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

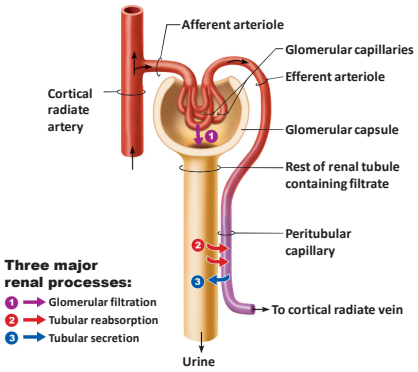
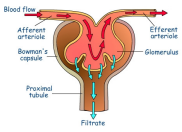


Figure 25.10

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



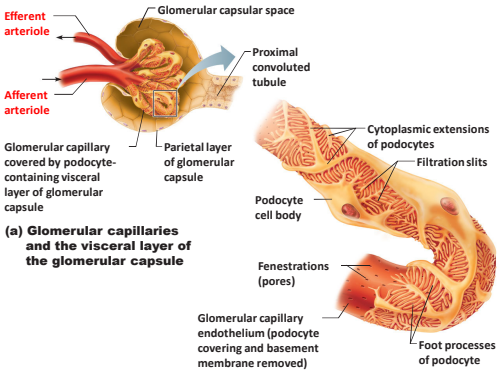
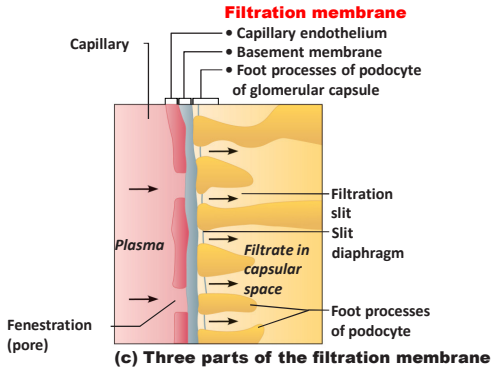


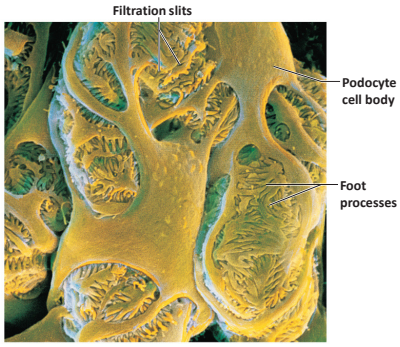
Figure 25.9a

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



(c) Three parts of the filtration membrane



(b) Filtration slits between the podocyte foot processes

Glomerular Filtration

- Net Filtration Pressure (NFP)
  - Glomerular hydrostatic pressure (HP_g)
  - Capsular hydrostatic pressure (HP_c)
  - Blood osmotic pressure (OP_g)

Glomerular Filtration

- Net Filtration Pressure (NFP)
  - The pressure responsible for filtrate formation

$$NFP = HP_g - (OP_g + HP_c)$$

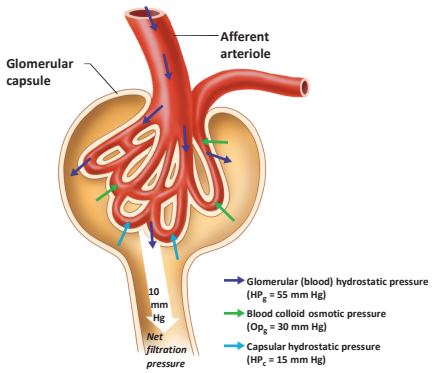


Figure 25.11

Net Filtration Pressure

$NFP = HP_G - (OP_G + HP_C)$

= 55 mm Hg – (30 mmHg + 15 mmHg)

= 10 mmHg

Glomerular Filtration

- Glomerular Filtration Rate (GFR)
  - 125 ml/min

1800 liters of blood through kidneys/day

= 1200 ml/min = about 180 liters filtrate/day

Glomerular Filtration

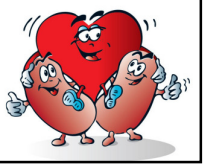
- Factors affecting GFR
  - Kidney disease
    - ↓ blood osmotic pressure, ↑ capsular osmotic pressure
  - Hemorrhage
    - ↓ glomerular blood hydrostatic pressure
  - Hypotension
    - Glomerular blood hydrostatic pressure = capsule hydrostatic and blood osmotic pressure = filtration stops!
      - Termed renal suppression

Glomerular Filtration

- 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

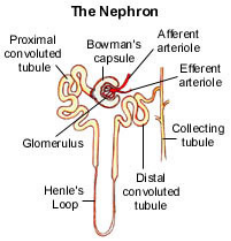
- Sympathetic nervous system
  - At rest
    - Renal blood vessels are dilated
    - Renal autoregulation mechanisms prevail
    - GFR maintained
  - Extreme stress
    - Norepinephrine and epinephrine released
    - Both cause constriction of afferent arterioles
      - Inhibits filtration
      - Shunts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

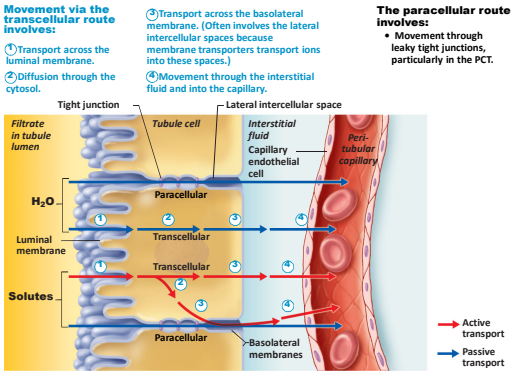


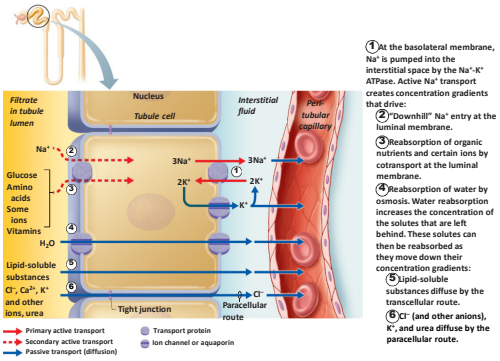
Figure 25.13

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



① At the basolateral membrane, Na^+ is pumped into the interstitial space by the Na^+-K^+ ATPase. Active Na^+ transport creates concentration gradients that drive:

② "Downhill" Na^+ entry at the luminal membrane.

③ Reabsorption of organic nutrients and certain ions by cotransport at the luminal membrane.

④ 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:

⑤ Lipid-soluble substances diffuse by the transcellular route.

⑥ Cl^- (and other anions), K^+, and urea diffuse by the paracellular route.

Figure 25.14

Tubular Reabsorption

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

Tubular Maximum

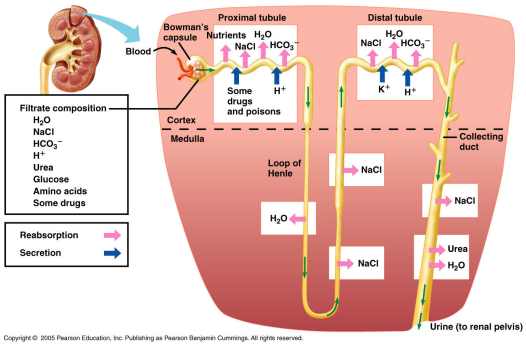
- Transport maximum (T_m) reflects the number of carriers in the renal tubules available
- When the carriers are saturated, excess of that substance is excreted
- Example: too much glucose in the blood entering glomerulus will cause glucosuria

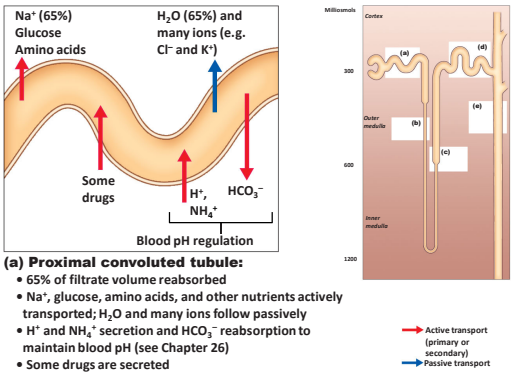
Tubular Reabsorption

- 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
  - K^+, H^+, 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





(a) Proximal convoluted tubule:
- 65% of filtrate volume reabsorbed
- Na^+, glucose, amino acids, and other nutrients actively transported; H_2O and many ions follow passively
- H^+ and NH_4^+ secretion and HCO_3^- reabsorption to maintain blood pH (see Chapter 26)
- Some drugs are secreted

Figure 25.18a

Tubular Secretion

- Principle effects
  - Rids body of
    - Foreign substances (penicillin and other drugs)
    - Nitrogenous wastes
    - Excess K^+
  - Controls blood pH:
    - Altering amounts of H^+ or 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

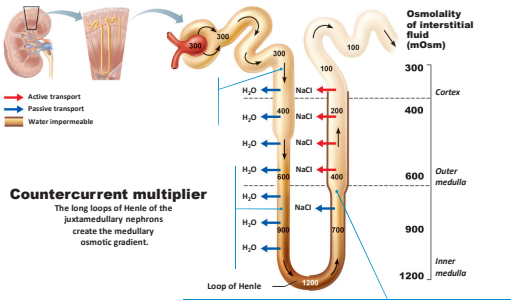


Figure 25.16a

Formation of Concentrated Urine

- Depends on the medullary osmotic gradient and the ability to alter permeability of the collecting tubules

↑ osmolarity of extracellular fluid (also ↓ plasma volume)
↓
↑ ADH release
↓
↑ aquaporins in collecting duct
↓
↑ H_2O reabsorption in collecting duct
↓
Small volume of concentrated urine

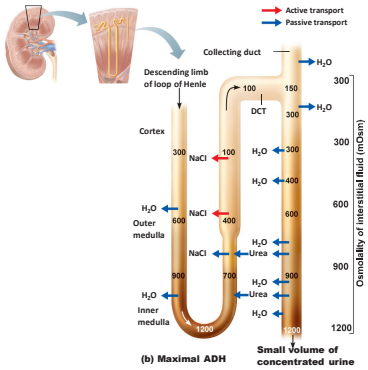


Figure 25.17b

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

↓ osmolarity of extracellular fluid
↓
↓ ADH release
↓
↓ aquaporins in collecting duct
↓
↓ H_2O reabsorption in collecting duct
↓
Large volume of dilute urine

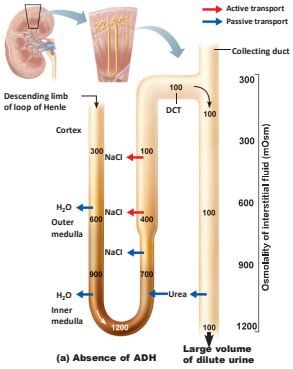


Figure 25.17a

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
  - $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$
- Lungs
  - Regulate carbonic acid levels by CO_2 manipulation
- Kidneys
  - Selectively secrete and reabsorb to maintain pH

Acid-Base Balance

- Most important renal mechanisms:
  - Conserving (reabsorbing) HCO_3^-
  - Excreting HCO_3^-
  - Secretion of H^+
    - H^+ secretion occurs in the PCT and in collecting tubules

Acid-Base Balance

- Examples
  - Respiratory Acidosis
    - Lungs are unable to eliminate CO_2 adequately
    - Kidneys reabsorb HCO_3^-, secrete H^+ (and $NH4^+$)
  - Respiratory Alkalosis
    - CO_2 levels are low
    - Kidneys secrete HCO_3^-, retain H^+ (and NH

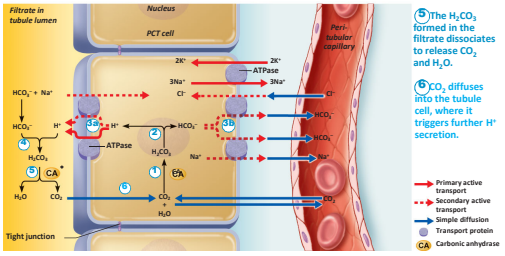


Figure 26.12

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)

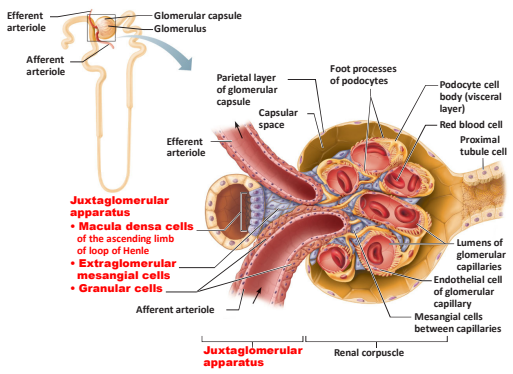


Figure 25.8

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?

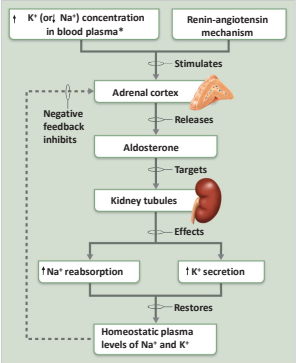


Figure 26.8

Blood Pressure Control

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

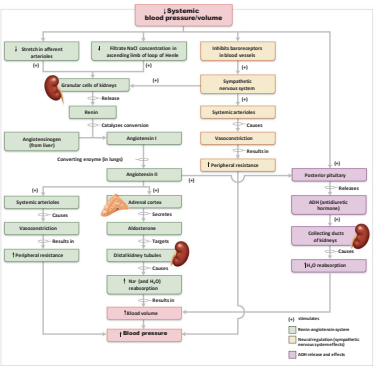


Figure 26.10

Factors Affecting Urine Volume

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

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