Chapter 25
The Urinary System
Kidney Functions

- Removal of toxins, metabolic wastes, and excess ions from the blood
- Regulation of blood volume, chemical composition, and pH
- Gluconeogenesis during prolonged fasting
- Endocrine functions
  - Renin: regulation of blood pressure and kidney function
  - Erythropoietin: regulation of RBC production
- Activation of vitamin D
Figure 25.9 A schematic, uncoiled nephron showing the three major renal processes that adjust plasma composition.

Three major renal processes:
1. Glomerular filtration
2. Tubular reabsorption
3. Tubular secretion

To cortical radiate vein

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Figure 25.5  Location and structure of nephrons. (3 of 7)

- Basement membrane
- Podocyte
- Fenestrated endothelium of the glomerulus

Glomerular capsule: visceral layer

10/30/2013  MDufilho
Figure 25.10a The filtration membrane.

(a) Glomerular capillaries and the visceral layer of the glomerular capsule

- Efferent arteriole
- Afferent arteriole
- Glomerular capillary covered by podocytes that form the visceral layer of glomerular capsule
- Parietal layer of glomerular capsule
- Proximal convoluted tubule
- Glomerular capsular space
- Cytoplasmic extensions of podocytes
- Filtration slits
- Podocyte cell body
- Fenestrations (pores)
- Glomerular capillary endothelium (podocyte covering and basement membrane removed)
- Foot processes of podocyte
Figure 25.10c The filtration membrane.

- Capillary endothelium
- Basement membrane
- Foot processes of podocyte of glomerular capsule

**Filtration membrane**

- Capillary endothelium
- Basement membrane
- Foot processes of podocyte

**Filtration slit**

**Slit diaphragm**

**Filtrate in capsular space**

**Foot processes of podocyte**

(c) Three layers of the filtration membrane
Terminology

• Renal Fraction = % of blood flow passing through kidneys = 20 – 25%

• Filtration Fraction = % plasma (in renal fraction) that passes through the filtration membrane to become filtrate = 20%
Net Filtration Pressure (NFP)

- The pressure responsible for filtrate formation (10 mm Hg)

- Determined by
  
  - Glomerular hydrostatic pressure \( (HP_g) \) the chief force
  
  - Two opposing forces:
    
    - Colloid osmotic pressure of glomerular blood \( (OP_g) \)
    
    - Capsular hydrostatic pressure \( (HP_c) \)

\[
NFP = HP_g - (OP_g + HP_c)
\]
Figure 25.11 Forces determining net filtration pressure (NFP).

NFP = Net filtration pressure
    = outward pressures – inward pressures
    = \((HP_{gc}) - (HP_{cs} + OP_{gc})\)
    = (55) – (15 + 30)
    = 10 mm Hg
Glomerular Filtration Rate (GFR)

• Volume of filtrate formed per minute by the kidneys (120–125 ml/min)

• Governed by (and directly proportional to)
  • Total surface area available for filtration
  • Filtration membrane permeability
  • NFP
Tubular Maximum

• Also called transport maximum
• When tubular load exceeds tubular maximum, the substances show up in urine
  • e. g. Glucosuria
Clinical Applications – What if…..

• Hemorrhage –
  - Blood Pressure?
  - NFP?
  - GFR?
  - Result

• Fight or flight situation
  - Sympathetic stimulation?
  - Blood Pressure?
  - Result?

• Kidney Infection
  - Result
Regulation of Glomerular Filtration

- GFR is tightly controlled by two types of mechanisms
  - Intrinsic controls (renal autoregulation)
    - Act locally within the kidney
  - Extrinsic controls
    - Nervous and endocrine mechanisms that maintain blood pressure, but affect kidney function
Intrinsic Controls

• Maintains a nearly constant GFR when MAP is in the range of 80–180 mm Hg

• Two types of renal autoregulation
  • Myogenic mechanism (Chapter 19)
  • Tubuloglomerular feedback mechanism, which senses changes in the juxtaglomerular apparatus
Figure 25.8  Juxtaglomerular complex (JGC) of a nephron.

- Glomerular capsule
- Efferent arteriole
- Afferent arteriole
- Glomerulus
- Parietal layer of glomerular capsule
- Capsular space
- Foot processes of podocytes
- Podocyte cell body (visceral layer)
- Red blood cell
- Proximal tubule cell
- Lumens of glomerular capillaries
- Endothelial cell of glomerular capillary
- Glomerular mesangial cells
- Juxtaglomerular complex
  - Macula densa cells of the ascending limb of nephron loop
  - Extraglomerular mesangial cells
  - Granular cells
- Juxtaglomerular complex
- Renal corpuscle
Intrinsic Controls: Tubuloglomerular Feedback Mechanism

Macula densa cells monitor Na\(^+\) and Cl\(^-\) in filtrate

- Macula densa cells of the JGA respond to ↑NaCl by releasing a vasoconstricting chemical that acts on the afferent arteriole → ↓GFR
- The opposite occurs if GFR decreases.
Intrinsic Controls

• Compensate for MAP of 80 – 180 mmHg to maintain GFR at 125 ml/min (+/- 30%)
• Kidney function suffers if MAP < 80 mmHg
• Then extrinsic controls are needed
Extrinsic Controls: Sympathetic Nervous System

• Under extreme stress
  • Norepinephrine is released by the sympathetic nervous system
  • Epinephrine is released by the adrenal medulla
  • Both cause constriction of afferent arterioles, inhibiting filtration and triggering the release of renin
Extrinsic Controls: Renin-Angiotensin Mechanism

• Triggered when the granular cells of the JGA release renin

\[
\text{angiotensinogen} \ (a \ plasma \ globulin) \\
\text{renin} \rightarrow \text{angiotensin I} \\
\text{angiotensin converting enzyme (ACE)} \rightarrow \text{angiotensin II}
\]
Other Factors Affecting GFR

• Prostaglandin E$_2$
  • Vasodilator that counteracts vasoconstriction by norepinephrine and angiotensin II
  • Prevents renal damage when peripheral resistance is increased

• Intrarenal angiotensin II
  • Reinforces the effects of hormonal angiotensin II

• Adenosine
  • A vasoconstrictor of renal vasculature
Figure 25.12 Physiological mechanisms regulating glomerular filtration rate (GFR) in the kidneys.

**SYSTEMIC BLOOD PRESSURE**

- **↓ Blood pressure in afferent arterioles; ↓ GFR**
- **↓ Stretch of smooth muscle in walls of afferent arterioles**
- **Vasodilation of afferent arterioles**
  - Release of vasoactive chemicals inhibited
  - ↑ GFR

- **↓ GFR**
- **Filtrate flow and NaCl in ascending limb of nephron loop**
- **Target**

- **Granular cells of juxtaglomerular complex of kidney**
  - Release
  - Renin
  - Catalyzes cascade resulting in formation of
  - Angiotensin II

- **Macula densa cells of juxtaglomerular complex of kidney**
  - ↑ Aldosterone secretion by adrenal cortex
  - Vasoconstriction of systemic arterioles; ↑ peripheral resistance
  - ↑ Na⁺ reabsorption by kidney tubules; water follows
  - ↑ Blood volume
  - ↑ Systemic blood pressure

- **Inhibits baroreceptors in blood vessels of systemic circulation**
- **Sympathetic nervous system**

**Myogenic mechanism of autoregulation**
- **Tubuloglomerular mechanism of autoregulation**
- **Hormonal (renin-angiotensin-aldosterone) mechanism**
- **Neural controls**

**Intrinsic mechanisms** directly regulate GFR despite moderate changes in blood pressure (between 80 and 180 mm Hg mean arterial pressure).

**Extrinsic mechanisms** indirectly regulate GFR by maintaining systemic blood pressure, which drives filtration in the kidneys.
Regulation of Urine Concentration and Volume – Really ECF

- Osmolality - number of solute particles in 1Kg of solvent
- Osmolarity – number of solute particles in 1 liter of solvent
- Both terms reflect the solution’s ability to cause osmosis
- Body fluids are measured in milliosmols (mOsm)
- The kidneys keep the solute load of body fluids constant at about 285 - 300 mOsm
- This is accomplished by the countercurrent mechanism
Countercurrent Mechanism

• Occurs when fluid flows in opposite directions in two adjacent segments of the same tube
  • Filtrate flow in the loop of Henle (countercurrent multiplier)
  • Blood flow in the vasa recta (countercurrent exchanger)
Figure 25.7a Blood vessels of cortical and juxtamedullary nephrons.

**Cortical nephron**
- Short nephron loop
- Glomerulus further from the cortex-medulla junction
- Efferent arteriole supplies peritubular capillaries

**Juxtamedullary nephron**
- Long nephron loop
- Glomerulus closer to the cortex-medulla junction
- Efferent arteriole supplies vasa recta

- Renal corpuscle
- Glomerulus (capillaries)
- Glomerular capsule
- Proximal convoluted tubule
- Peritubular capillaries
- Ascending limb of nephron loop
- Arcuate vein
- Arcuate artery
- Nephron loop
- Descending limb of nephron loop
- Cortex-medulla junction
- Vasa recta
Figure 25.16a Juxtamedullary nephrons create an osmotic gradient within the renal medulla that allows the kidney to produce urine of varying concentration. (4 of 4)

(a) (continued) As water and solutes are reabsorbed, the loop first concentrates the filtrate, then dilutes it.

1. Filtrate entering the nephron loop is isosmotic to both blood plasma and cortical interstitial fluid.

2. Water moves out of the filtrate in the descending limb down its osmotic gradient. This concentrates the filtrate.

3. Filtrate reaches its highest concentration at the bend of the loop.

4. Na⁺ and Cl⁻ are pumped out of the filtrate. This increases the interstitial fluid osmolality.

5. Filtrate is at its most dilute as it leaves the nephron loop. At 100 mOsm, it is hypo-osmotic to the interstitial fluid.
Countercurrent Exchanger: Vasa Recta

• The vasa recta
  • Maintain the osmotic gradient
  • Deliver blood to the medullary tissues
  • Protect the medullary osmotic gradient by preventing rapid removal of salt, and by removing reabsorbed H₂O
The entire length of the vasa recta is highly permeable to water and solutes. Due to countercurrent exchanges between each section of the vasa recta and its surrounding interstitial fluid, the blood within the vasa recta remains nearly isosmotic to the surrounding fluid. As a result, the vasa recta do not undo the osmotic gradient as they remove reabsorbed water and solutes.

The countercurrent flow of fluid moves through two adjacent parallel sections of the vasa recta.
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
- Na$^+$ and other ions may be selectively removed in the DCT and collecting duct, decreasing osmolality to as low as 50 mOsm
Figure 25.17a  Mechanism for forming dilute or concentrated urine.

(a) If we were so overhydrated we had no ADH...

- Osmolality of extracellular fluids
- ADH release from posterior pituitary
- Number of aquaporins (H$_2$O channels) in collecting duct
- H$_2$O reabsorption from collecting duct
- Large volume of dilute urine

Descending limb of nephron loop

Collecting duct

Cortex

Outer medulla

Inner medulla

Large volume of dilute urine

Active transport

Passive transport
Formation of Concentrated Urine

• Depends on the medullary osmotic gradient and ADH

• ADH triggers reabsorption of H$_2$O in the collecting ducts

• Facultative water reabsorption occurs in the presence of ADH so that 99% of H$_2$O in filtrate is reabsorbed
Figure 25.17b Mechanism for forming dilute or concentrated urine.

(b) If we were so dehydrated we had maximal ADH...

- ↑ Osmolality of extracellular fluids
- ↑ ADH release from posterior pituitary
- ↑ Number of aquaporins (H₂O channels) in collecting duct
- ↑ H₂O reabsorption from collecting duct

Small volume of concentrated urine

Urea contributes to the osmotic gradient. ADH increases its recycling.
Diuretics

• Chemicals that enhance the urinary output
  • Osmotic diuretics: substances not reabsorbed, (e.g., high glucose in a diabetic patient)
  • ADH inhibitors such as alcohol
  • Substances that inhibit Na$^+$ reabsorption and obligatory H$_2$O reabsorption such as caffeine, Lasix, Diuril, HCTZ (hydrochlorothiazide) and others
Solvent Drag

• Collecting ducts – water reabsorbed toward hypertonic medullary ISF

• What is happening to the remaining filtrate?

• What happens with concentration gradient?

• Urea, toxins and lipid soluble drugs can be dragged back into blood by water reabsorption – solvent drag
Renal Clearance

• Volume of plasma cleared of a particular substance in a given time

• Renal clearance tests are used to
  • Determine GFR
  • Detect glomerular damage
  • Follow the progress of renal disease
Renal Clearance

\[ RC = \frac{UV}{P} \]

RC = renal clearance rate (ml/min)

U = concentration (mg/ml) of the substance in urine

V = flow rate of urine formation (ml/min)

P = concentration of the same substance in plasma
Renal Clearance

- For any substance freely filtered and neither reabsorbed nor secreted by the kidneys (e.g., inulin),
  \[ RC = \text{GFR} = 125 \text{ ml/min} \]
  Kidneys have cleared all inulin present in 125ml plasma in 1 min
- If \( RC < 125 \text{ ml/min} \), the substance is reabsorbed
- If \( RC = 0 \), the substance is completely reabsorbed
- If \( RC > 125 \text{ ml/min} \), the substance is secreted (most drug metabolites)