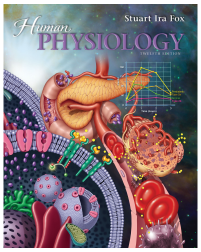



# Chapter 17

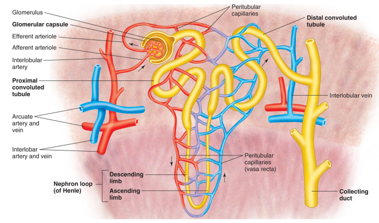
**Physiology of the Kidneys**

Lecture PowerPoint



# I. Structure and Function of the Kidneys






# Kidney Functions

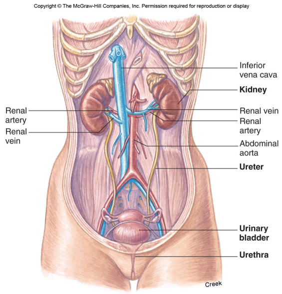
- Regulation of the extracellular fluid environment in the body, including:
  - Volume of blood plasma (affects blood pressure)
  - Wastes
  - Electrolytes
  - pH

# Kidney Structure

- Urine made in the kidneys pools into the renal pelvis, then down the ureter to the urinary bladder.
- It passes from the bladder through the urethra to exit the body.
- Urine is transported using peristalsis.

# Kidney Structure



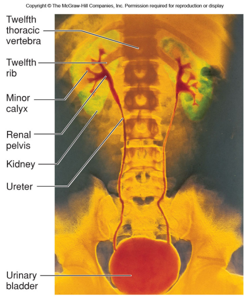



# Kidney Structure

- The kidney has two distinct regions:
  - Renal cortex
  - Renal medulla, made up of renal pyramids and columns
- Each pyramid drains into a minor calyx → major calyx → renal pelvis.

## Kidney Structure






## Control of Micturition

- Detrusor muscles line the wall of the urinary bladder.
  - Gap junctions connect smooth muscle cells.
  - Innervated by parasympathetic neurons, which release acetylcholine onto muscarinic ACh receptors
- Sphincters surround urethra.
  - Internal urethral sphincter: smooth muscle
  - External urethral sphincter: skeletal muscle

## Control of Micturition

- Stretch receptors in the bladder send information to S1−S4 regions of the spinal cord.
  - These neurons normally inhibit parasympathetic nerves to the detrusor muscles, while somatic motor neurons to the external urethral sphincter are stimulated.
  - Called the guarding reflex
  - Prevents involuntary emptying of bladder

## Control of Micturition

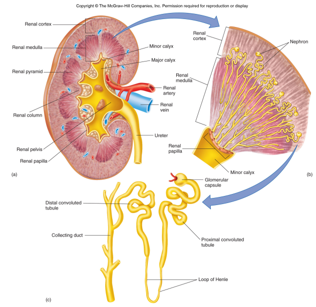
- Stretch of the bladder initiates the voiding reflex.
  - Information about stretch passes up the spinal cord to the micturition center of the pons.
  - Parasympathetic neurons cause detrusor muscles to contract.
  - Sympathetic innervation of the internal urethral sphincter causes it to relax.
  - Person feels the need to urinate and can control when with external urethral sphincter.

## Microscopic Kidney Structure

- Nephron: functional unit of the kidney
  - Each kidney has more than a million nephrons.
  - Nephron consists of small tubules and associated blood vessels.

## Microscopic Kidney Structure

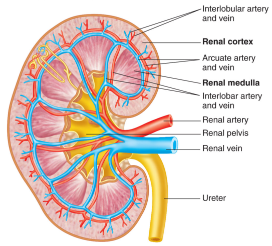




## Renal Blood Vessels

Renal artery →
Interlobar arteries →
Arcuate arteries →
Interlobular arteries →
Afferent arterioles
Glomerulus →
Efferent arterioles →
Peritubular capillaries →
Interlobular veins →
Arcuate veins →
Interlobar veins →
Renal vein






## Nephron Tubules

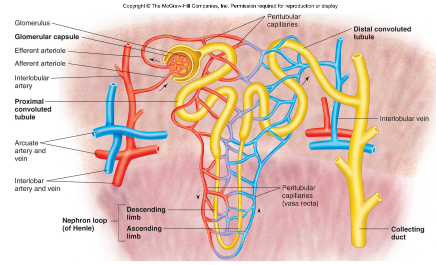
- Glomerular (Bowman's) capsule surrounds the glomerulus. Together, they make up the renal corpuscle.
- Filtrate produced in renal corpuscle passes into the proximal convoluted tubule.
- Next, fluid passes into the descending and ascending loop of Henle.

## Nephron Tubules

- After the loop of Henle, fluid passes into the distal convoluted tubule.
- Finally, fluid passes into the collecting duct.
  - The fluid is now urine and will drain into a minor calyx.

## Nephron Tubules

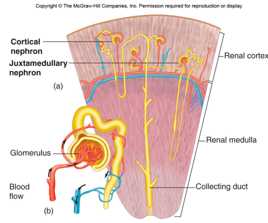





## Two Types of Nephrons

- Juxtamedullary: better at making concentrated urine
- Cortical






## II. Glomerular Filtration

## Glomerular Corpuscle

- Capillaries of the glomerulus are fenestrated.
  - Large pores allow water and solutes to leave but not blood cells and plasma proteins.
- Fluid entering the glomerular capsule is called filtrate

## Glomerular Corpuscle

- Filtrates must pass through:
  1. Capillary fenestrae
  2. Glomerular basement membrane
  3. Visceral layer of the glomerular capsule composed of cells called podocytes with extensions called pedicles

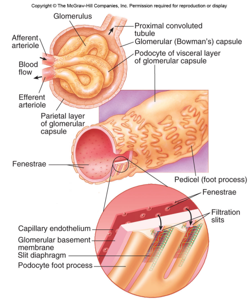
## Glomerular Corpuscle



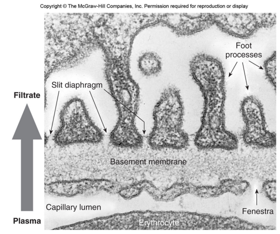



## Glomerular Corpuscle









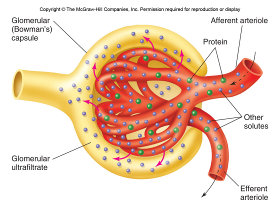

## Glomerular Corpuscle

- Slits in the pedicles called slit diaphragm pores are the major barrier for the filtration of plasma proteins.
  - Defect here causes proteinuria = proteins in urine.
  - Some albumin is filtered out but is reabsorbed by active endocytosis.

## Ultrafiltrate

- Fluid in glomerular capsule gets there via hydrostatic pressure of the blood, colloid osmotic pressure, and very permeable capillaries.





## Filtration Rates

- Glomerular filtration rate (GFR): volume of filtrate produced by both kidneys each minute = 115−125 ml.
  - 180 ml/ day
  - Total blood volume filtered every 40 minutes
  - Most must be reabsorbed immediately

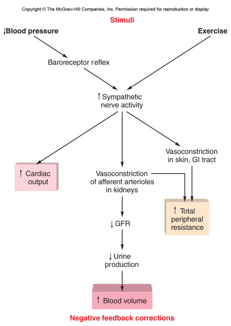
## Regulation of Filtration Rate

- Vasoconstriction or dilation of afferent arterioles changes filtration rate.
  - Extrinsic regulation via sympathetic nervous system
  - Intrinsic regulation via signals from the kidneys; called renal autoregulation

## Sympathetic Nerve Effects

- In a fight/flight reaction, there is vasoconstriction of the afferent arterioles.
  - Helps divert blood to heart and muscles
  - Urine formation decreases

## Sympathetic Nerve Effects




## Renal Autoregulation

- GFR is maintained at a constant level even when blood pressure (BP) fluctuates greatly.
  - Afferent arterioles dilate if BP < 70.
  - Afferent arterioles constrict if BP > normal.

1. Myogenic constriction: Smooth muscles in arterioles sense blood pressure.

## Renal Autoregulation

2. Tubuloglomerular feedback: Cells in the ascending limb of the loop of Henle called macula densa sense a rise in water and sodium as occurs with increased blood pressure (and filtration rate).
   – They send a chemical signal to constrict the afferent arterioles.

## Regulation of Filtration Rate

- Summary:



**Table 17.1 | Regulation of the Glomerular Filtration Rate (GFR)**

| Regulation | Stimulus | Afferent Arteriole | GFR |
|---|---|---|---|
| Sympathetic nerves | Activation by baroreceptor reflex or by higher brain centers | Constricts | Decreases |
| Autoregulation | Decreased blood pressure | Dilates | No change |
| Autoregulation | Increased blood pressure | Constricts | No change |

## III. Reabsorption of Salt and Water

## Reabsorption

- 180 ml of water is filtered per day, but only 1−2 ml is excreted as urine.
  - This will increase when well hydrated and decrease when dehydrated.
  - A minimum 400 ml must be excreted to rid the body of wastes = obligatory water loss.
  - 85% of reabsorption occurs in the proximal tubules and descending loop of Henle.This portion is unregulated.

## Reabsorption in the Proximal Tubule

- The osmolality of filtrate in the glomerular capsule is equal to that of blood plasma.
- $Na^+$ is actively transported out of the filtrate into the peritubular blood to set up a concentration gradient to drive osmosis.

## Active Transport

- Cells of the proximal tubules are joined by tight junctions on the apical side (facing inside the tubule).
  - The apical side also contains microvilli.
  - These cells have a lower $Na^+$ concentration than the filtrate inside the tubule due to $Na^+/K^+$ pumps on the basal side of the cells.
  - $Na^+$ from the filtrate diffuses into these cells and is then pumped out the other side.

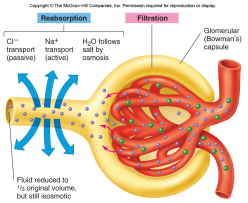
## Passive Transport

- The pumping of sodium into the interstitial space attracts negative $Cl^-$ out of the filtrate.
- Water then follows $Na^+$ and $Cl^-$ into the tubular cells and the interstitial space.
- The increased concentration of salts and water diffuses into the peritubular capillaries.

## Proximal Tubular Fluid

- Reduced by 1/3 but still isosmotic
  - Plasma membrane is freely permeable to water and salts.






## Descending Loop of Henle

- An additional 20% of water is reabsorbed here.
  - Happens continuously and is unregulated
  - The final 15% of water (~27 L) is absorbed later in the nephron under hormonal control.
- Fluid entering loop of Henle is isotonic to extracellular fluids.

## Countercurrent Multiplier System

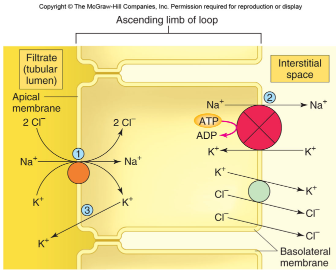
- Water cannot be actively pumped out of the tubes, and it will not cross if isotonic to extracellular fluid.
- The structure of the loop of Henle allows for a concentration gradient to be set up for the osmosis of water.
- The ascending portion sets up this gradient.

## Ascending Loop of Henle

- Salt (NaCl) is actively pumped into the interstitial fluid.
  - Movement of $Na^+$ down its electrochemical gradient from filtrate into tubule cells powers the secondary active transport of $Cl^-$ and $K^+$.
  - $Na^+$ is moved into interstitial space via $Na^+/K^+$ pump. $Cl^-$ follows $Na^+$ passively due to electrical attraction, and $K^+$ passively diffuses back into filtrate.

## Ascending Loop of Henle






## Ascending Loop of Henle

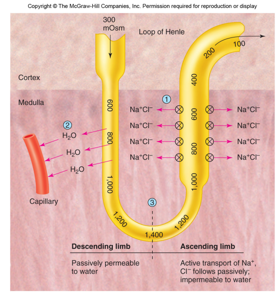
- Walls are not permeable to water, so osmosis cannot occur from the ascending part of the loop.
- Surrounding interstitial fluid becomes increasingly solute concentrated at the bottom of the tube.
- Tubular fluid entering the descending loop of Henle becomes more hypotonic as it descends the loop.

## Descending Loop of Henle

- *Is not* permeable to salt but *is* permeable to water
- Water is drawn out of the filtrate and into the interstitial space where it is quickly picked up by capillaries.
- As it descends, the fluid becomes more solute concentrated.
  - This is perfect for salt transport out of the fluid in the ascending portion.

## Loop of Henle: Solute and Water Transport






## Countercurrent Multiplication

- Positive feedback mechanism is created between the two portions of the loop of Henle.
  - The more salt the ascending limb removes, the saltier the fluid entering it will be (due to loss of water in descending limb).

## Vasa Recta

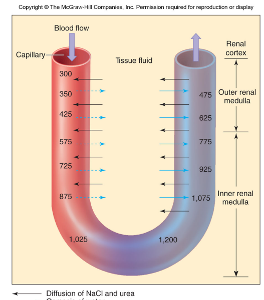
- Specialized blood vessels around loop of Henle, which also have a descending and ascending portion
- Help create the countercurrent system because they take in salts in the descending region but lose them again in the ascending region
  - Keep salts in the interstitial space

## Vasa Recta

- High salt concentration at the beginning of the ascending region pulls in water, which is removed from the interstitial space.
  - Also keeps salt concentration in the interstitial space high

## Vasa Recta

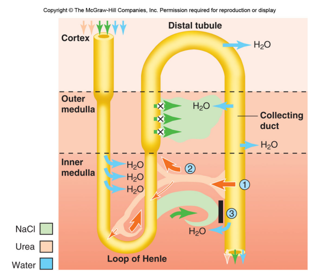




# Urea

- A waste product of protein metabolism
- Contributes to countercurrent system
  - Transported out of collecting duct and into interstitial fluid
  - Diffuses back into ascending limb and cycles around continuously
  - Helps set up solute concentration gradients

# Urea




# Renal Tubule Transport Properties

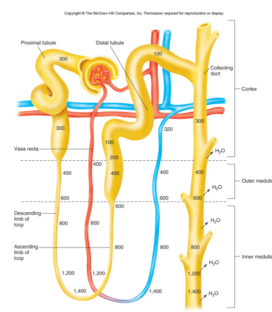


**Table 17.2 | Transport Properties of Different Segments of the Renal Tubules and the Collecting Ducts**

| | | Passive Transport | | |
|---|---|---|---|---|
| **Nephron Segment** | **Active Transport** | **Salt** | **Water** | **Urea** |
| Proximal tubule | $Na^+$ | $Cl^-$ | Yes | Yes |
| Descending limb of Henle's loop | None | Maybe | Yes | No |
| Thin segment of ascending limb | None | NaCl | No | Yes |
| Thick segment of ascending limb | $Na^+$ | $Cl^-$ | No | No |
| Distal tubule | $Na^+$ | $Cl^-$ | No** | No |
| Collecting duct* | Slight $Na^+$ | No | Yes (ADH) or slight (no ADH) | Yes |

*The permeability of the collecting duct to water depends on the presence of ADH.
**The last part of the distal tubule, however, is permeable to water.

# Renal Tubule Osmolality



# Collecting Duct and ADH

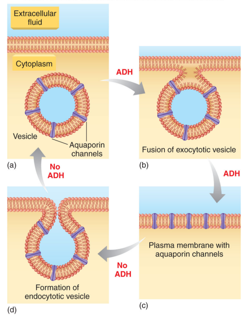
- Last stop in urine formation
- Also influenced by hypertonicity of interstitial space – water will leave via osmosis if able to
- Permeability to water depends on the number of aquaporin channels in the cells of the collecting duct
  - Availability of aquaporins determined by ADH

# Collecting Duct and ADH

- ADH binds to receptors on collecting duct cells →
  cAMP →
  Protein kinase →
  Vesicles with aquaporin channels fuse to plasma membrane.
- Water channels are removed without ADH.

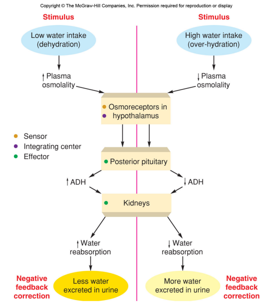
## Collecting Duct and ADH






## Role of ADH in Plasma Concentration






## Summary of ADH Action



**Table 17.3 | Antidiuretic Hormone Secretion and Action**

| Stimulus | Receptors | Secretion of ADH | Effects on Urine Volume | Effects on Blood |
|---|---|---|---|---|
| ↑Osmolality (dehydration) | Osmoreceptors in hypothalamus | Increased | Decreased | Increased water retention; decreased blood osmolality |
| ↓Osmolality | Osmoreceptors in hypothalamus | Decreased | Increased | Water loss increases blood osmolality |
| ↑Blood volume | Stretch receptors in left atrium | Decreased | Increased | Decreased blood volume |
| ↓Blood volume | Stretch receptors in left atrium | Increased | Decreased | Increased blood volume |

## IV. Renal Plasma Clearance

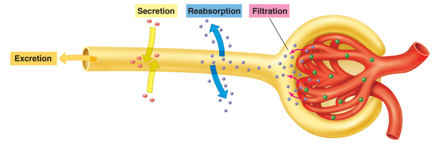
## Secretion

- Kidneys must also remove excess ions and wastes from the blood.
  - Sometimes called renal plasma clearance
  - Filtration in the glomerular capsule begins this process.
  - Secretion finishes the process when substances are moved from the peritubular capillaries into the tubules.

## Excretion Rate

- Excretion rate = filtration rate + secretion rate – reabsorption rate
- Used to measure glomerular filtration rate (GFR), an indicator of renal health





## Secretion of Drugs

- Membrane carriers specific to foreign substances transport them into the tubules.
  - Called organic anion transporters (OATs) or organic cation transporters
  - Very fast; may interfere with action of therapeutic drugs

## Clearance of Inulin

- Inulin is a compound found in garlic, onion, and artichokes.
  - Great marker of glomerular filtration rate because it is filtered but not reabsorbed or secreted

$$GFR = \frac{V \times U}{P}$$

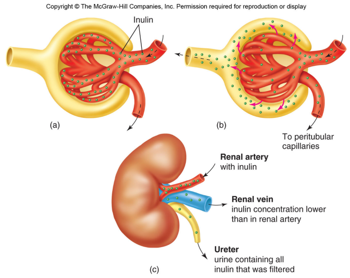
V = rate of urine formation

U = inulin concentration in urine

P = inulin concentration in plasma

## Clearance of Inulin






## Renal Plasma Clearance

- Volume of plasma from which a substance is completely removed by the kidneys in 1 minute
  - Inulin is filtered only. Clearance = GFR
  - Anything that can be reabsorbed has a clearance < GFP.
  - If a substance is filtered *and* secreted, it will have a clearance > GFR.
  - Renal plasma clearance uses same formula as GFR.

## Renal Plasma Clearance



**Table 17.4 | Effects of Filtration, Reabsorption, and Secretion on Renal Plasma Clearance**

| Term | Definition | Effect on Renal Clearance |
|---|---|---|
| Filtration | A substance enters the glomerular ultrafiltrate. | Some or all of a filtered substance may enter the urine and be "cleared" from the blood. |
| Reabsorption | A substance is transported from the filtrate, through tubular cells, and into the blood. | Reabsorption decreases the rate at which a substance is cleared; clearance rate is less than the glomerular filtration rate (GFR). |
| Secretion | A substance is transported from peritubular blood, through tubular cells, and into the filtrate. | When a substance is secreted by the nephrons, its renal plasma clearance is greater than the GFR. |



**Table 17.5 | Renal "Handling" of Different Plasma Molecules**

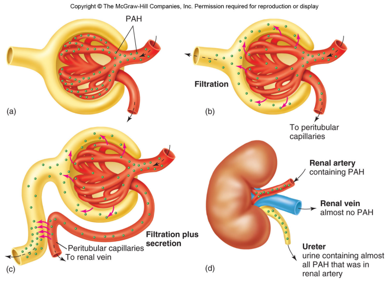
| If Substance Is: | Example | Concentration in Renal Vein | Renal Clearance Rate |
|---|---|---|---|
| Not filtered | Proteins | Same as in renal artery | Zero |
| Filtered, not reabsorbed or secreted | Inulin | Less than in renal artery | Equal to GFR (115–125 ml/min) |
| Filtered, partially reabsorbed | Urea | Less than in renal artery | Less than GFR |
| Filtered, completely reabsorbed | Glucose | Same as in renal artery | Zero |
| Filtered and secreted | PAH | Less than in renal artery; approaches zero | Greater than GFR; up to total plasma flow rate (~625 ml/min) |
| Filtered, reabsorbed, and secreted | $K^+$ | Variable | Variable |

## Clearance of PAH

- Exogenous molecule injected for measurement of total renal blood flow
- All PAH in the peritubular capillaries will be secreted by OATs, so the time it takes to clear all PAH injected indicates blood flow to these capillaries.

## Clearance of PAH



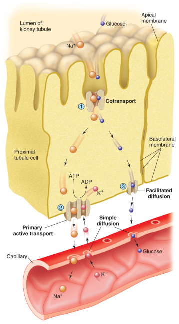



## Reabsorption of Glucose and Amino Acids

- Easily filtered out in the glomerular capsule
- Completely reabsorbed in the proximal tubule via secondary active transport with sodium, facilitated diffusion, and simple diffusion

## Reabsorption of Glucose and Amino Acids






## Transporter Saturation

- Glucose/$Na^+$ cotransporters have a transport maximum.
  - If there is too much glucose in the filtrate, it will not be completely reabsorbed.
  - Glucose in the urine = glycosuria and is a sign of diabetes mellitus.
  - Extra glucose in the blood also results in decreased water reabsorption and possible dehydration.

## V. Renal Control of Electrolyte and Acid-Base Balance

## Electrolyte Balance

- Kidneys match electrolyte ($Na^+$, $K^+$, $Cl^-$, bicarbonate, phosphate) excretion to ingestion.
  - Control of $Na^+$ levels is important in blood pressure and blood volume.
  - Control of $K^+$ levels is important in healthy skeletal and cardiac muscle activity.
  - Aldosterone plays a big role in $Na^+$ and $K^+$ balance.

## Aldosterone

- About 90% of filtered $Na^+$ and $K^+$ is reabsorbed early in the nephron.
  - This is not regulated.
- An assessment of what the body needs is made, and aldosterone controls additional reabsorption of $Na^+$ and secretion of $K^+$ in the distal tubule and collecting duct.

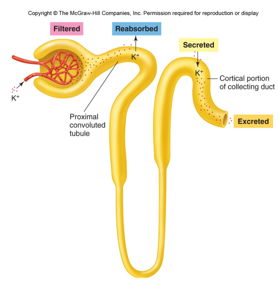
## Potassium Secretion

- Aldosterone independent response: Increase in blood $K^+$ triggers an increase in the number of $K^+$ channels in the cortical collecting duct.
  - When blood $K^+$ levels drop, these channels are removed.

## Potassium Secretion

- Aldosterone-dependent response: Increase in blood $K^+$ triggers adrenal cortex to release aldosterone.
  - This increases $K^+$ secretion in the distal tubule and collecting duct.

## Potassium Secretion




## Sodium and Potassium

- Increases in sodium absorption drive extra potassium secretion.
- Due to:
  - Potential difference created by $Na^+$ reabsorption driving $K^+$ through $K^+$ channels
  - Stimulation of renin-angiotensin-aldosterone system by water and $Na^+$ in filtrate
  - Increased flow rates bend cilia on the cells of the distal tubule, resulting in activation of $K^+$ channels

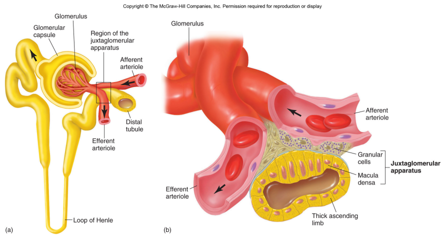
## Control of Aldosterone Secretion

- A rise in blood $K^+$ directly stimulates production of aldosterone in the adrenal cortex.
- A fall in blood $Na^+$ indirectly stimulates production of aldosterone via the renin-angiotensin-aldosterone system.

## Juxtaglomerular Apparatus

- Located where the afferent arteriole comes into contact with the distal tubule






## Juxtaglomerular Apparatus

- A decrease in plasma $Na^+$ results in a fall in blood volume.
  - Sensed by juxtaglomerular apparatus
  - Granular cells secrete renin into the afferent arteriole.
  - This converts angiotensinogen into angiotensin I.
  - Angiotensin-converting enzyme (ACE) converts this into angiotensin II.

## Angiotensin II

- Stimulates adrenal cortex to make aldosterone
  - Promotes the reabsorption of $Na^+$ from cortical collecting duct
  - Promotes secretion of $K^+$
  - Increases blood volume and raises blood pressure

## Regulation of Renin Secretion

- Low salt levels result in lower blood volume due to inhibition of ADH secretion.
  - Less water is reabsorbed in collecting ducts and more is excreted in urine.
- Reduced blood volume is detected by granular cells that act as baroreceptors. They then secrete renin.
  - Granular cells are also stimulated by sympathetic innervation from the baroreceptor reflex.

## Macula Densa

- Part of the distal tubule that forms the juxtaglomerular apparatus
- Sensor for tubuloglomerular feedback needed for regulation of glomerular filtration rate
  - When there is more $Na^+$ and $H_2O$ in the filtrate, a signal is sent to the afferent arteriole to constrict limiting filtration rate.
  - Controlled via negative feedback

## Macula Densa

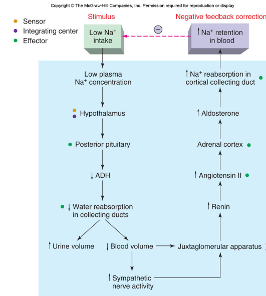
- When there is more $Na^+$ and $H_2O$ in the filtrate, a signal is sent to the afferent arteriole to inhibit the production of renin.
  - This results in less reabsorption of $Na^+$, allowing more to be excreted.
  - This helps lower $Na^+$ levels in the blood.

## Atrial Natriuretic Peptide

- Increases in blood volume also increase the release of atrial natriuretic peptide hormone from the atria of the heart when atrial walls are stretched.
  - Stimulates kidneys to excrete more salt

## Plasma Sodium Balance






## Regulation of Renin and Aldosterone Secretion



**Table 17.6 | Regulation of Renin and Aldosterone Secretion**

| Stimulus | Effect on Renin Secretion | Angiotensin II Production | Aldosterone Secretion | Mechanisms |
|---|---|---|---|---|
| ↓Blood volume | Increased | Increased | Increased | Low blood volume stimulates renal baroreceptors; granular cells release renin. |
| ↑Blood volume | Decreased | Decreased | Decreased | Increased blood volume inhibits baroreceptors; increased $Na^+$ in distal tubule acts via macula densa to inhibit release of renin from granular cells. |
| ↑ $K^+$ | None | Not changed | Increased | Direct stimulation of adrenal cortex |
| ↑Sympathetic nerve activity | Increased | Increased | Increased | α-adrenergic effect stimulates constriction of afferent arterioles; β-adrenergic effect stimulates renin secretion directly. |

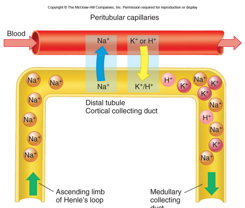
## Relationship Between $Na^+$, $K^+$, and $H^+$

- Reabsorption of $Na^+$ stimulates the secretion of other positive ions.
  - $K^+$ and $H^+$ compete.
- Acidosis stimulates the secretion of $H^+$ and inhibits the secretion of $K^+$ ions.
  - Acidosis can lead to hyperkalemia.
- Alkalosis stimulates the secretion and excretion of more $K^+$.

## Relationship Between $Na^+$, $K^+$, and $H^+$

- Hyperkalemia stimulates the secretion of $K^+$ and inhibits secretion of $H^+$.
  - Can lead to acidosis






## Acid-Base Regulation

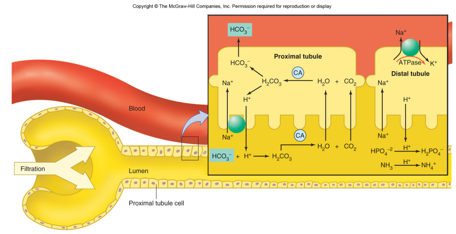
- Kidneys maintain blood pH by reabsorbing bicarbonate and secreting $H^+$.
  - Urine is thus acidic.
- Proximal tubule uses $Na^+/H^+$ pumps to exchange $Na^+$ out and $H^+$ in.
  - Some of the $H^+$ brought in is used for the reabsorption of bicarbonate.

## Acid-Base Regulation

- Bicarbonate cannot cross the inner tubule membrane so must be converted to $CO_2$ and $H_2O$ using carbonic anhydrase.
  - Bicarbonate + $H^+$ → carbonic acid
  - Carbonic acid (w/ carbonic anhydrase) → $H_2O$ + $CO_2$
- $CO_2$ can cross into tubule cells, where the reaction reverses and bicarbonate is made again.
- This diffuses into the interstitial space.

## Reabsorption of Bicarbonate






## Secretion of $H^+$

- Aside from the $Na^+/H^+$ pumps in the proximal tubule, the distal tubule has $H^+$ ATPase pumps to increase $H^+$ secretion.

## pH Disturbances

- Alkalosis: Less $H^+$ is available to transport bicarbonate into tubule cells, so less bicarbonate is reabsorbed.
  - Extra bicarbonate secretion compensates for alkalosis.

## pH Disturbances

- Acidosis: Proximal tubule can make extra bicarbonate through the metabolism of the amino acid glutamine.
  - Extra bicarbonate enters the blood to compensate for acidosis.
  - Ammonia stays in urine to buffer $H^+$.

## pH Disturbances



**Table 17.7 | Categories of Disturbances in Acid-Base Balance**

| | Bicarbonate (mEq/L)* | | |
|---|---|---|---|
| $P_{CO_2}$ (mmHg) | *Less than 21* | *21–26* | *More than 26* |
| More than 45 | Combined metabolic and respiratory acidosis | Respiratory acidosis | Metabolic alkalosis and respiratory acidosis |
| 35–45 | Metabolic acidosis | Normal | Metabolic alkalosis |
| Less than 35 | Metabolic acidosis and respiratory alkalosis | Respiratory alkalosis | Combined metabolic and respiratory alkalosis |

*mEq/L = milliequivalents per liter. This is the millimolar concentration of $HCO_3^-$ multiplied by its valence (× 1).

## Urinary Buffers

- Nephrons cannot produce urine with a pH below 4.5.
- To increase $H^+$ secretion, urine must be buffered.
  - Phosphates and ammonia buffer the urine.
  - Phosphates enter via filtration.
  - Ammonia comes from the deamination of amino acids.

## VI. Clinical Applications

## Diuretics

- Used clinically to control blood pressure and relieve edema (fluid accumulation)
  - Diuretics increase urine volume, decreasing blood volume and interstitial fluid volume.
  - Many types act on different portions of the nephron.

## Types of Diuretics

- Loop diuretics: most powerful; inhibit salt transport out of ascending loop of Henle
  - Example: Lasix
  - Can inhibit up to 25% of water reabsorption
- Thiazide diuretics: inhibit salt transport in distal tubule
  - Can inhibit up to 8% of water reabsorption

## Types of Diuretics

- Carbonic anhydrase inhibitors: much weaker; inhibit water reabsorption when bicarbonate is reabsorbed
  - Also promote excretion of bicarbonate
- Osmotic diuretics: reduce reabsorption of water by adding extra solutes to the filtrate
  - Example: Mannitol
  - Can occur as a side effect of diabetes

## Types of Diuretics

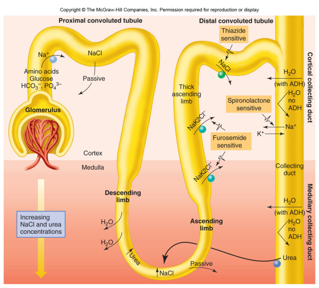
- Potassium-sparing diuretics: Aldosterone antagonists block reabsorption of $Na^+$ and secretion of $K^+$.



**Table 17.8 | Actions of Different Classes of Diuretics**

| Category of Diuretic | Example | Mechanism of Action | Major Site of Action |
|---|---|---|---|
| Loop diuretics | Furosemide | Inhibits sodium transport | Thick segments of ascending limbs |
| Thiazides | Hydrochlorothiazide | Inhibits sodium transport | Last part of ascending limb and first part of distal tubule |
| Carbonic anhydrase inhibitors | Acetazolamide | Inhibits reabsorption of bicarbonate | Proximal tubule |
| Osmotic diuretics | Mannitol | Reduces osmotic reabsorption of water by reducing osmotic gradient | Last part of distal tubule and cortical collecting duct |
| Potassium-sparing diuretics | Spironolactone | Inhibits action of aldosterone | Last part of distal tubule and cortical collecting duct |
| | Triamterene | Inhibits $Na^+$ reabsorption and $K^+$ secretion | Last part of distal tubule and cortical collecting duct |

## Action of Diuretics




## Renal Function Tests

- PAH and inulin clearance
  - Can diagnose nephritis or renal insufficiency
- Urinary albumin excretion rate: detects above-normal albumin excretion
  - Called microalbuminuria
  - Signifies renal damage due to hypertension or diabetes
- Proteinuria: overexcretion of proteins; signifies nephrotic syndrome

## Acute Renal Failure

- Ability of kidneys to regulate blood volume, pH, and solute concentrations crashes in a matter of hours/days.
  - Usually due to decreased blood flow through kidneys due to:
    - Atherosclerosis of renal arteries
    - Inflammation of renal tubules
    - Use of certain drugs (NSAIDs)

## Glomerulonephritis

- Inflammation of the glomerulus
  - Autoimmune disease
  - Many glomeruli are destroyed, and others are more permeable to proteins.
  - Loss of proteins from blood reduces blood osmotic pressure and leads to edema.

## Renal Insufficiency

- Any reduction in renal activity
  - Can be caused by glomerulonephritis, diabetes, atherosclerosis, or blockage by kidney stones
  - Can lead to high blood pressure, high blood $K^+$ and $H^+$, and uremia = urea in the blood.
  - Patients with uremia are placed on a dialysis machine to clear blood of these solutes.