Physiology 12

Kidney and Fluid regulation

Guyton Ch 20, 21,22,23

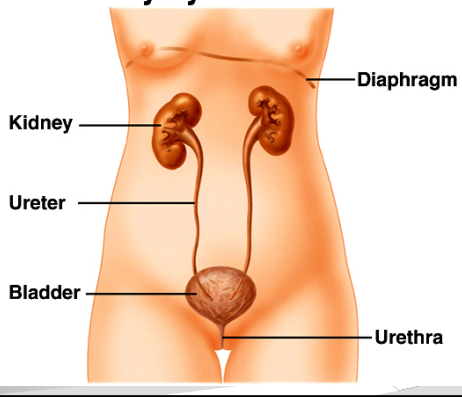
Roles of the Kidney

- 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

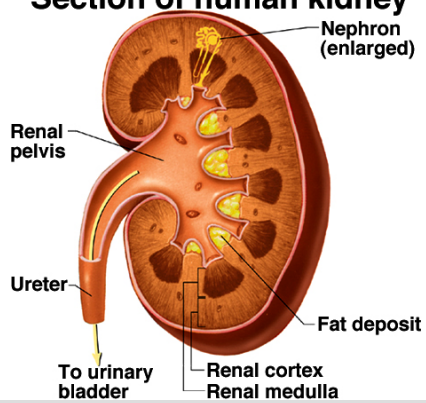
Renal Physiology
The Nephron and GFR

- Kidney Gross Anatomy
- The Nephron
- Glomerular Filtration Rate (GFR)
- Regulation of GFR

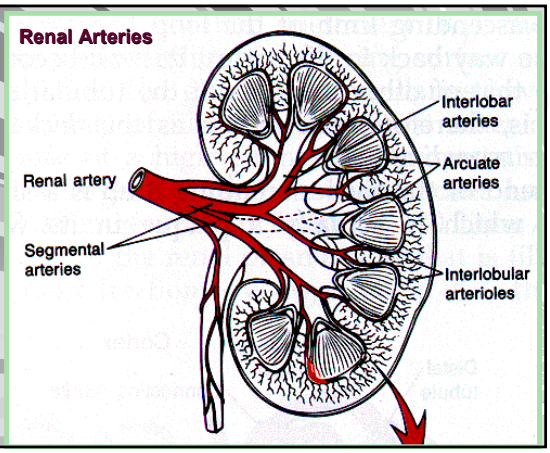
Urinary system/woman

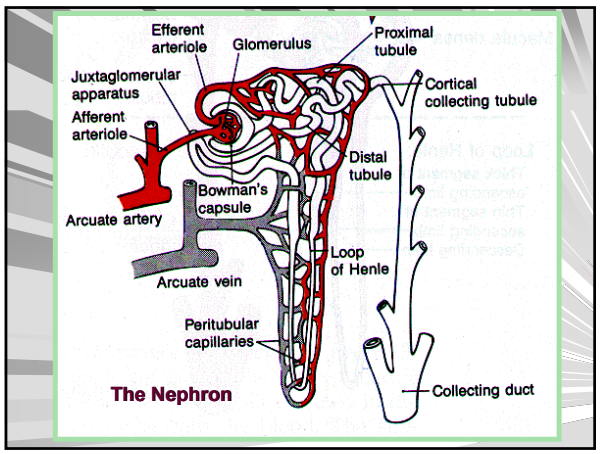


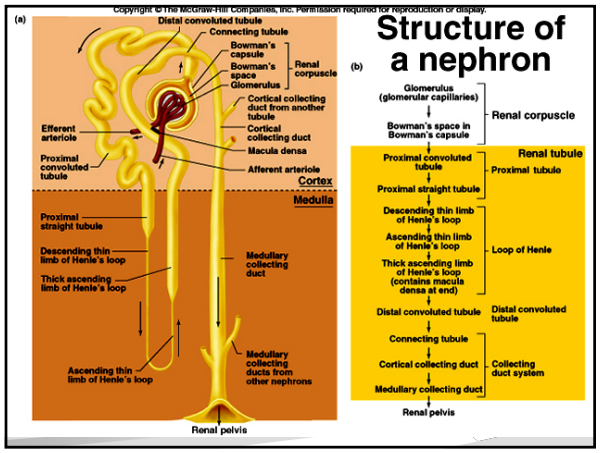
Section of human kidney

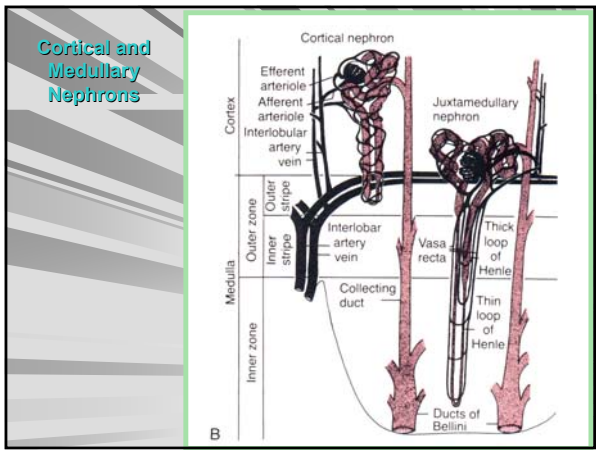


Renal Arteries

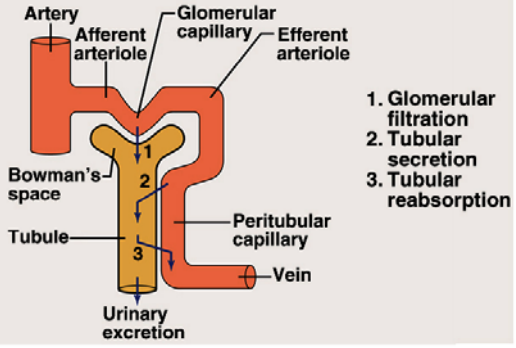



Efferent arteriole
Glomerulus
Proximal tubule
Juxtaglomerular apparatus
Cortical collecting tubule
Afferent arteriole
Distal tubule
Bowman's capsule
Arcuate artery
Loop of Henle
Arcuate vein
Peritubular capillaries
The Nephron
Collecting duct


Structure of a nephron
Distal convoluted tubule
Connecting tubule
Bowman's capsule
Bowman's space
Glomerulus
Renal corpuscle
Cortical collecting duct from another tubule
Efferent arteriole
Cortical collecting duct
Macula densa
Proximal convoluted tubule
Afferent arteriole
Cortex
Medulla
Proximal straight tubule
Descending thin limb of Henle's loop
Medullary collecting duct
Thick ascending limb of Henle's loop
Medullary collecting ducts from other nephrons
Ascending thin limb of Henle's loop
Renal pelvis
Glomerulus (glomerular capillaries)
Bowman's space in Bowman's capsule
Renal corpuscle
Renal tubule
Proximal convoluted tubule
Proximal tubule
Proximal straight tubule
Descending thin limb of Henle's loop
Ascending thin limb of Henle's loop
Loop of Henle
Thick ascending limb of Henle's loop (contains macula densa at end)
Distal convoluted tubule
Distal convoluted tubule
Connecting tubule
Cortical collecting duct
Collecting duct system
Medullary collecting duct
Renal pelvis

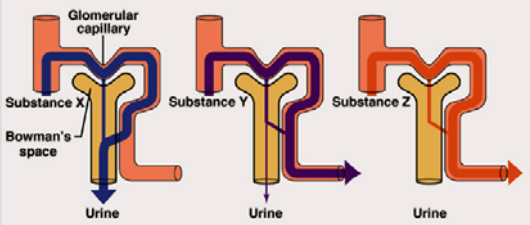

Cortical and Medullary Nephrons
Cortical nephron
Efferent arteriole
Afferent arteriole
Interlobular artery
vein
Cortex
Juxtamedullary nephron
Outer stripe
Outer zone
Inner stripe
Medulla
Interlobar artery
vein
Vasa recta
Thick loop of Henle
Collecting duct
Thin loop of Henle
Inner zone
Ducts of Bellini
B

Components of renal function

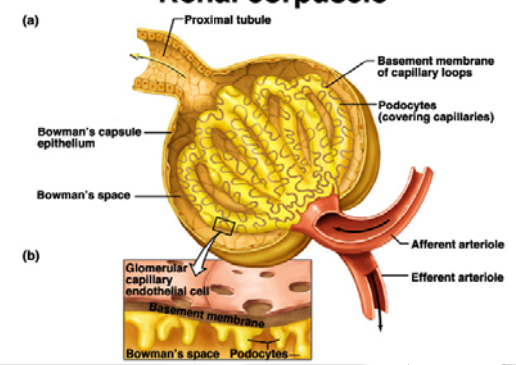


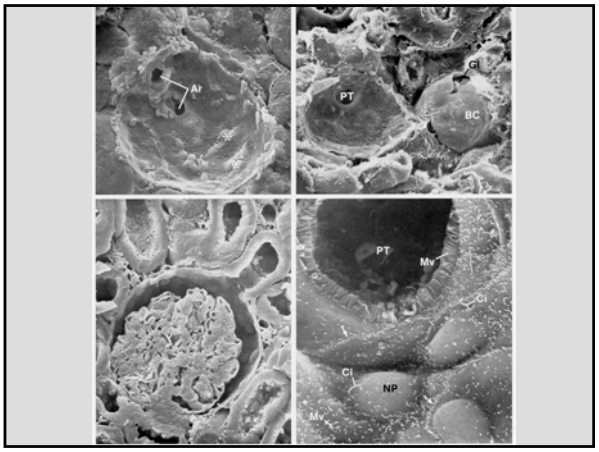
1. Glomerular filtration
2. Tubular secretion
3. Tubular reabsorption

Renal handling



Renal corpuscle





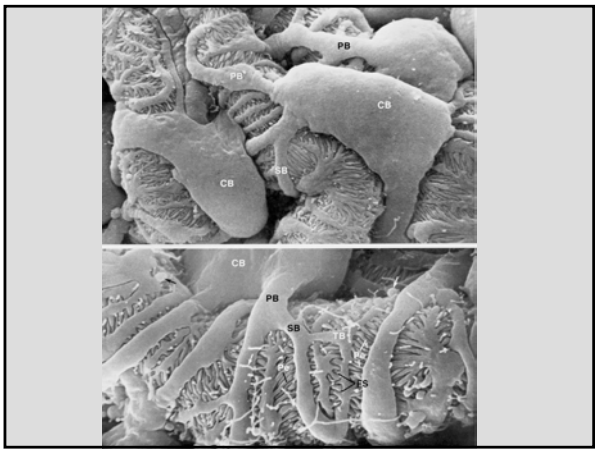


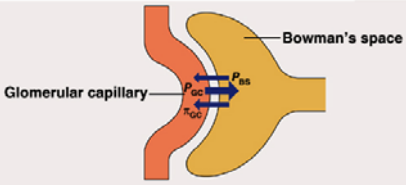
TABLE 21–1 FILTERABILITY OF SUBSTANCES BY GLOMERULAR CAPILLARIES DECREASES WITH INCREASING MOLECULAR WEIGHT

Substance	Molecular Weight	Filterability
Water	18	1.0
Sodium	23	1.0
Glucose	180	1.0
Inulin	5,500	1.0
Myoglobin	17,000	0.75
Albumin	69,000	0.005

Glomerular Filtration Rate (GFR)

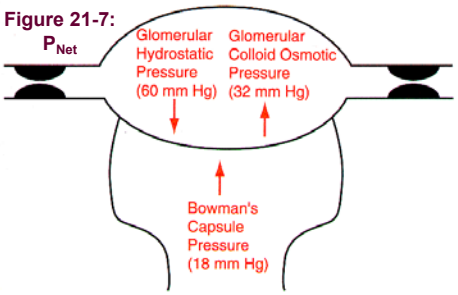
- Glomerular capillaries have higher filter rate than other capillaries
  - Due to higher hydrostatic pressure and leakier capillaries
- GFR = 125 ml/min = 180 L/day
- Filtered fraction =
  GFR/Renal plasma flow = 20%

Glomerular filtration



Forces	mmHg
Favoring filtration:	
Glomerular capillary blood pressure (P_{GC})	60
Opposing filtration:	
Fluid pressure in Bowman's space (P_{BS})	15
Osmotic force due to protein in plasma (π_{GC})	29
Net glomerular filtration pressure = $P_{GC} - P_{BS} - \pi_{GC}$	16

Figure 21-7:

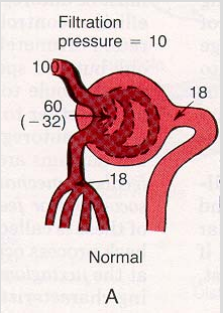


$P_{Net} = P_G - P_B - \pi_G$

Net Filtration Pressure (10 mm Hg) = Glomerular Hydrostatic Pressure (60 mm Hg) − Bowman's Capsule Pressure (18 mm Hg) − Glomerular Oncotic Pressure (32 mm Hg)

Influences on GFR

- GFR = K_f x 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



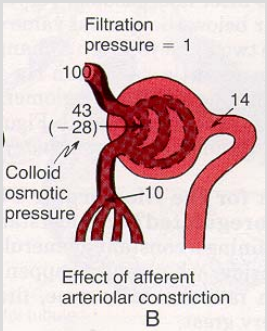
Capillary Pressure (out) = 60 mmHg

Bowmans Pressure (in) = 18 mmHg

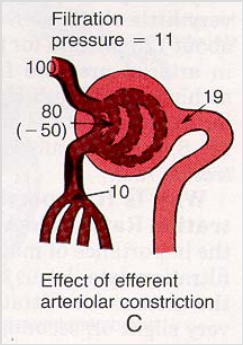
Plasma Colloidal (in) = 32 mmHg

Bowman's Colloidal (out) = 0 mmHg

10 mmHg outward pressure



↑ Afferent Constriction = ↓ Filtration



↑ Efferent Constriction = ↑ Filtration

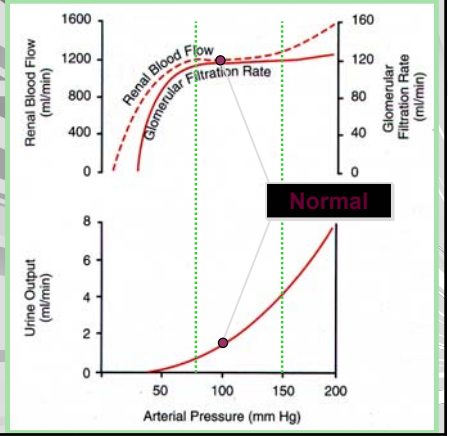
GFR Increases with:

- 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

Figure 21-9:
Autoregulation of Renal Blood Flow and GFR

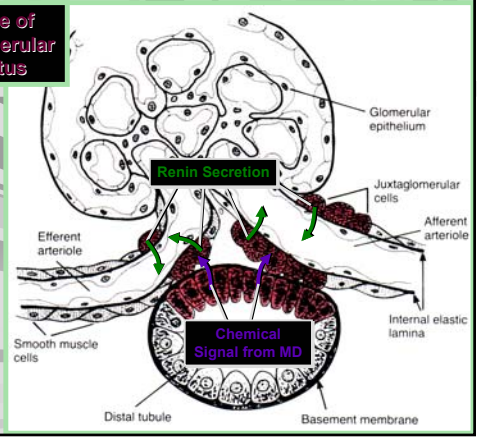


Pressure Diuresis

Autoregulation of GFR

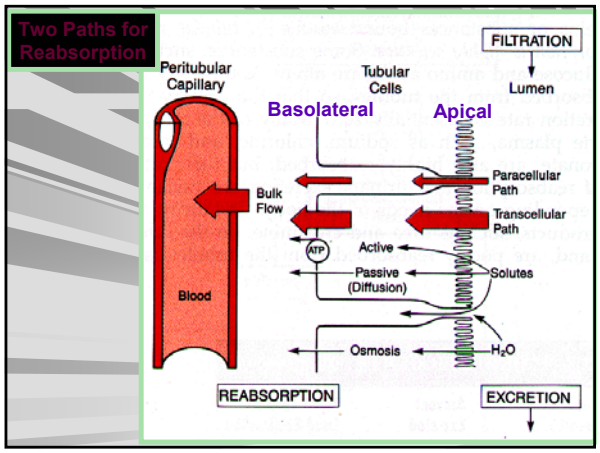
- Mediated by Tubuloglomerular Feedback
- Low NaCl (flow) at Macula Densa:
  - Lowers afferent arteriolar resistance (?)
  - Raises efferent arteriolar resistance (AII)
- Macula Densa also regulates renal BP via renin-angiotensin-aldosterone

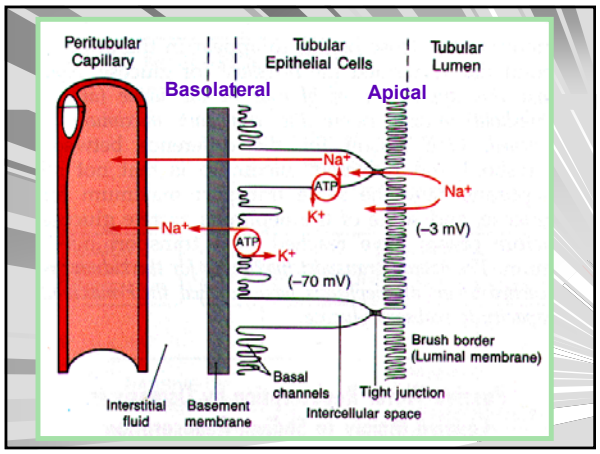
Structure of Juxtaglomerular Apparatus

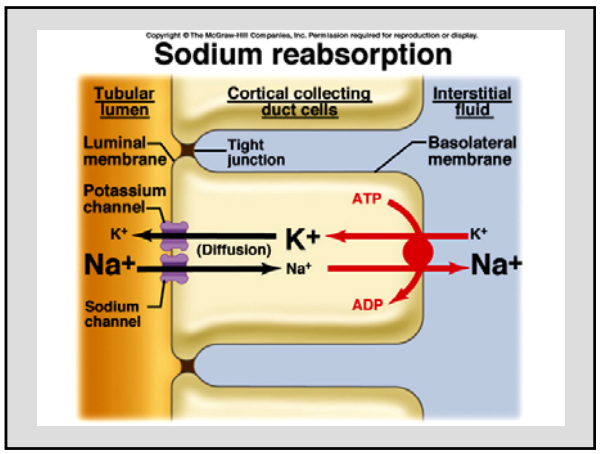


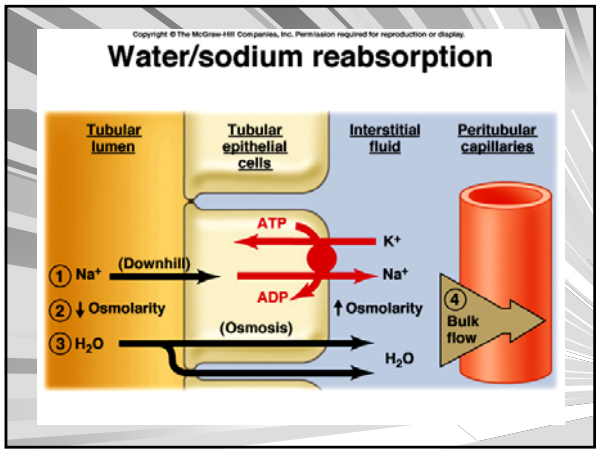
Renal Physiology
Filtration and Reabsorption

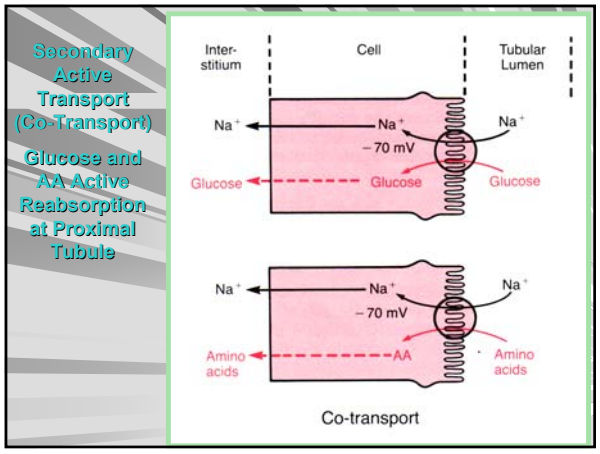
- 1° and 2° Active Transport
  - Passive diffusion of Cl, urea, water
- Saturable reabsorption of glucose & AAs
- Tour of reabsorption and secretion along the tubule
- Renal Clearance





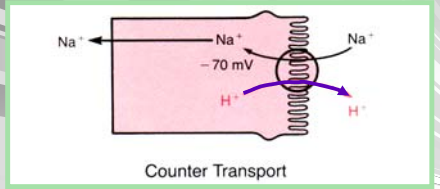

Sodium reabsorption
Tubular lumen
Cortical collecting duct cells
Interstitial fluid
Luminal membrane
Tight junction
Basolateral membrane
Potassium channel
ATP
K+
(Diffusion)
K+
K+
Na+
Na+
Na+
ADP
Sodium channel


Water/sodium reabsorption
Tubular lumen
Tubular epithelial cells
Interstitial fluid
Peritubular capillaries
ATP
K+
1 Na+
(Downhill)
Na+
ADP
2 ↓ Osmolarity
↑ Osmolarity
(Osmosis)
4 Bulk flow
3 H2O
H2O


Secondary Active Transport (Co-Transport)
Glucose and AA Active Reabsorption at Proximal Tubule
Inter-stitium
Cell
Tubular Lumen
Na+
Na+
Na+
– 70 mV
Glucose
Glucose
Glucose
Na+
Na+
Na+
– 70 mV
Amino acids
AA
Amino acids
Co-transport

Secondary Active Transport (Counter Transport)

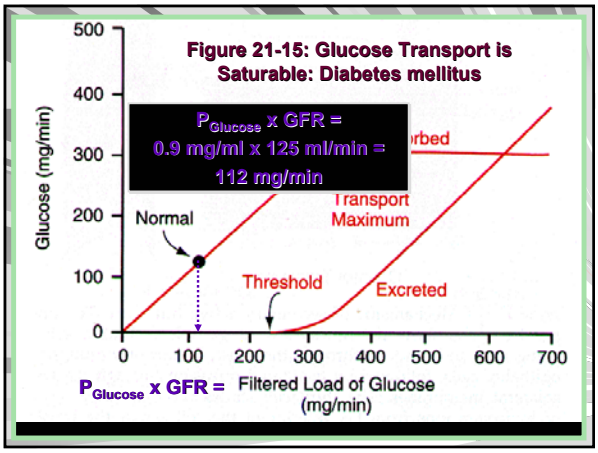
H^+ Secretion

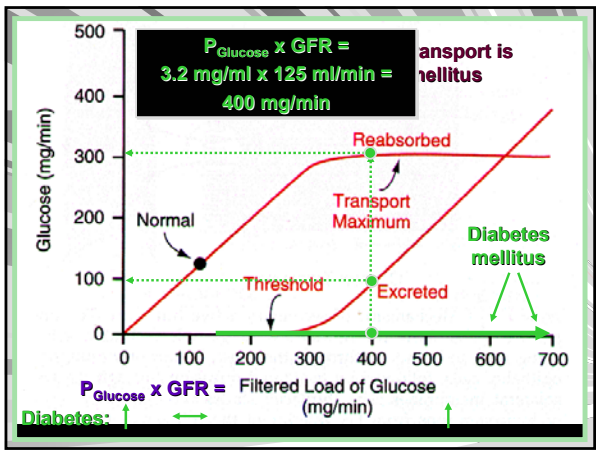


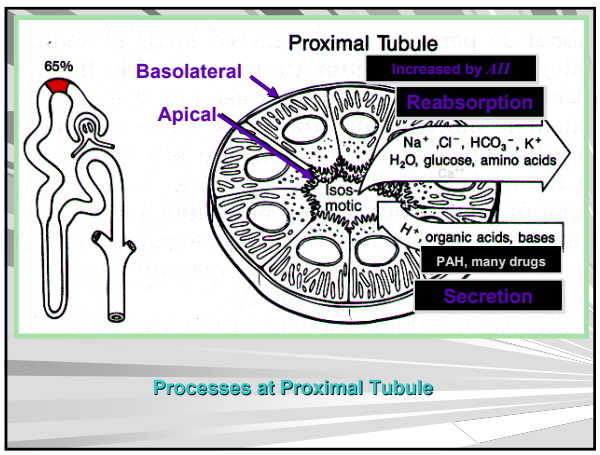
Counter Transport

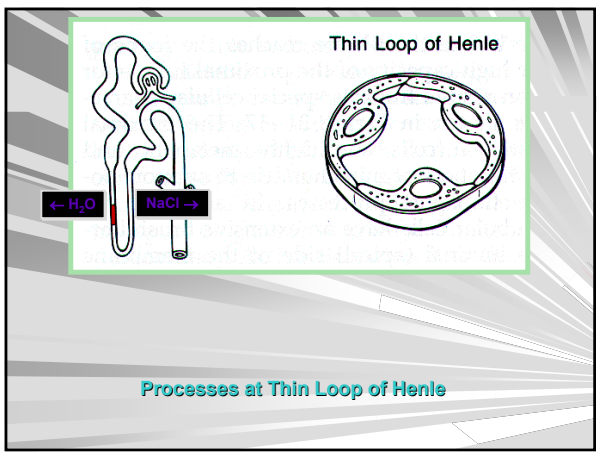
Filtration

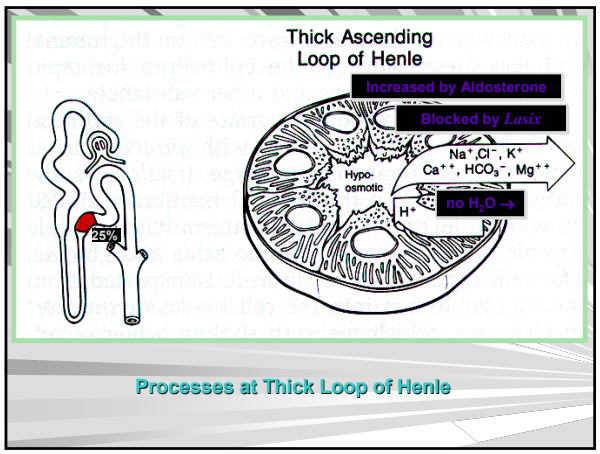
- Filtration = P_S x GFR, where P_S is the plasma concentration of substance S
- This represent the tubular load or filtered load that must be handled
- Units: mg/ml x ml/min = mg/min



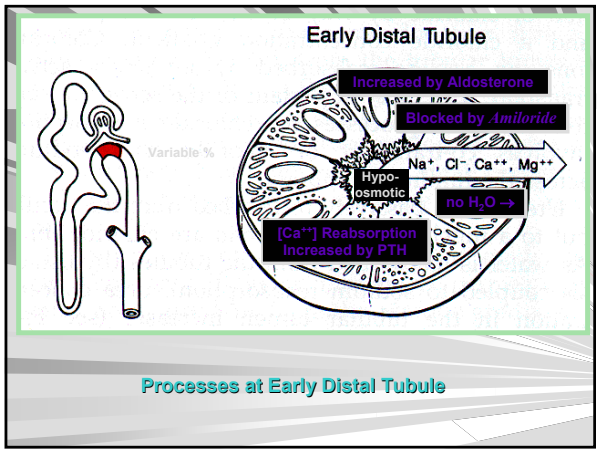

$P_{Glucose}$ x GFR =
3.2 mg/ml x 125 ml/min =
400 mg/min
ansport is
ellitus
Glucose (mg/min)
500
400
300
200
100
0
Reabsorbed
Transport
Maximum
Normal
Diabetes
mellitus
Threshold
Excreted
0
100
200
300
400
500
600
700
$P_{Glucose}$ x GFR =
Filtered Load of Glucose
(mg/min)
Diabetes:


Proximal Tubule
65%
Basolateral
Apical
Increased by AII
Reabsorption
Na^+ ,Cl^-, HCO_3^-, K^+
H_2O, glucose, amino acids
Isos-
motic
H^+, organic acids, bases
PAH, many drugs
Secretion
Processes at Proximal Tubule


Thin Loop of Henle
← H_2O
NaCl →
Processes at Thin Loop of Henle



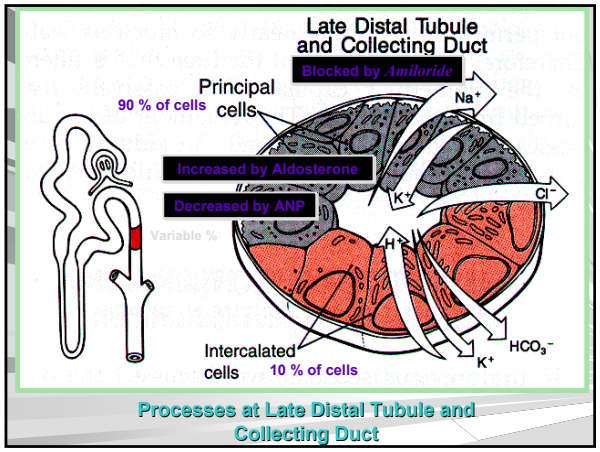
Processes at Thick Loop of Henle

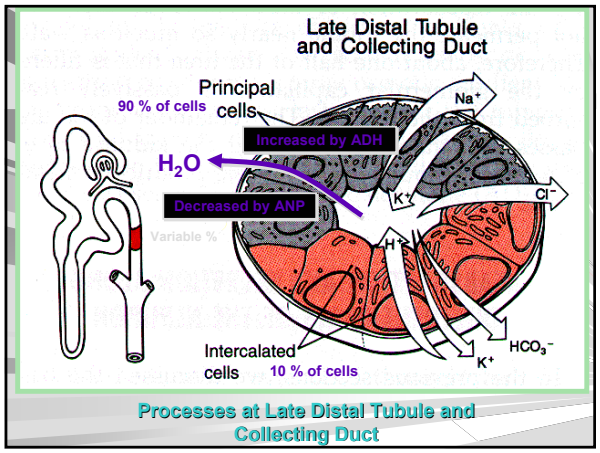


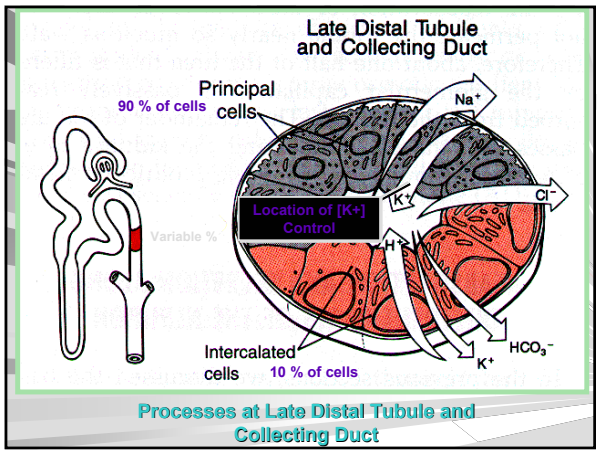
Processes at Early Distal Tubule

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

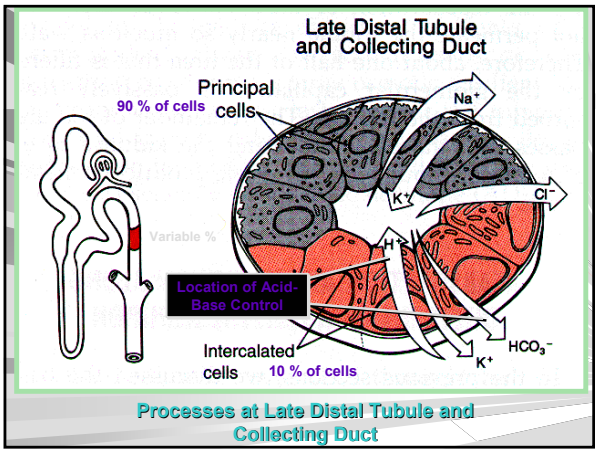

Late Distal Tubule
and Collecting Duct
Blocked by Amiloride
Principal
cells
90 % of cells
Increased by Aldosterone
Decreased by ANP
Variable %
Intercalated
cells
10 % of cells
Na+
K+
Cl−
H+
K+
HCO3−
Processes at Late Distal Tubule and
Collecting Duct


Late Distal Tubule
and Collecting Duct
Principal
cells
90 % of cells
Increased by ADH
H2O
Decreased by ANP
Variable %
Intercalated
cells
10 % of cells
Na+
K+
Cl−
H+
K+
HCO3−
Processes at Late Distal Tubule and
Collecting Duct


Late Distal Tubule
and Collecting Duct
Principal
cells
90 % of cells
Location of [K+]
Control
Variable %
Intercalated
cells
10 % of cells
Na+
K+
Cl−
H+
K+
HCO3−
Processes at Late Distal Tubule and
Collecting Duct

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

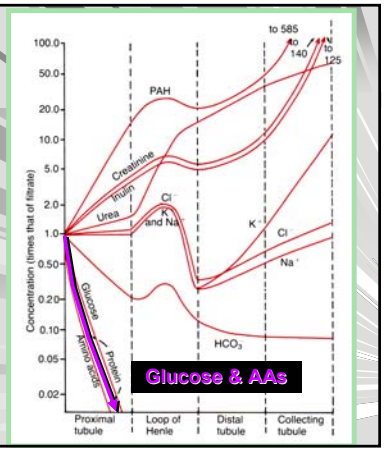
Acid-Base Homeostasis

- Diet usually generates an excess of acid
- Most HCO_3^- is reabsorbed by PT (85%), remainder by TAL and CD
- Controlled by tubule cells, which sense pH and [CO_2]
  - Secrete more H^+ if pH too low
  - Secrete less H^+ if pH too high

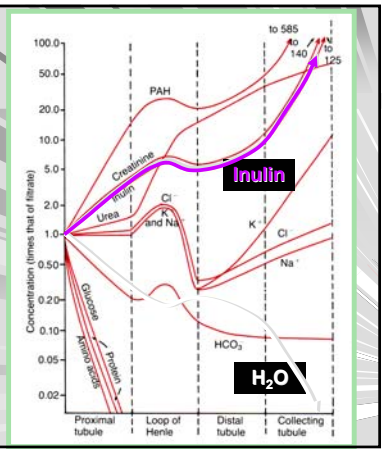
Acid-Base Homeostasis

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

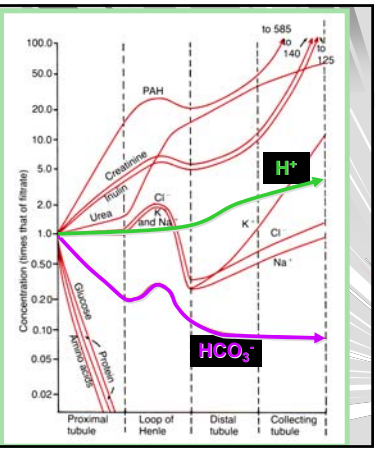
Relative Concentrations of Substances along Tubule



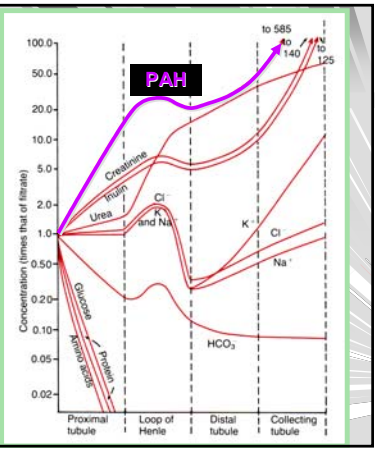
Relative Concentrations of Substances along Tubule



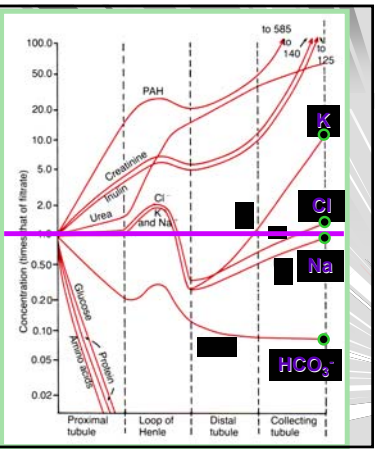
Relative Concentrations of Substances along Tubule



Relative Concentrations of Substances along Tubule



Relative Concentrations of Substances along Tubule



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

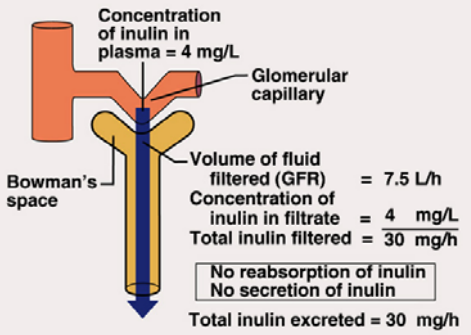
Renal Clearance

- 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 handling of inulin

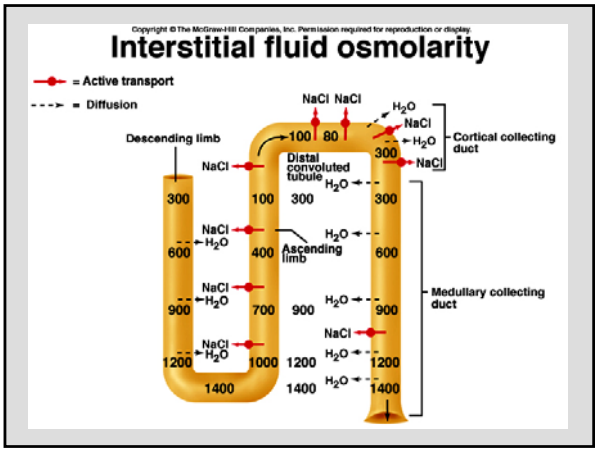


Renal Physiology: Renal Exchange Mechanisms

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.**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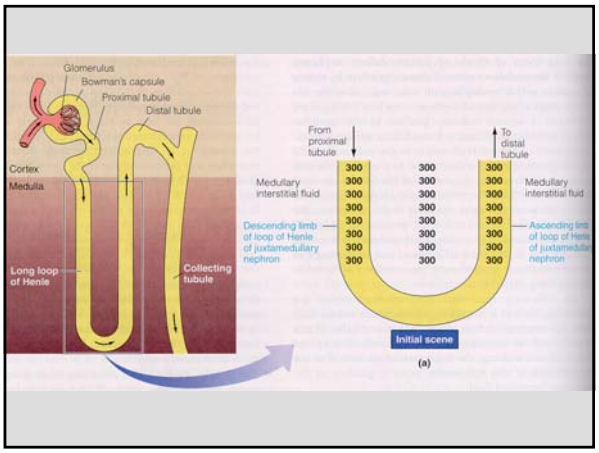
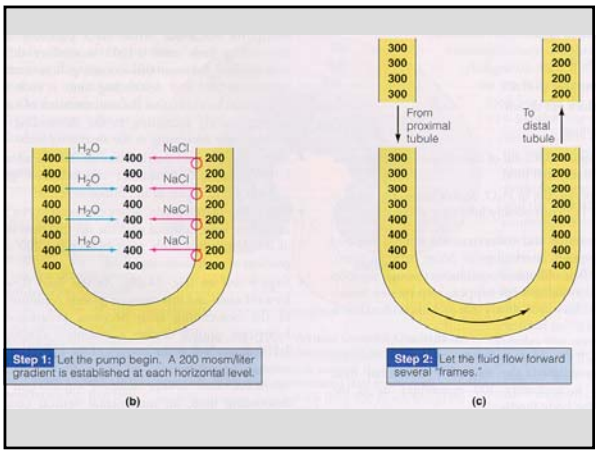
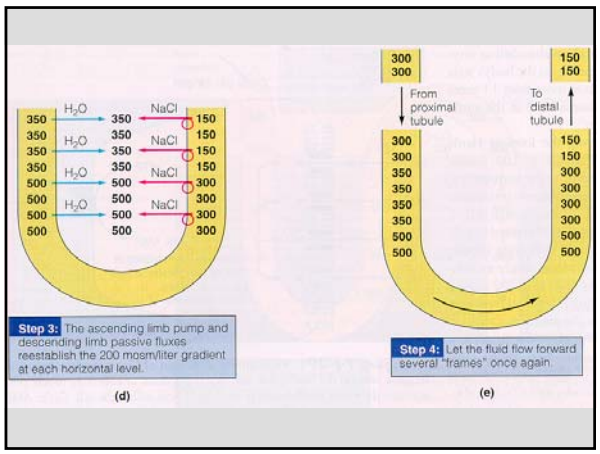
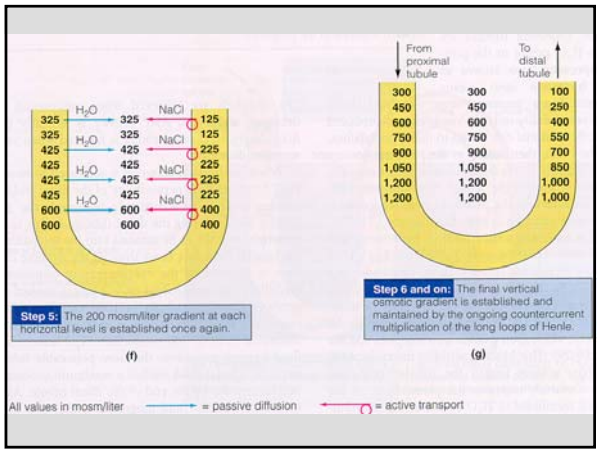
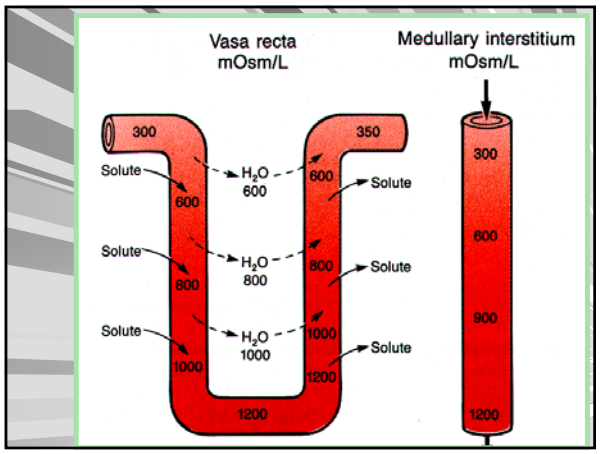
Interstitial fluid osmolarity
= Active transport
= Diffusion
Descending limb
Distal convoluted tubule
Ascending limb
Cortical collecting duct
Medullary collecting duct
NaCl
H_2O
100
80
300
600
400
900
700
1000
1200
1400


Glomerulus
Bowman's capsule
Proximal tubule
Distal tubule
Cortex
Medulla
Long loop of Henle
Collecting tubule
From proximal tubule
To distal tubule
Medullary interstitial fluid
Descending limb of loop of Henle of juxtamedullary nephron
Initial scene
(a)


H_2O
NaCl
Step 1: Let the pump begin. A 200 mosm/liter gradient is established at each horizontal level.
From proximal tubule
To distal tubule
Step 2: Let the fluid flow forward several "frames."
(b)
(c)


H_2O
NaCl
350 350 150
350 350 150
350 350 150
350 500 300
500 500 300
500 500 300
500 500 300
Step 3: The ascending limb pump and descending limb passive fluxes reestablish the 200 mosm/liter gradient at each horizontal level.
(d)
300 300
150 150
From proximal tubule
To distal tubule
300 300 150
300 350 150
350 350 300
350 350 300
350 350 300
500 500 500
500 500 500
Step 4: Let the fluid flow forward several "frames" once again.
(e)


H_2O
NaCl
325 325 125
325 325 125
425 425 225
425 425 225
425 425 225
425 425 225
600 600 400
600 600 400
Step 5: The 200 mosm/liter gradient at each horizontal level is established once again.
(f)
From proximal tubule
To distal tubule
300 300 100
450 450 250
600 600 400
750 750 550
900 900 700
1,050 1,050 850
1,200 1,200 1,000
1,200 1,200 1,000
Step 6 and on: The final vertical osmotic gradient is established and maintained by the ongoing countercurrent multiplication of the long loops of Henle.
(g)
All values in mosm/liter
= passive diffusion
= active transport


Vasa recta mOsm/L
Medullary interstitium mOsm/L
300
Solute
600
H_2O 600
350
600
Solute
300
600
Solute
800
H_2O 800
800
Solute
900
Solute
1000
H_2O 1000
1000
Solute
1200
1200
1200

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.

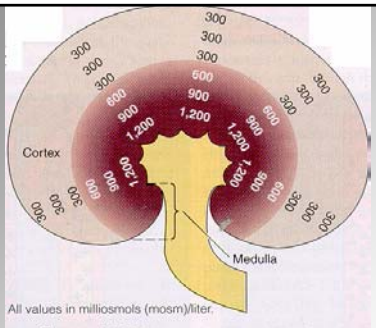
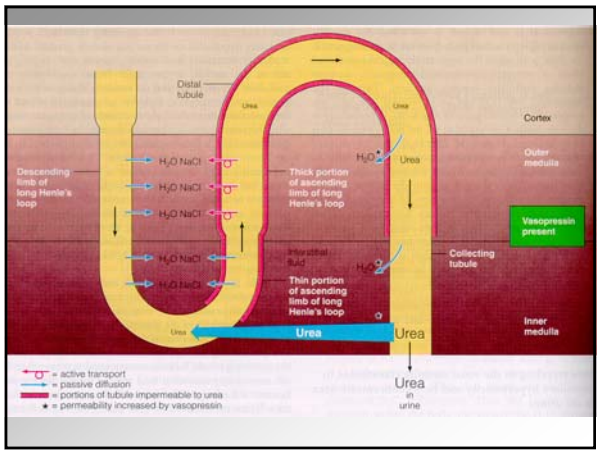
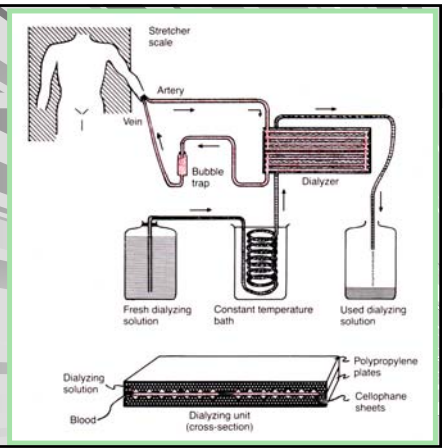


Figure 14-27 **Vertical Osmotic Gradient in the Renal Medulla** The osmolarity of the interstitial fluid throughout the renal cortex is isotonic at 300 mosm/liter, but the osmolarity of the interstitial fluid in the renal medulla increases progressively from 300 mosm/liter at the boundary with the cortex to a maximum of 1,200 mosm/liter at the junction with the renal pelvis.

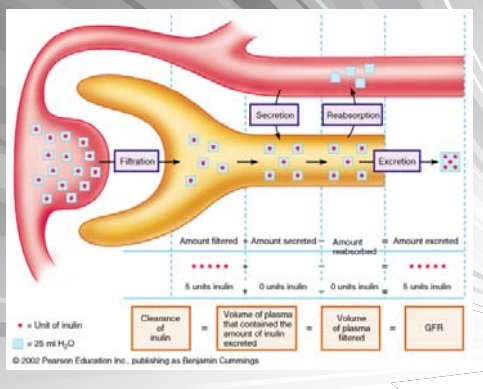


Kidney Dialysis



Regulation of Renal Output and Cardio-vascular Volume Control

Germann Ch 18



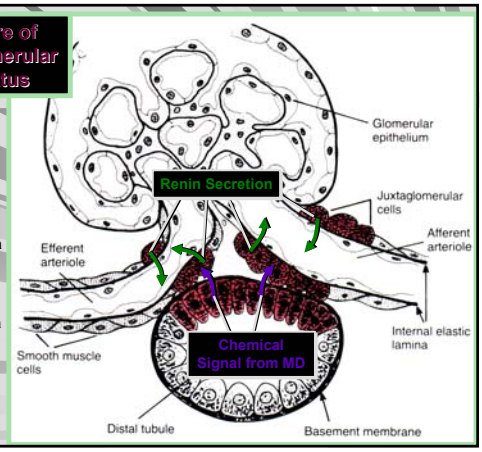
Hormonal Control of Renal Output and Cardiovascular Pressure

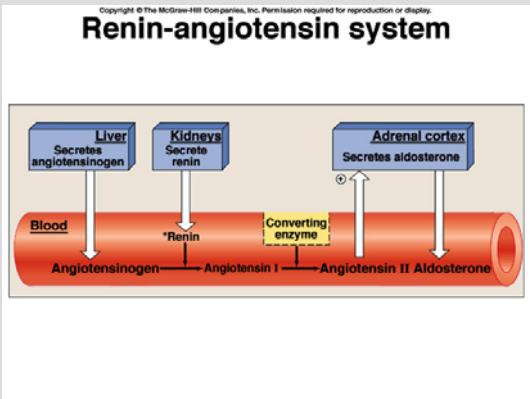
Three main systems:

- **Renin-Angiotension System**
- **Aldosterone**
- **Antidiuretic Hormone**

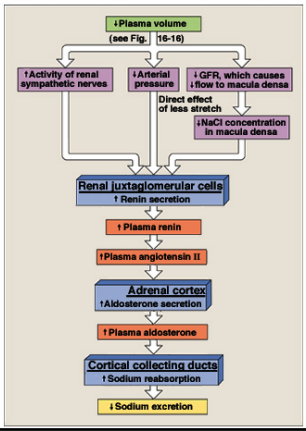
Structure of Juxtaglomerular Apparatus

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





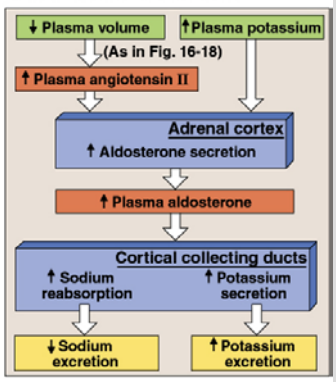
Decreased plasma volume

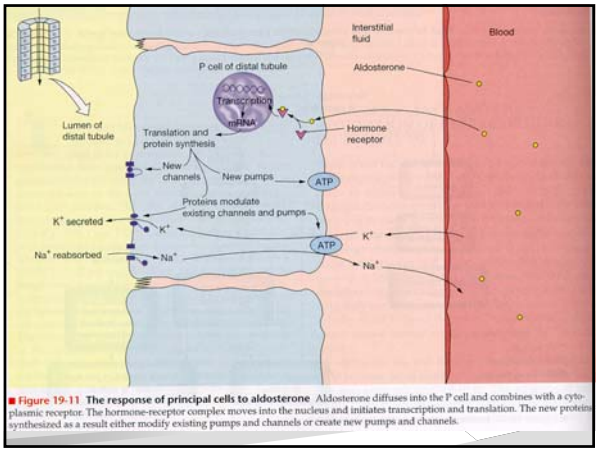


Renin-Angiotension System:

- 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.

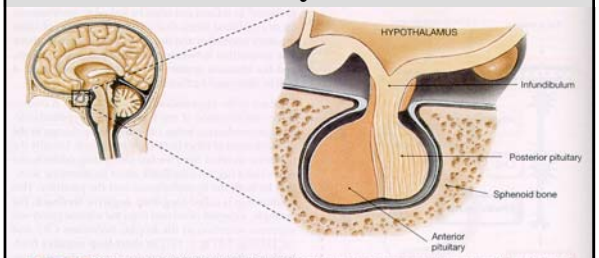
Control of aldosterone





■ Figure 19-11 **The response of principal cells to aldosterone** Aldosterone diffuses into the P cell and combines with a cytoplasmic receptor. The hormone-receptor complex moves into the nucleus and initiates transcription and translation. The new proteins synthesized as a result either modify existing pumps and channels or create new pumps and channels.

Antidiuretic Hormone Regulation of Urine Secretion and Body Fluids

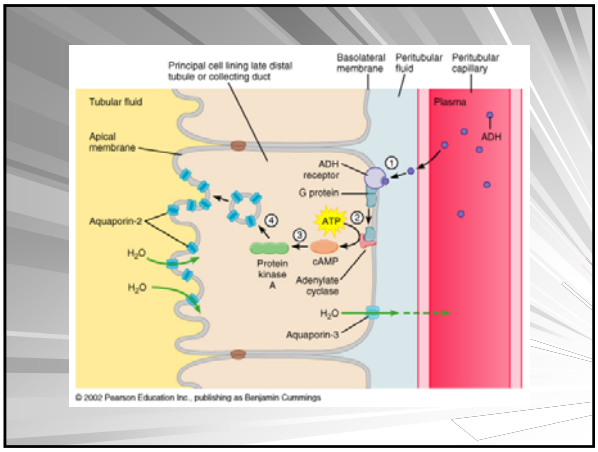


■ Figure 7-12 **Cross section of skull showing pituitary** The pituitary gland is composed of two types of tissue. The posterior pituitary is an extension of the neural tissue of the brain. The anterior pituitary is true endocrine tissue of epithelial origin. The pituitary sits in a protected pocket of bone, connected to the brain by a thin stalk, the infundibulum.

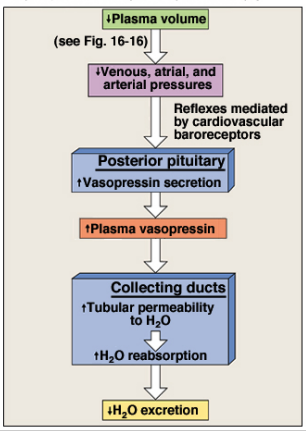
Anteroventral Border of the Third Ventricle (AV3V Nucleus of the Hypothalamus)

↑ extracellular fluid osmolarity - ↑ ADH Secretion

Induce thirst



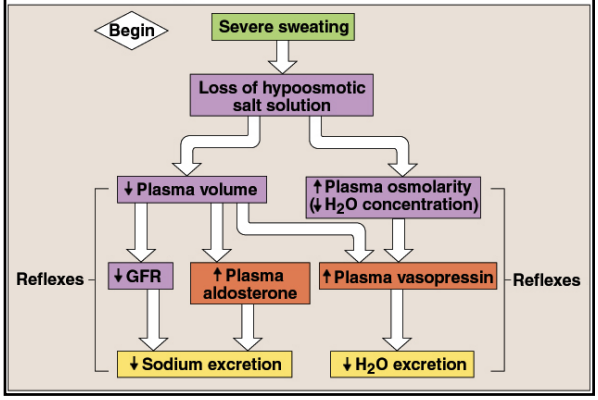
Baroreceptor pathway



ADH effects on the body

- Vasoconstriction
- 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.

Descreasing of sodium/water excretion



Osmoreceptor pathway

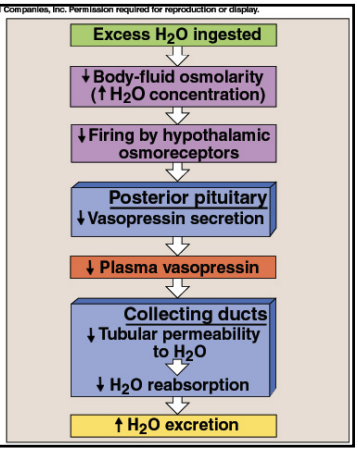


TABLE 21–7 HORMONES THAT REGULATE TUBULAR REABSORPTION

Hormone	Site of Action	Effects
Aldosterone	Distal tubule/collecting duct	↑ NaCl, H_2O reabsorption, ↑ K^+ secretion
Angiotensin II	Proximal tubule	↑ NaCl, H_2O reabsorption, ↑ H^+ secretion
Antidiuretic hormone	Distal tubule/collecting duct	↑ H_2O reabsorption
Atrial natriuretic peptide	Distal tubule/collecting duct	↓ NaCl reabsorption
Parathyroid hormone	Proximal tubules, thick ascending loop of Henle/distal tubules	↓ PO_4^{--} reabsorption, ↑ Ca^{++} reabsorption

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 -

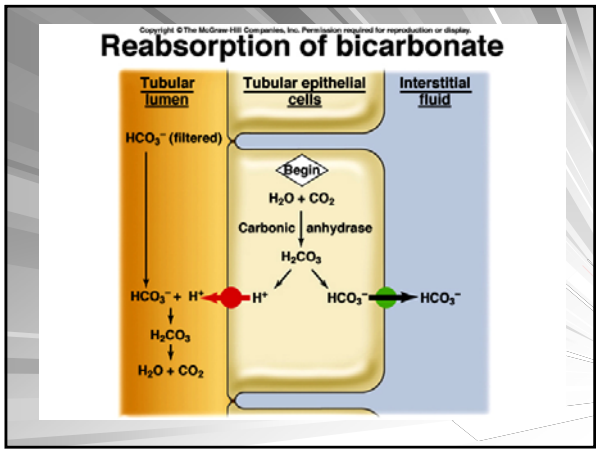
- **Excessive Ingestion of Alkaline Drugs**
- **Excessive Vomiting (loss of Cl-)**
- **Excess Aldosterone (reabsorption of Na+, release of H+)**

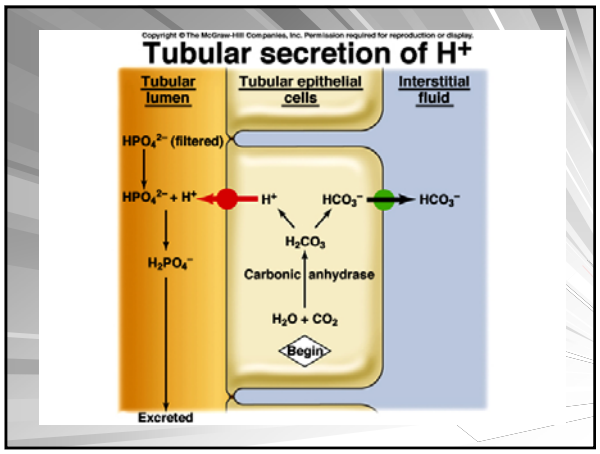
Hydrogen Ion Regulation

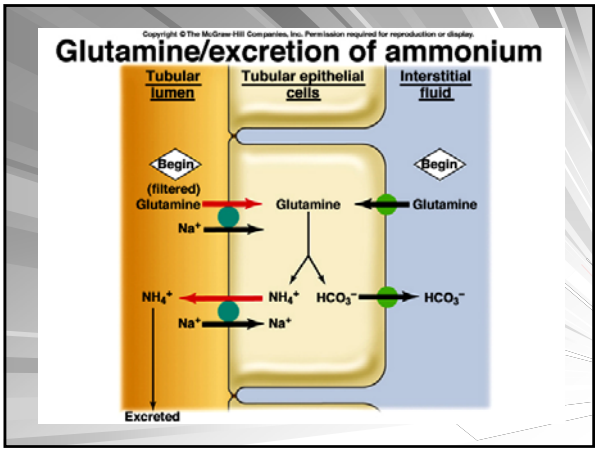
Hydrogen Ion buffer system

Carbonic Anhydrase

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$$



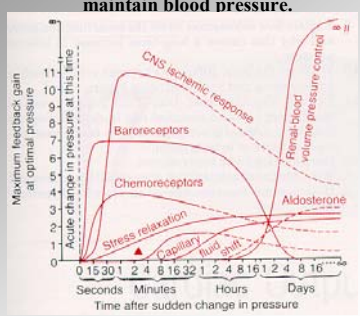




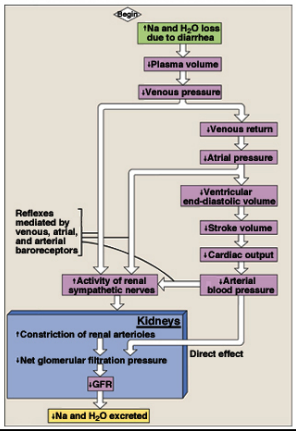
Take home message

- 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.



Reflex pathways



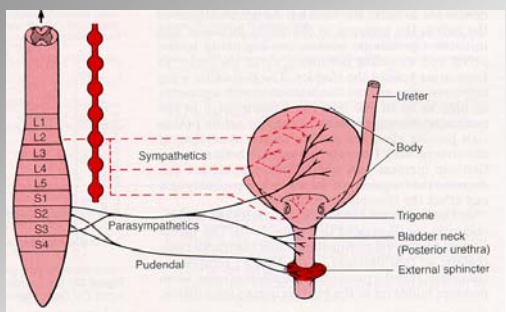
Urea Secretion

~ 30 grams daily

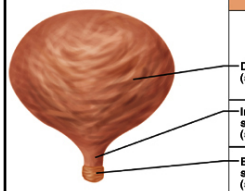
Factors determining excretion:

- Concentration in Plasma
- Glomerular Filtration Rate

Micturition



Control of the bladder



Muscle	Innervation		
	Type	During filling	During micturition
Detrusor (smooth muscle)	Parasympathetic (causes contraction)	Inhibited	Stimulated
Internal urethral sphincter (smooth muscle)	Sympathetic (causes contraction)	Stimulated	Inhibited
External urethral sphincter (skeletal muscle)	Somatic motor (causes contraction)	Stimulated	Inhibited