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Chapter 17 Outline

- Structure and Function of the Kidney
- Glomerular Filtration
- Reabsorption of Salt and Water
- Renal Plasma Clearance
- Renal Control of Electrolyte and Acid-Base Balance
- Clinical Applications

Kidney Function

- Is to regulate plasma and interstitial fluid by formation of urine
- In process of urine formation, kidneys regulate:
  - Volume of blood plasma, which contributes to BP
  - Waste products in plasma
  - Concentration of electrolytes
    - Including Na⁺, K⁺, HCO₃⁻ and others
  - Plasma pH

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Gross Structure of the Urinary System

Paired kidneys are on either side of vertebral column below diaphragm.
- About size of fist
- Urine flows from kidneys into ureters which empty into bladder.
- Urethra drains urine from bladder.

Structure of Kidney
- Cortex contains many capillaries and outer parts of nephrons.
- Medulla consists of renal pyramids separated by renal columns.
- Pyramid contains minor calyces which unite to form a major calyx.
Structure of Kidney

- Major calyces join to form renal pelvis which collects urine
- Conducts urine to ureters which empty into bladder

Microscopic Structure of the Kidney

Renal Blood Vessels

- Blood enters kidney through **renal artery**
  - Which divides into **interlobar arteries**
    - That divide into **arcuate arteries** that give rise to **interlobular arteries**
  - Interlobular arteries give rise to **afferent arterioles** which supply **glomeruli**
  - Glomeruli are mass of capillaries inside glomerular capsule that gives rise to filtrate that enters nephron tubule
  - **Efferent arteriole** drains glomerulus and delivers that blood to **peritubular capillaries** (**vasa recta**)
  - Blood from peritubular capillaries enters interlobular veins
Summary of Blood Vessels Supplying the Kidney

- Aorta
- Renal artery
- Segmental artery
- Interlobar artery
- Arcuate artery
- Cortical radiate artery
- Afferent arteriole
- Glomerulus (capillaries)
- Nephron-associated blood vessels (see Figure 24.9)
- Efferent arteriole
- Peritubular capillaries and vasa recta
- Interlobar vein
- Arcuate vein
- Cortical radiate vein
- Renal vein
- Inferior vena cava

(b) Path of blood flow through renal blood vessels

Nephron

- Is functional unit of kidney; responsible for forming urine
- >1 million nephrons/kidney
- Consists of small tubes and associated small blood vessels
Type of Nephrons

- **Cortical nephrons** originate in outer 2/3 of cortex
- **Juxtamedullary nephrons** originate in inner 1/3 cortex
- Have long LHs
- Important in producing concentrated urine

Formation of Urine
Glomerular Filtration

- Glomerular capillaries and Bowman's capsule form a filter for blood
  - Glomerular Caps are fenestrated—have large pores between its endothelial cells
    - Big enough to allow any plasma molecule to pass
    - 100-400 times more permeable than other Caps

Glomerular Filtration continued

- To enter tubule filtrate must pass through narrow slit diaphragms formed between pedicels (foot processes) of podocytes of glomerular capsule
Plasma proteins are mostly excluded from the filtrate because of large size and negative charge.

The slit diaphragms are lined with negative charges which repel negatively-charged proteins.

Some protein (especially albumin) normally enters the filtrate but most is reabsorbed by receptor-mediated endocytosis.

**Proteinuria** = Defects in the slit diaphragm results in massive leakage of protein in the filtrate and thus appears in the urine.

Proteinuria

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Scanning electron micrograph of glomerular caps and capsule.

An electron micrograph of the filtration barrier between the cap lumen & glomer. capsule.
The Formation of Glomerular Ultrafiltrate

- Only a fraction of plasma proteins (green) are filtered.
- Smaller plasma solutes (purple) easily enter the glomerular ultrafiltrate.

Glomerular Filtration Rate (GFR)

- Is volume of filtrate produced by both kidneys/min.
- Averages 115 ml/min in women; 125 ml/min in men.
- Totals about 180L/day (45 gallons).
- So most filtered water must be reabsorbed or death would ensue from water lost through urination.

Regulation of GFR

- Is controlled by extrinsic (sympathetic nervous system) and intrinsic (renal autoregulation) mechanisms - vasoconstriction or dilation of afferent arterioles affects rate of blood flow to glomeruli and thus GFR.
Sympathetic Effects

- Sympathetic activity constricts afferent arteriole
- Helps maintain BP and shunts blood to heart and muscles

Renal Autoregulation

- Defined as the ability of kidneys to maintain relatively constant GFR in the face of fluctuating B.P.
- 2 mechanisms responsible:
  - **Myogenic constriction** of afferent arteriole due to smooth muscle responding to an increase in arterial pressure
  - Achieved via effects of locally produced chemicals on afferent arterioles part of **tubuloglomerular feedback**

Renal Autoregulation – Myogenic Constriction

<table>
<thead>
<tr>
<th>Regulation</th>
<th>Stimulus</th>
<th>Afferent Arteriole</th>
<th>GFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sympathetic</td>
<td>Activation by baroreceptor reflex or by higher brain centers</td>
<td>Constricts</td>
<td>Decreases</td>
</tr>
<tr>
<td>Autoregulation</td>
<td>Decreased blood pressure</td>
<td>Dilates</td>
<td>No change</td>
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Renal Autoregulation

- Is also maintained by negative feedback between afferent arteriole and volume of filtrate (tubuloglomerular feedback)
  - Increased flow of filtrate sensed by macula densa (part of juxtaglomerular apparatus) in thick ascending LH
    - Signals afferent arterioles to constrict
Reabsorption of Salt and H₂O
- In PCT returns most molecules and H₂O from filtrate back to peritubular capillaries
- About 180 L/day (45 gallons) of ultrafiltrate produced; only 1–2 L of urine excreted/24 hours
- Urine volume varies according to needs of body
- Minimum of 400 ml/day urine necessary to excrete metabolic wastes (obligatory water loss)

Reabsorption of Salt and H₂O
- The transport of molecules out of the tubular filtrate back into the blood = reabsorption
- Water is never transported
- Other molecules are transported and water follows by osmosis

The Mech. of Reabsorption in the proximal tubule
- There is coupled transport of glucose and Na⁺ into the cytoplasm &
- Primary active transport of Na⁺ across basolateral membrane by Na⁺/K⁺ pump
- Glucose is then transported out of cell by facilitated diffusion and is reabsorbed into the blood
Salt and water reabsorption in the proximal tubules:

- ~65% Na⁺, Cl⁻, and H₂O is reabsorbed in PCT and returned to bloodstream.
- An additional 20% is reabsorbed in descending loop of Henle.
- Thus 85% of filtered H₂O and salt are reabsorbed early in tubule.
  - This is constant and independent of hydration levels.
  - Energy cost is 6% of calories consumed at rest.
  - The remaining 15% is reabsorbed variably, depending on level of hydration.

Concentration Gradient in Kidney:

- In order for H₂O to be reabsorbed, interstitial fluid must be hypertonic.
- Osmolality of medulla interstitial fluid (1200-1400 mOsm) is 4X that of cortex and plasma (300 mOsm).
  - This concentration gradient results largely from loop of Henle which allows interaction between descending and ascending limbs.
The Countercurrent Multiplier System

- Extrusion of NaCl from ascending limb makes surrounding interstitial fluid more concentrated.
- Multiplication of concentration due to descending limb passively permeable to water—causing fluid to become more concentrated.
- Deepest region of medulla at 1,400 mOsm.

Ascending Limb Loop of Henle

- Has a thin segment in the depths of medulla and thick part toward cortex.
- Impermeable to H₂O; permeable to salt; thick part actively transports salt out of filtrate.
  - Active transport of salt causes filtrate to become dilute (100 mOsm) by end of Loop of Henle.

The Transport of Ions in the Ascending Limb

- In thick segment, Na⁺ and K⁺ together with 2 Cl⁻ enter tubule cells.
- Na⁺ then actively transported out into interstitial space and Cl⁻ follows passively.
- K⁺ diffuses back into filtrate; some also enters interstitial space.
Na⁺ is Actively Transported across basolateral membrane by Na⁺/K⁺ pump
Cl⁻ passively follows Na⁺ down electrical gradient
K⁺ passively diffuses back into filtrate

Countercurrent Multiplier System
- Countercurrent flow and proximity allow descending and ascending limbs of Loop of Henle to interact in way that causes osmolality to build in medulla
- Salt pumping in thick ascending part raises osmolality around descending limb, causing more H₂O to diffuse out of filtrate
  - This raises osmolality of filtrate in descending limb which causes more concentrated filtrate to be delivered to ascending limb
  - As this concentrated filtrate is subjected to Active Transport of salts, it causes even higher osmolality around descending limb (positive feedback)
- Process repeats until equilibrium is reached when osmolality of medulla is 1400

The Role of Urea in Urine Concentration
- Urea diffuses out of inner collect. duct into interstitial fluid in medulla
- Urea then passes into ascend. limb so it recirculates in interstitial fluid in medulla
- Water is reabsorbed by osmosis from collect. duct
Collecting Duct (CD)
- Plays important role in water conservation
- Is impermeable to salt in medulla
- Permeability to H₂O depends on levels of ADH

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>Secretion of ADH</th>
<th>Effect on Urine Volume</th>
<th>Effect on Blood</th>
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<tbody>
<tr>
<td>Osmolarity (dehydration)</td>
<td>Osmoregulator in hypothalamus</td>
<td>Increased</td>
<td>Increased urine volume; decreased blood osmolality</td>
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Homeostasis of Plasma Concentration Maintained by ADH
- Is secreted by post pituitary in response to dehydration
- Stimulates insertion of aquaporins (water channels) into plasma membrane of Collect. Duct
- When ADH is high, H₂O is drawn out of CD by high osmolality of interstitial fluid
- And reabsorbed by vasa recta

Osmolality of Different Regions of the Kidney
Role of Aldosterone in Na⁺/K⁺ Balance

- 90% filtered Na⁺ and K⁺ reabsorbed before Distal Tub.
- Remaining is variably reabsorbed in Distal Tub. and Collect. Duct according to bodily needs
- Regulated by aldosterone (controls K⁺ secretion and Na⁺ reabsorption)
- In the absence of aldosterone, 80% of remaining Na⁺ is reabsorbed in Distal Tub. and cortical Collect. Duct
- When aldosterone is high all remaining Na⁺ is reabsorbed

K⁺ is Reabsorbed and Secretion

- K⁺ almost completely reabsorbed in prox. tubule
- Under aldosterone stim. secreted into cortical collect. Ducts
- All K⁺ in urine from secretion rather than filtration

Juxtaglomerular Apparatus (JGA)

- Is specialized region in each nephron where afferent arteriole comes in contact with thick ascending limb LH
Renin-Angiotensin-Aldosterone System

- Is activated by release of renin from granular cells within afferent arteriole
- Renin converts angiotensinogen to angiotensin I
  - Which is converted to Angio II by angiotensin-converting enzyme (ACE) in lungs
- Angio II stimulates release of aldosterone

Macula Densa

- Located where tubule cells make contact with granular cells
- Acts as sensor for tubuloglomerular feedback, needed for autoreg. of GFR
  - Signals afferent arteriole to constrict
  - Signals granular cells to decrease secretion of renin when blood Na+ and water is high.
Atrial Natriuretic Peptide (ANP)

- Is produced by atria due to stretching of walls
- An aldosterone antagonist
- Stimulates salt and H2O excretion
- Acts as an endogenous diuretic