pressure (in) = 18 mmHg
Plasma Colloidal (in) = 32 mmHg
Bowman’s Colloidal (out) = 0 mmHg

10 mmHg outward pressure

\( \uparrow \) Afferent Constriction = \( \downarrow \) Filtration
↑ Efferent Constriction = ↑ Filtration

GFR Increases with:
- Increased glomerular blood flow
- Decreased afferent arteriolar resistance
- Increased efferent arteriolar resistance
- Sympathetic stimulation (extreme situations only) lowers GFR
  - NE and Epi lower GFR

Autoregulation of GFR
- GFR is relatively constant over arterial BPs of 80-170 mm Hg
- Persists in isolated kidney
  - Independent of nervous system
- No autoregulation would create 46 liters/day of urine if BP = 125 mm Hg
  - = 6 liters/day with autoregulation
Autoregulation of GFR

- Mediated by Tubuloglomerular Feedback
- Low NaCl (flow) at Macula Densa:
  - Lowers afferent arteriolar resistance (?)
  - Raises efferent arteriolar resistance (AII)
- Macula Densa also regulates renal BP via renin-angiotensin-aldosterone
Renal Physiology
Filtration and Reabsorption

- 1\textsuperscript{st} and 2\textsuperscript{nd} Active Transport
  - Passive diffusion of Cl, urea, water
- Saturable reabsorption of glucose & AAs
- Tour of reabsorption and secretion along the tubule
- Renal Clearance

Two Paths for Reabsorption

![Diagram showing two paths for reabsorption](image-url)
Secondary Active Transport

Glucose and Amino Acids - Active Reabsorption in Proximal Tubule
Secondary Active Transport (Counter Transport)

H⁺ Secretion

Filtration

\[ \text{Filtration} = P_S \times \text{GFR}, \text{ where } P_S \text{ is the plasma concentration of substance } S \]

This represents the tubular load or filtered load that must be handled.

Units: mg/ml x ml/min = mg/min

\[ P_{\text{Glucose}} \times \text{GFR} = 0.9 \text{ mg/ml} \times 125 \text{ ml/min} = 112 \text{ mg/min} \]
Figure 21

**Glucose Transport is Saturable: Diabetes mellitus**

\[ P_{\text{Glucose}} \times GFR = 3.2 \text{ mg/ml} \times 125 \text{ ml/min} = 400 \text{ mg/min} \]

**Processes at Proximal Tubule**

- Basolateral
- Apical
- Reabsorption
- Secretion
- \( \text{Na}^+ \), \( \text{K}^+ \), \( \text{HCO}_3^- \), \( \text{H}^+ \), amino acids
- \( \text{PAH, many drugs} \)

**Processes at Thin Loop of Henle**

- \( \text{NaCl} \rightarrow 20\% \leftarrow \text{H}_2\text{O} \)

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**Diabetes mellitus**

\[ P_{\text{Glucose}} \times GFR = 3.2 \text{ mg/ml} \times 125 \text{ ml/min} = 400 \text{ mg/min} \]
Processes at Thick Loop of Henle

- Increases by Aldosterone
- Blocked by Lasix

Processes at Early Distal Tubule

- Variable %
- Hypo-osmotic
- Blocked by Amiloride
- Increases by Aldosterone

Calcium Homeostasis

- 90% dietary Ca excreted in feces, 10% in urine
- Low [Ca] in plasma causes parathyroid cells to secrete PTH
  - ↑Ca reabsorption from distal tubule
  - ↑Ca reabsorption from intestine
  - ↑Release of Ca stored in bone
- Can eventually strip bone of Ca supply
Potassium Homeostasis

- Most K⁺ is inside cells (140 mM), not outside (4.2 mM)
- ↑ plasma [K⁺] causes ↑ K⁺ secretion from principal cells:
  - Direct ↑ Na/K pump
  - ↑ Aldosterone secretion => ↑ Na/K pump

Processes at Late Distal Tubule and Collecting Duct

- 90% of cells: Principal cells
- 10% of cells: Intercalated cells

Acid-Base Homeostasis

- Diet usually generates an excess of acid
- Most HCO₃⁻ is reabsorbed by PT (85%), remainder by TAL and CD
- Controlled by tubule cells, which sense pH and [CO₂]
  - Secrete more H⁺ if pH too low
  - Secrete less H⁺ if pH too high
Acid-Base Homeostasis

- Excess H⁺ is secreted by Intercalated Cells in DT and CD
  - Urinary H⁺ is buffered by phosphate and ammonia so that pH ≥ 4.5

Relative Concentrations of Substances along Tubule

Glucose & AAs

Inulin
Renal Clearance

Renal Clearance (C_S) is the volume of plasma completely cleared of a substance (S) per minute.
- Units are ml/min
- \( C_S = (U_S \times V)/P_S \)
  - \( U_S \) is [S] in urine, \( V \) is urine flow rate, \( P_S \) is [S] in plasma

Filtered-Only substances (no secretion or reabsorption) have \( C_S = GFR \)
- Example: Inulin

Secreted substances have \( C_S > GFR \)
- Example: PAH

Reabsorbed substances have \( C_S < GFR \)
- Example: glucose

Renal Clearance

Renal clearance of inulin allows clinical determination of GFR
- \( GFR = (U_I \times V)/P_I \)

PAH is 90% secreted. Renal clearance of PAH allows clinical determination of Renal Plasma Flow
- \( RPF = (U_{PAH} \times V)/(P_{PAH} \times 0.9) \)
Renal Physiology: Renal Exchange Mechanisms

Excrete excess solutes
And/or
Concentrating the Urine

Create a very high osmotic pressure in the interstitial fluid

• Created by active transport of ions.
• Increase the interstitial fluid Osmolarity.
Create a very high osmotic pressure in the interstitial fluid

- Created by active transport of ions.
- Increase the interstitial fluid Osmolarity.
- Arteriole and Capillary system transports ions to medullary areas of the kidney.
Regulation of Renal Output and Cardio-vascular Volume Control

Germann Ch 18
Hormonal Control of Renal Output and Cardiovascular Pressure

Three main systems:
- Renin-Angiotension System
- Aldosterone
- Antidiuretic Hormone

Structure of Juxtaglomerular Apparatus

Low glomerular filtration rate, excess in Na+ and Cl- reabsorption, decreased ion concentration in the filtrate.

Renin-angiotensin system

Linier Secretes angiotensinogen
Kidney Secretes renin
Adrenal cortex Secretes aldosterone

Angiotensinogen ---- Angiotensin I ---- Angiotensin II Aldosterone
Renin-Angiotension System:

• Act on vascular system (directly) to increase total peripheral resistance

• Act on the Kidney tubule system to increase retention of salts and water. (vasoconstriction of afferent arteriole and peritubular capillaries)

• Stimulation of Aldosterone System.
Antidiuretic Hormone
Regulation of Urine Secretion and Body Fluids

Anteroventral Border of the Third Ventricle (AV3V Nucleus of the Hypothalamus)

↑ extracellular fluid osmolarity - ↑ ADH Secretion

Induce thirst
ADH effects on the body

• Vasconstriction

• Stimulate reabsorption of Water from the Distal Convoluted Tubule and Collecting Ducts

• Binds to receptors on the basolateral membrane of the epithelial cells.

• Initiates a second (intracellular) messenger (cAMP)

• Cause the fusion of vesicles (containing pores) to the luminal membrane.

• Water rushes from the lumen into the cell and into the interstitium.
Metabolic Acidosis and Alkalosis

Abnormalities of Acid-Base balance besides those caused by excess or insufficient carbon dioxide in the body fluids

Effects of: Metabolic Acidosis

Signs or Symptoms -
• Depression of the Central Nervous System (< pH 7.0)
• Increased respiratory rate and depth. (H+)

Causes -
• Diarrhea - excess loss of sodium bicarbonate
• Uremia - failure of kidney filtration of H+
• Diabetes Mellitus - excess production of glucose based acids (acetoacetic acid)

Effects of: Metabolic Alkalosis

Signs or Symptoms -
• Overexcitability of the Central Nervous System (muscle tetany)

Causes -
• Excessive Ingestion of Alkaline Drugs
• Excessive Vomiting (loss of Cl-)
• Excess Aldosterone (reabsorption of Na+, release of H+)
Hydrogen Ion Regulation

Hydrogen Ion buffer system

Carbonic Anhydrase

\[ \text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \text{H}^+ \]
Take home message

- Kidneys are homeostatic regulators of the body’s Hydrogen Ion concentration (pH)
- Kidneys maintain balance by regulating plasma bicarbonate concentration

Kidneys and the Renal System are important for both short and long-term control of body fluid levels. By regulating these fluid levels the Renal system will work in conjunction with the Cardiovascular system to maintain blood pressure.
Urea Secretion

~ 30 grams daily

Factors determining excretion:

- Concentration in Plasma
- Glomerular Filtration Rate

Micturition