Urine Formation by the Kidneys Tubular Processing of the Glomerular Filtrate

Chapter 27
pages 327 – 347

OBJECTIVES

At the end of this lecture you should be able to describe:

- Absorptive Characteristics of different parts of nephrons
- Transport Mechanisms operating in nephrons
- Tubular Reabsoprtion and Secretion

NEXT

Characteristics

Volume	1 – 2 liters (quarts) per day (influenced by many factors)
Color	Yellow or Amber (varies with concentration and diet)
Turbidity	Transparent when fresh (becomes cloudy)
Odor	Aromatic (becomes ammonia-like)
pH	Averages 6.0 (ranges between 4.6 and 8.0)
Specific Gravity	1.001 – 1.035 (denser than water)

Organic Solutes

Nitrogenous Wastes	Urea; Creatinine; Uric Acid
Hippuric Acid	Derived from Benzoic Acid
Indican	Derived from Indole
Ketone Bodies	Derived from Triglycerides

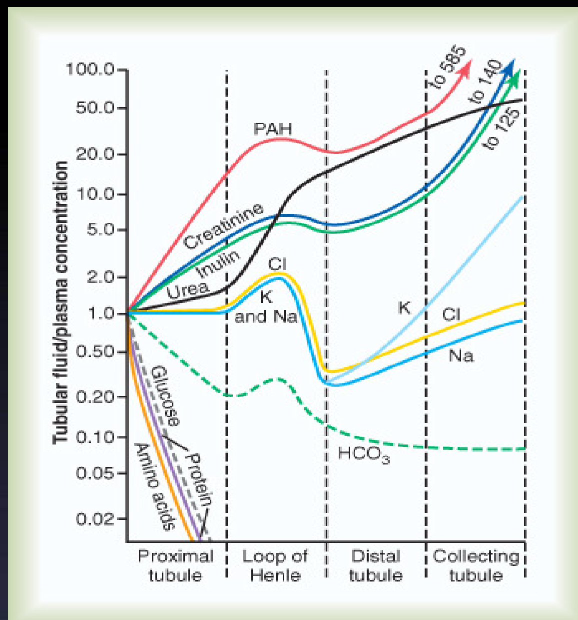
Inorganic Solutes

Cations	Sodium; Potassium; Ammonium; Magnesium; Calcium
Anions	Chloride; Sulfate; Phosphates

URINE COMPOSITION

pH	freshly voided urine is usually acidic (around pH 6), range=4.8 and 7.5
Colour	Bright Yellow & transparent
Specific Gravity	1.002 to 1.030
Volume	1-2 L per day
Albumin	20 μg of albumin per minute (30 mg in 24 hours)
Glucose	None

	Amount Filtered	Amount Reabsorbed	Amount Excreted	% of Filtered Load Reabsorbed
Glucose (g/day)	180	180	0	100
Bicarbonate (mEq/day)	4,320	4,318	2	>99.9
Sodium (mEq/day)	25,560	25,410	150	99.4
Chloride (mEq/day)	19,440	19,260	180	99.1
Potassium (mEq/day)	756	664	92	87.8
Urea (g/day)	46.8	23.4	23.4	50
Creatinine (g/day)	1.8	0	1.8	0



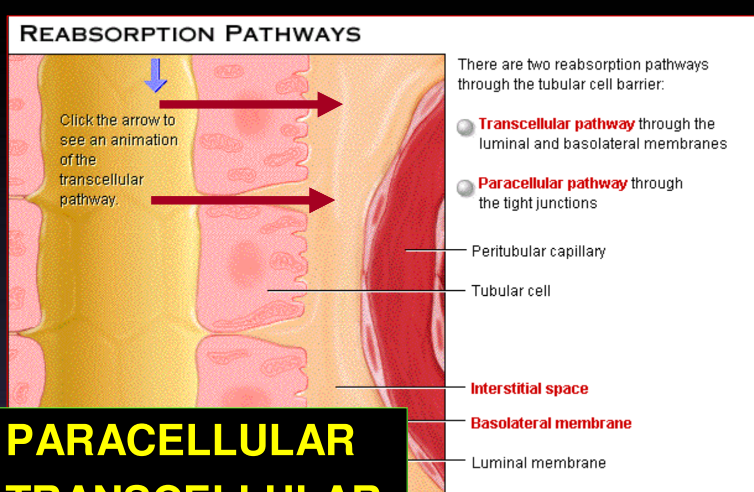
CLASSIFICATION OF TRANSPORT MECHANISMS

- SIMPE DIFFUSION
- FACILITATED DIFFUSION
- PRIMARY ACTIVE TRANSPORT
- SECONDARY ACTIVE TRANSPORT
- PINOCYTOSIS
- BULK FLOW

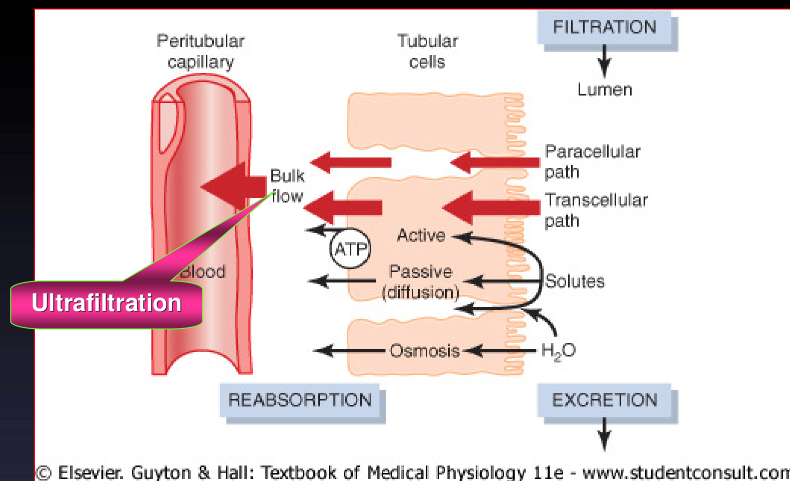
PRIMARY ACTIVE TRANSPORTERS

- Sodium-potassium ATPpase
- Hydrogen ATPpase
- Hydrogen-potassium ATPpase
- Calcium ATPpase.

REABSORTION PATHWAYS

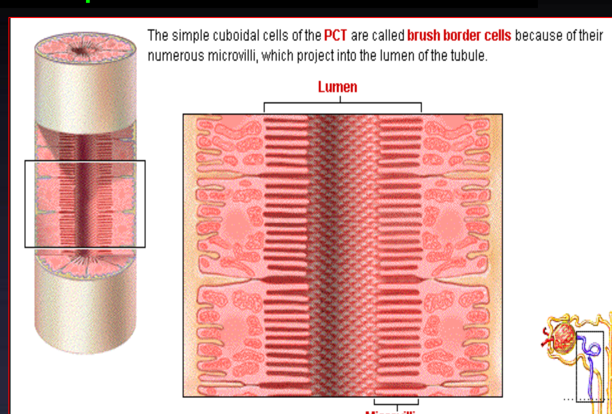


- PARACELLULAR
- TRANSCELLULAR

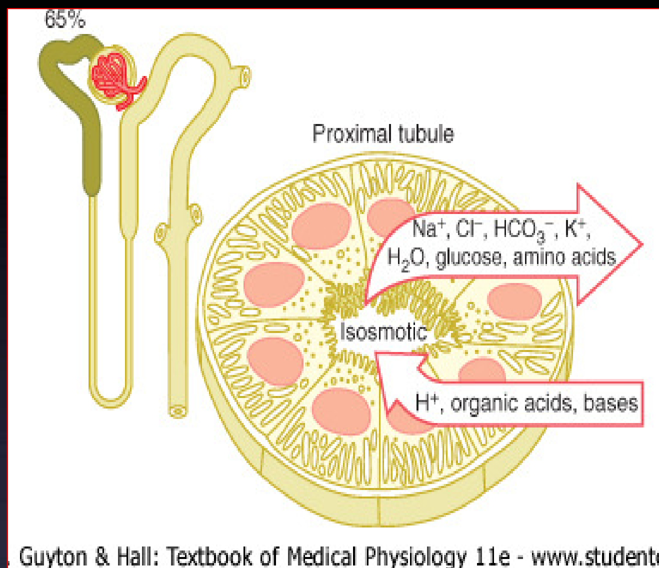


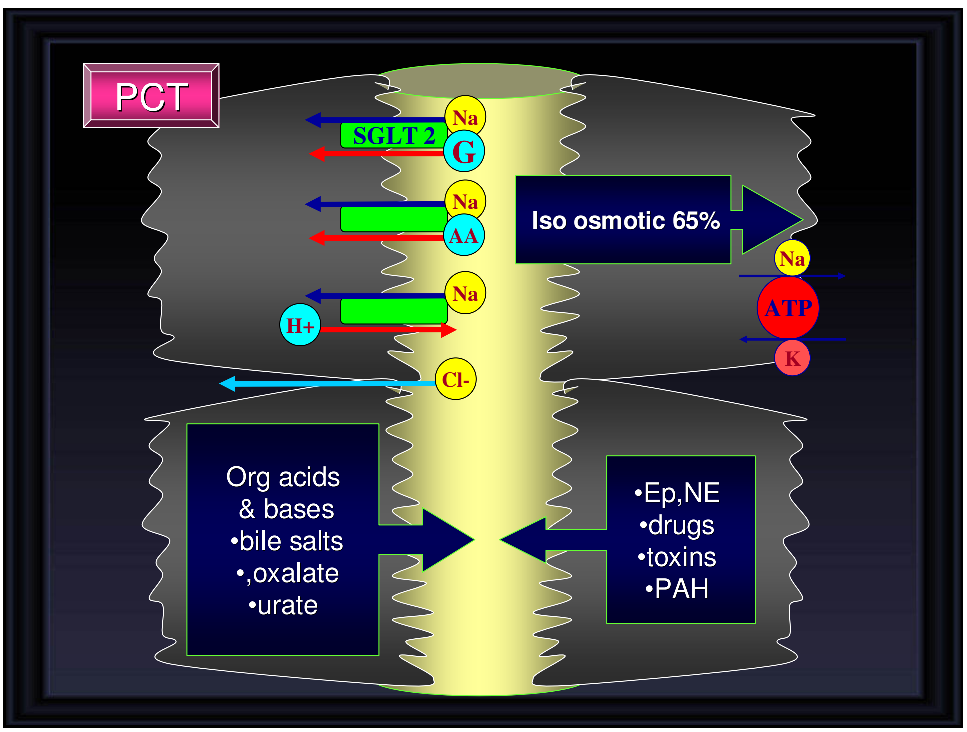
PROXIMAL CONVOLUTED TUBULE

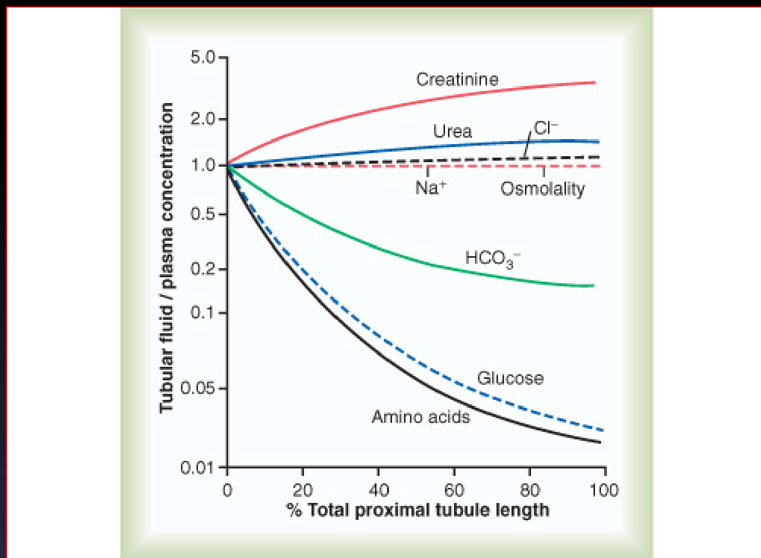
- **many mitochondria**
- **brush border multiplies the surface area about 20-fold.**
- **tight junctions**
- **lateral intercellular spaces.**



PROXIMAL CONVOLUTED TUBULE

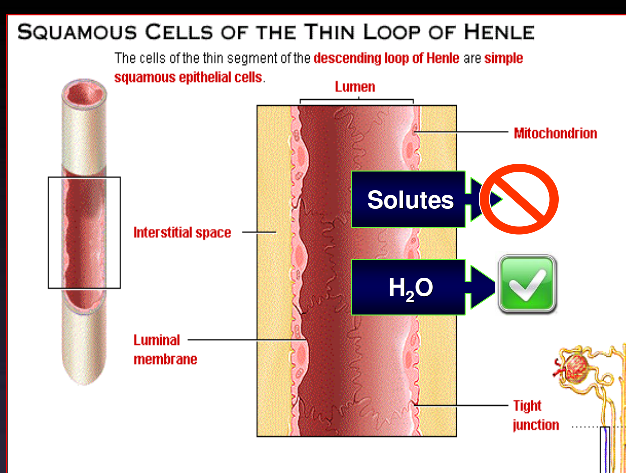




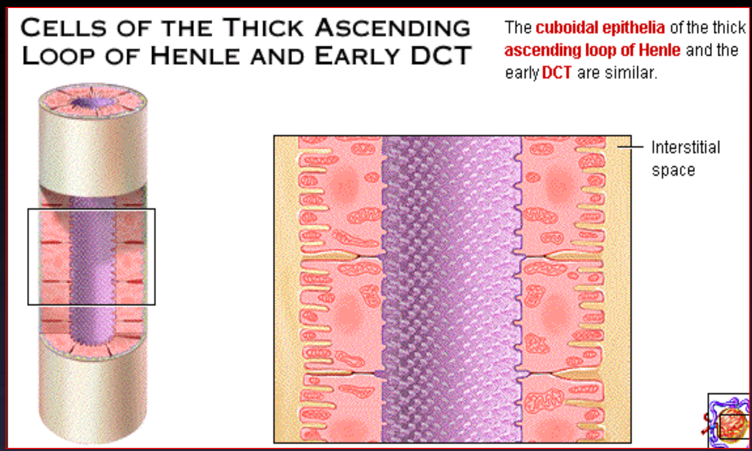


THIN DESCENDING SEGMENT OF LOOP OF HENLE

- few mitochondria
- flattened with few microvilli



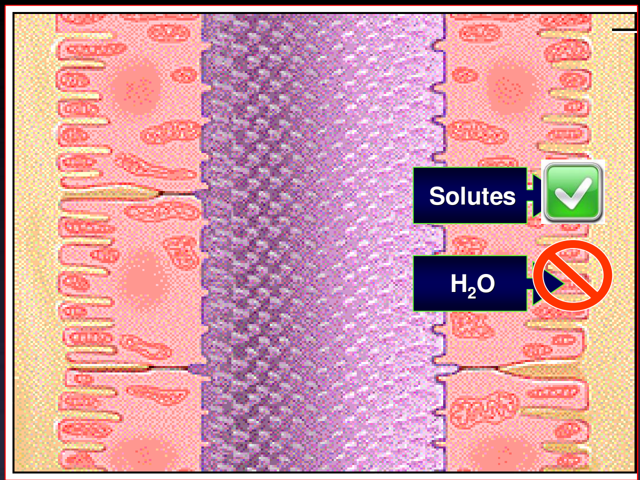
THICK ASCENDING LOOP OF HANLE AND EARLY DCT

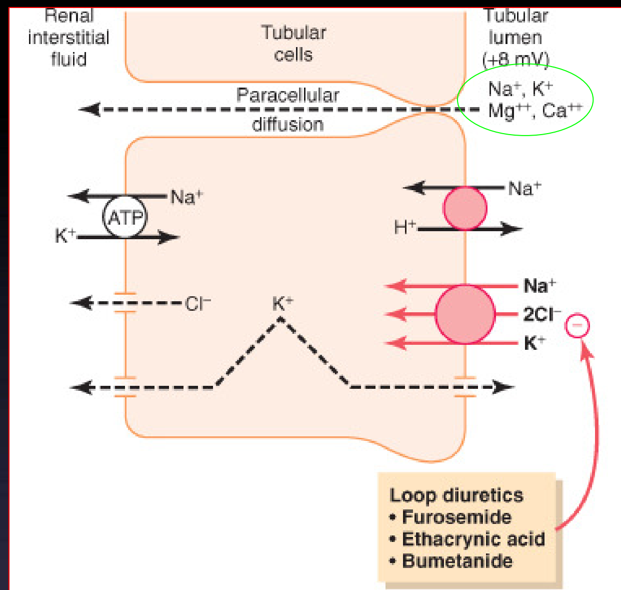


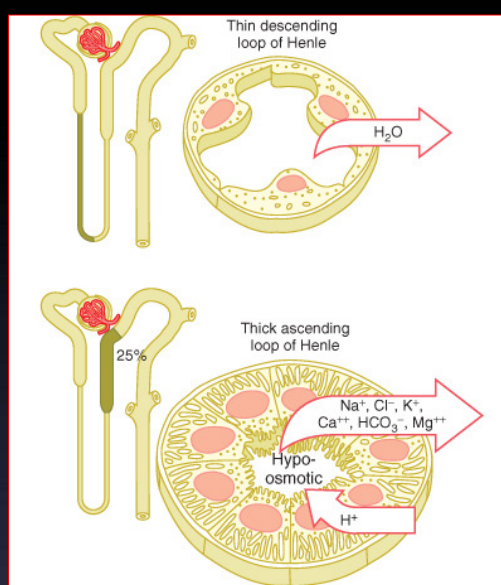
Many mitochondria and microvilli, but fewer than in the proximal tubule

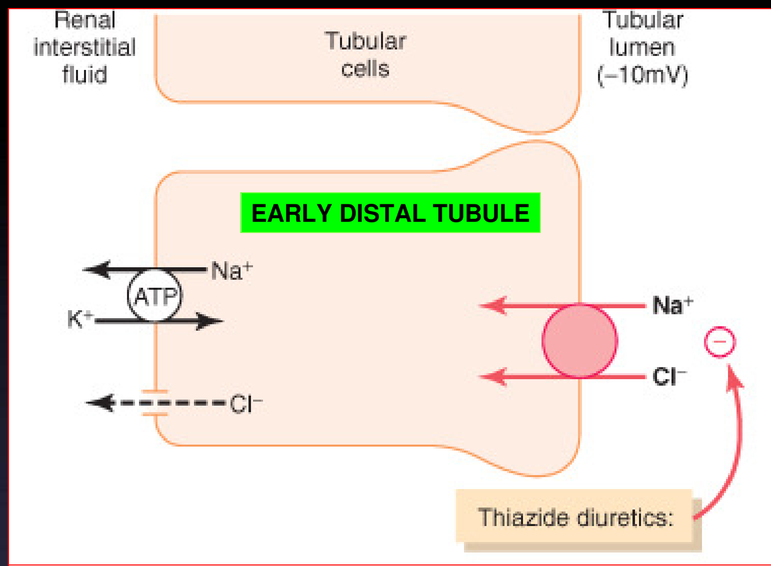
THICK ASCENDING LOOP OF HENLE AND EARLY DCT

Many mitochondria and microvilli, but fewer than in the proximal tubule



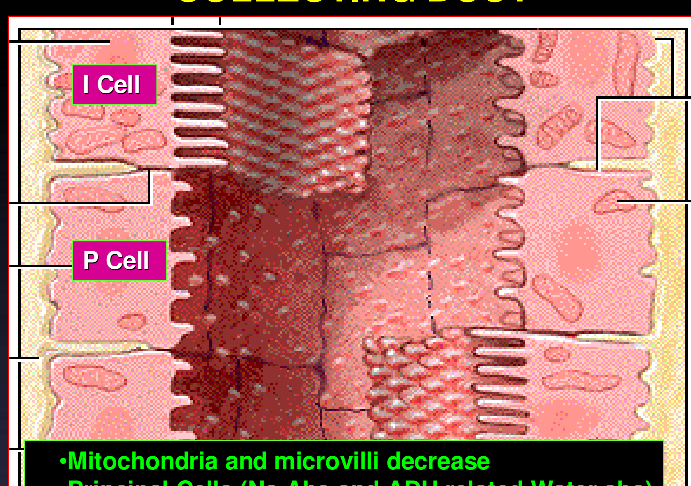

Renal interstitial fluid
Tubular cells
Tubular lumen (+8 mV)
Na+, K+
Mg++, Ca++
Paracellular diffusion
Na+
ATP
K+
Na+
H+
Cl−
K+
Na+
2Cl−
K+
Loop diuretics
• Furosemide
• Ethacrynic acid
• Bumetanide


Thin descending loop of Henle
H2O
Thick ascending loop of Henle
25%
Na+, Cl−, K+,
Ca++, HCO3−, Mg++
Hypo-osmotic
H+

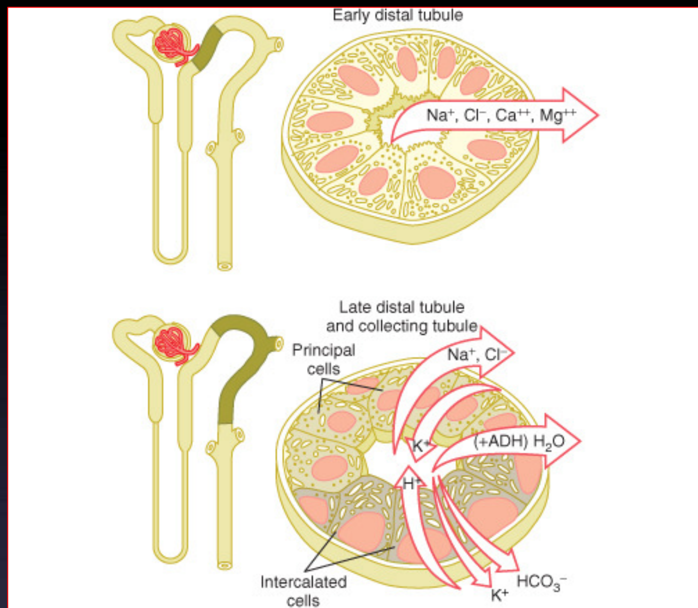


Mechanism of sodium chloride transport in the early distal tubule

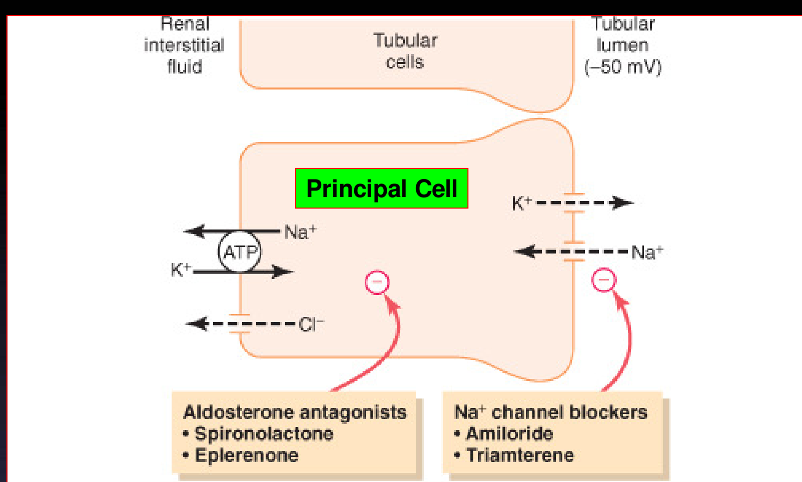
LATE DCT AND CORTICAL COLLECTING DUCT



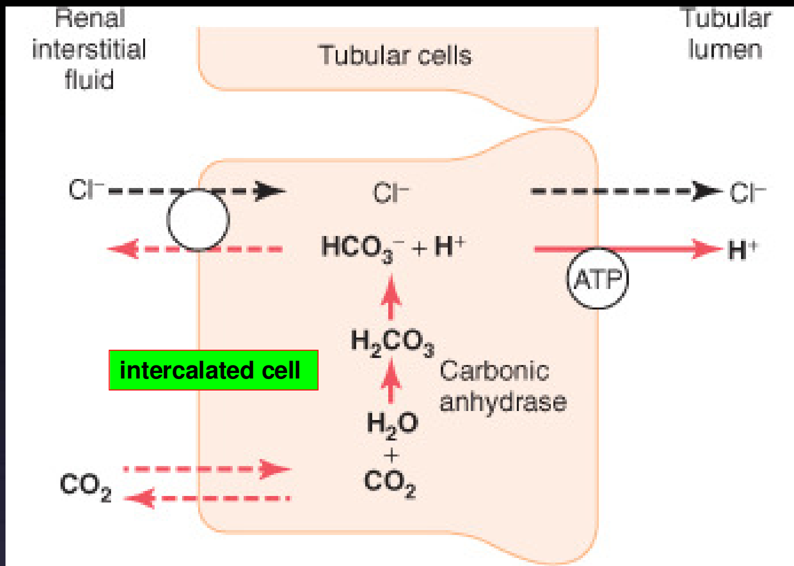
- Mitochondria and microvilli decrease
- Principal Cells (Na Abs and ADH related Water abs)
- Intercalated Cells (Acid Sec and HCO3 Transport)



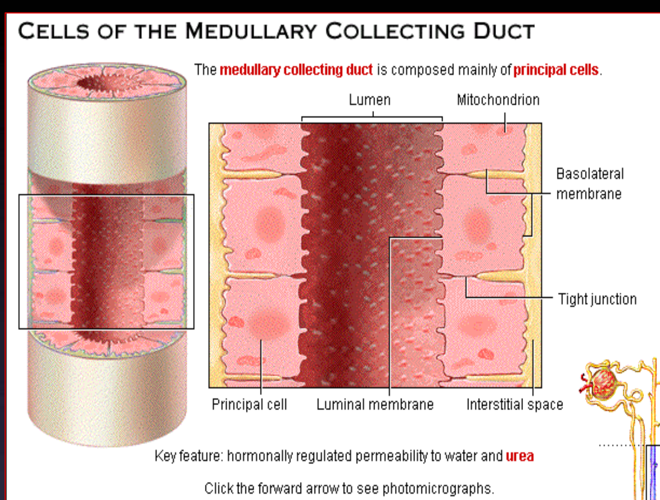
Early distal tubule
Na+, Cl−, Ca++, Mg++
Late distal tubule
and collecting tubule
Principal
cells
Na+, Cl−
K+
(+ADH) H2O
H+
Intercalated
cells
K+
HCO3−

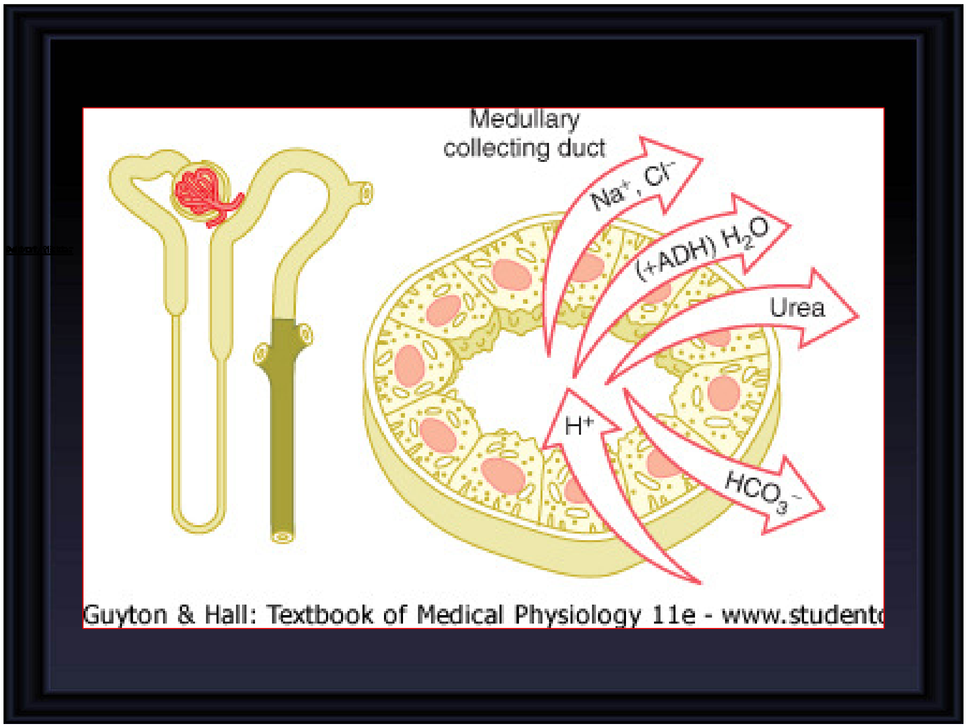


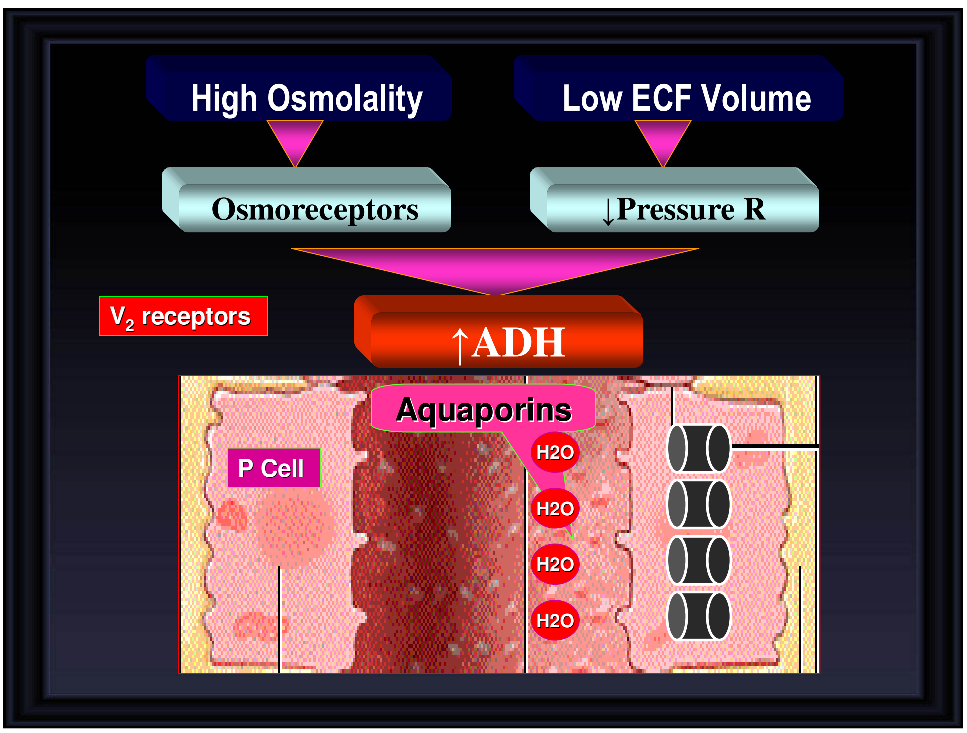
Renal
interstitial
fluid
Tubular
cells
Tubular
lumen
(−50 mV)
Principal Cell
K+
Na+
ATP
K+
Na+
Cl−
Aldosterone antagonists
• Spironolactone
• Eplerenone
Na+ channel blockers
• Amiloride
• Triamterene



MEDULLARY COLLECTING DUCT




Medullary
collecting duct
Na+, Cl-
(+ADH) H2O
Urea
H+
HCO3-
Guyton & Hall: Textbook of Medical Physiology 11e - www.studentc


High Osmolality
Low ECF Volume
Osmoreceptors
↓Pressure R
V2 receptors
↑ADH
Aquaporins
P Cell
H2O
H2O
H2O
H2O

REABSORPTION OF WATER IN DIFFERENT SEGMENTS OF TUBULES

PART OF NEPHRON	PERCENTAGE REABSORBED
Proximal tubules	65
Loop of Henle	15
Distal tubules	10
Collecting ducts	9.3
Passing into urine	**0.7**

REABSORPTION OF WATER IN DIFFERENT SEGMENTS OF TUBULES

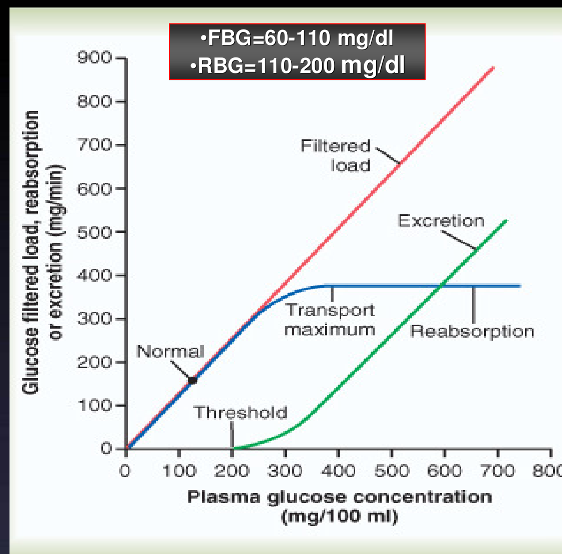
PART OF NEPHRON	AMOUNT REABSORBED
Glomerular Filtrate	125
Flowing into the loops of Henle	45
Flowing into the distal tubules	25
Flowing into the collecting tubules	12
Flowing into the urine	1

GLUCOSE REABSORPTION

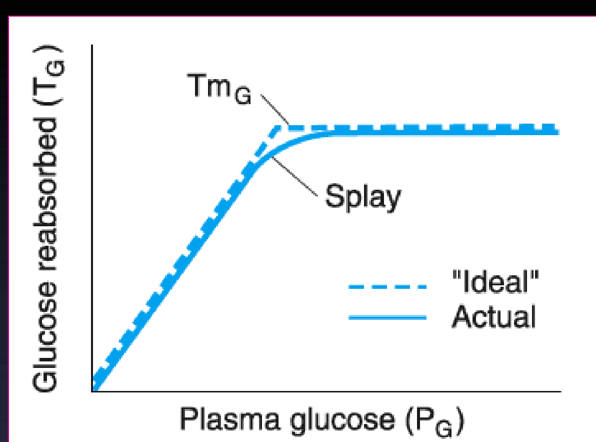
Tmax
375 mg/min

Filtered Load
125 mg/min
(GFRxPlasmaGlu)

Renal Threshold
200mg/dl



GLUCOSE REABSORPTION



TUBULAR TRANSPORT MAXIMUM

- The Maximum limit/rate at which a solute can be transported across the tubular cells of kidneys is called TUBULAR TRANSPORT MAXIMUM

Tm for Glucose is 375 mg/min

TUBULAR TRANSPORT MAXIMUM FOR DIFFERENT SUBSTANCES

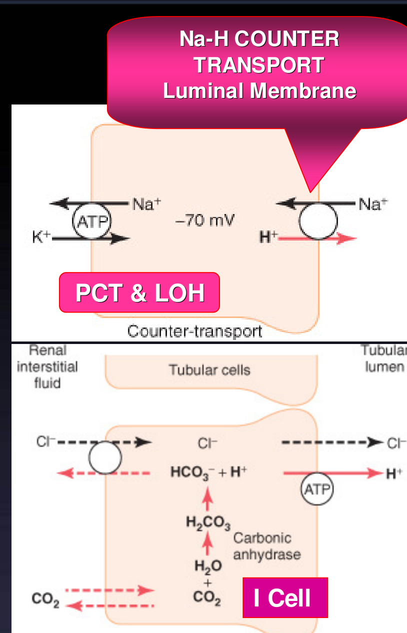
SUBSTANCE	Tm
Glucose	375 mg/min
Phosphate	0.1 mM/min
Sulfate	0.06 mM/min
Amino Acids	1.5 mM/min
Urate	15 mg/min
Plasma Protein	30 mg/min
Hemoglobin	1 mg/min
Lactate	75 mg/min
Acetoacetate	variable

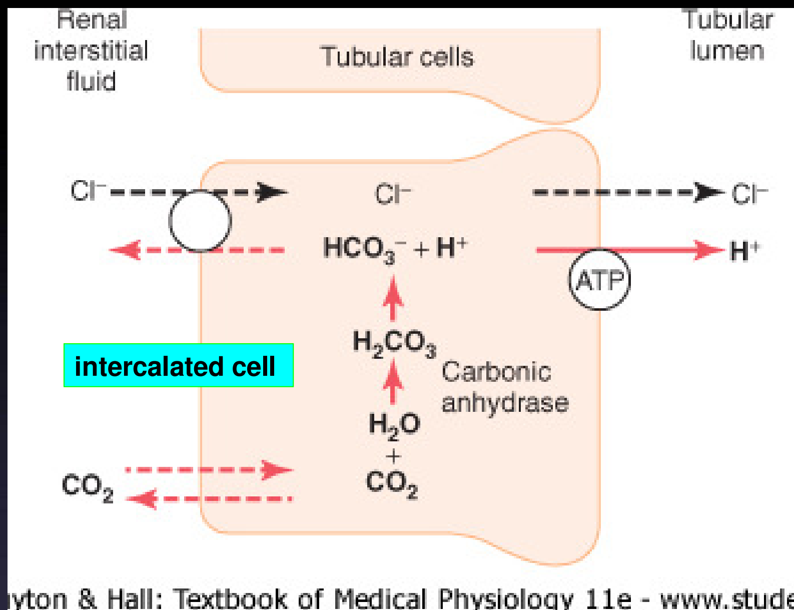
Transport Maximums for Substances That Are Actively Secreted

Substance	Transport Maximum
Creatinine	16 mg/min
Para-aminohippuric acid	80 mg/min

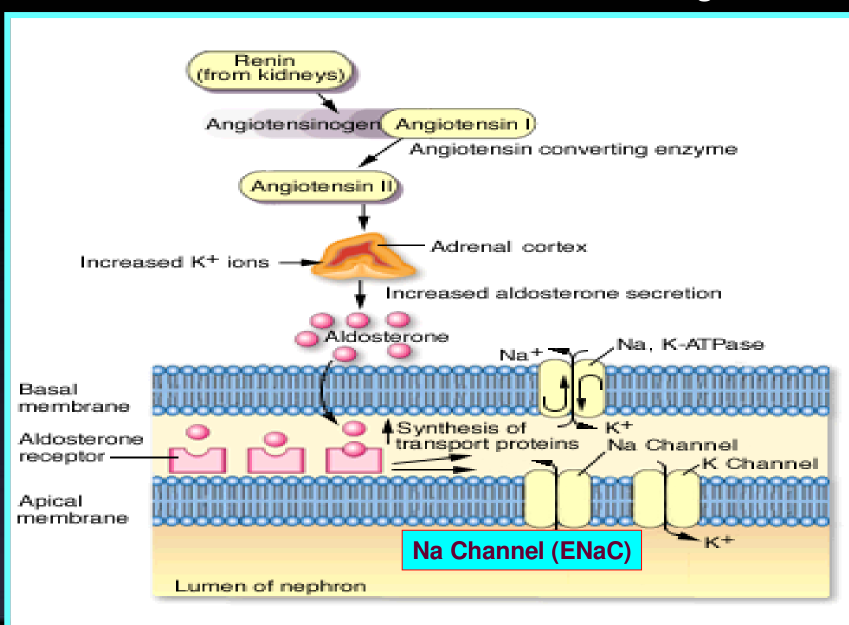
HYDROGEN

- Secreted in Proximal Tubule and Thick ascending LOH by Counter Transport with Na
- Secreted in DCT by H ATP ase





Effect Of Aldosterone On Cortical Collecting Duct



UREA

- Plasma concentration is 2.5 – 7.5 mmol/L
- 50 % is reabsorbed in PCT passively with water
- It is the only waste to be reabsorbed
- Creatinine and Phenol are not reabsorbed.

POTASSIUM

- It is both reabasorbed and secreted
- 67% of filtered load is reabsorbed by PCT
  - solvent drag
- Secreted by Thick Asc LOH, early distal tubule / collecting duct
  - correlated with dietary intake
    - 80% of filtered load appears in urine if dietary content high
    - 1% if dietary content low

CALCIUM

- Ionized Calcium is freely filtered and reabsorbed in PCT
- It moves into tubular cells passively (downhill)
- It moves out of the cell by Ca/Na Counter Transport or Actively by Ca ATP ase Mechanism
- Its reabsorption is Hormonally controlled

PHOSPHATE

- It is reabsorbed by cotransport with Na in PCT in luminal border
- Its reabsorption is Hormonally controlled
- It is increased by Vit D and decreased by Parathyroid Hormone

SULPHATE

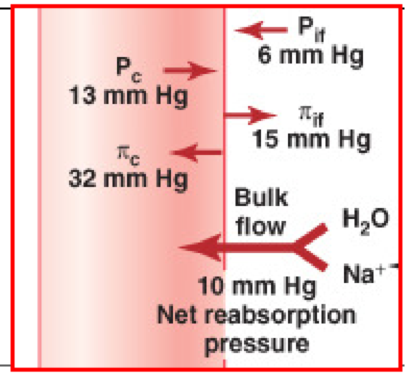
- Like PHOSPHATE reabsorbed with Na

Factors That Can Influence Peritubular Capillary Reabsorption

$\uparrow P_c \rightarrow \downarrow$ Reabsorption
- $\downarrow R_A \rightarrow \uparrow P_c$
- $\downarrow R_E \rightarrow \uparrow P_c$
- $\uparrow$ Arterial Pressure $\rightarrow \uparrow P_c$

$\uparrow \pi_c \rightarrow \uparrow$ Reabsorption
- $\uparrow \pi_A \rightarrow \uparrow \pi_c$
- $\uparrow FF \rightarrow \uparrow \pi_c$

$\uparrow K_f \rightarrow \uparrow$ Reabsorption

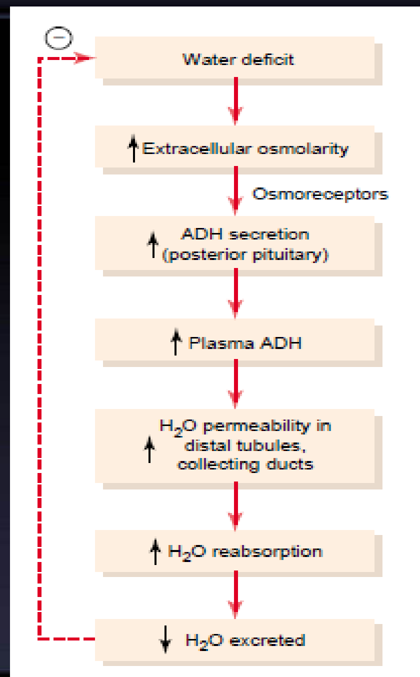


P_c, peritubular capillary hydrostatic pressure; R_A and R_E, afferent and efferent arteriolar resistances, respectively; π_c, peritubular capillary colloid osmotic pressure; π_A, arterial plasma colloid osmotic pressure; FF, filtration fraction; K_f, peritubular capillary filtration coefficient.

REGULATION OF EXTRACELLULAR FLUID VOLUME AND OSMOLALITY

Osmoreceptor ADH Feedback System

1. INCREASED OSMOLALITY
2. DECREASED ARTERIAL PRESSURE
3. DECREASED BLOOD VOLUME



FACTORS AFFECTING ADH

Increase ADH	Decrease ADH
$\uparrow$Osmolarity	$\downarrow$Osmolarity
$\downarrow$ Blood volume	$\uparrow$ Blood volume
$\downarrow$ Blood pressure	$\uparrow$ Blood pressure
Nausea	
Hypoxia	Alcohol
Drugs: Drugs:	Clonidine (antihypertensive drug)
Morphine	Haloperidol (dopamine blocker)
Nicotine	
Cyclophosphamide	

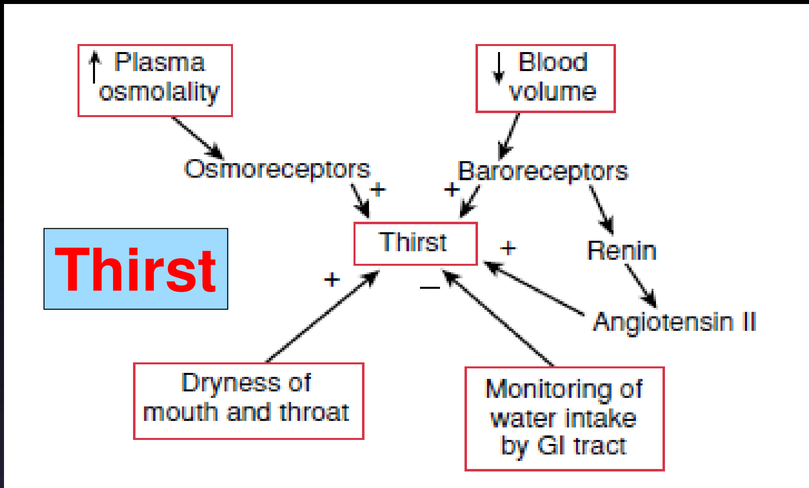
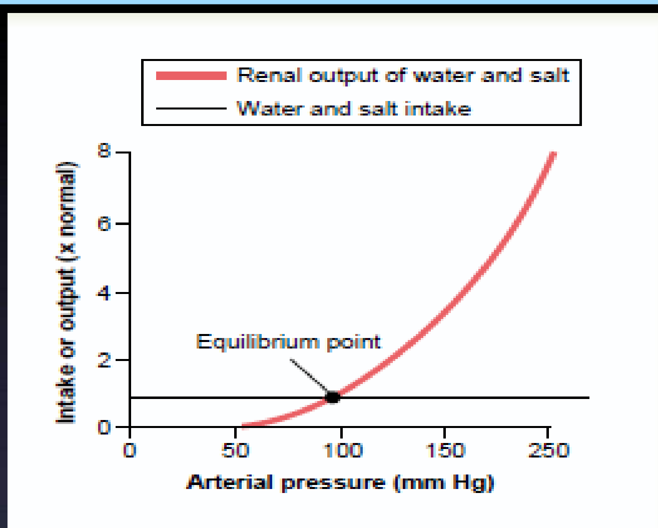


FIGURE 24.7 **Factors affecting the thirst sensation.** A plus sign indicates stimulation of thirst, the minus sign indicates an inhibitory influence.

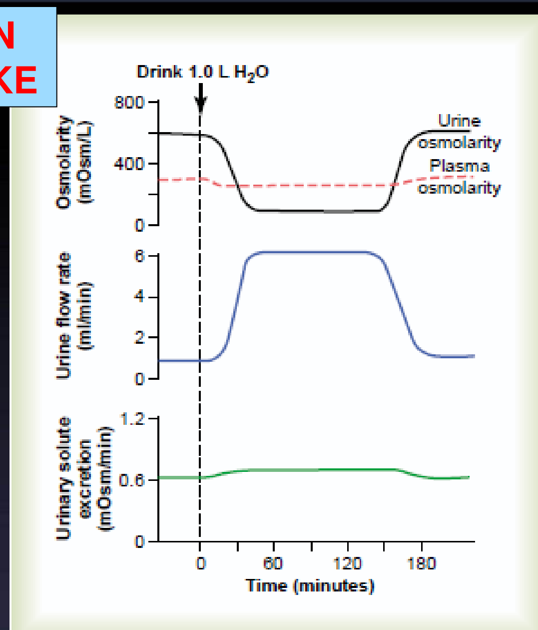
Role of Thirst in Controlling Extracellular Fluid Osmolarity and Sodium Concentration

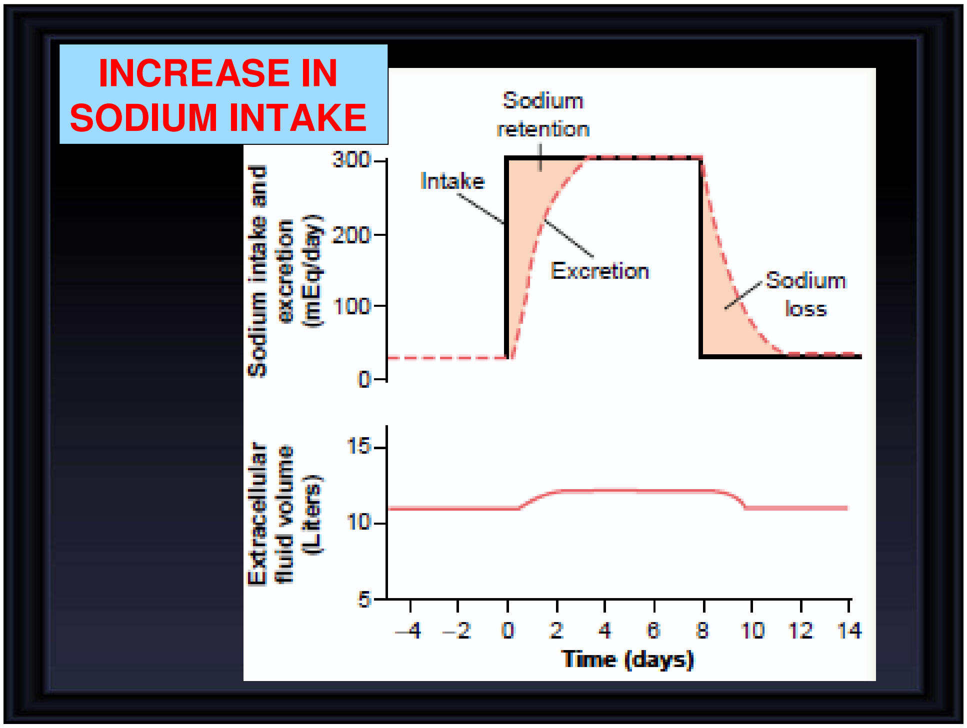
Increase Thirst	Decrease Thirst
↑Osmolarity	↓Osmolarity
↓ Blood volume	↑ Blood volume
↓ Blood pressure	↑ Blood pressure
↑ Angiotensin	↓Angiotensin II
Dryness of mouth	Gastric distention

Pressure Natriuresis and Pressure Diuresis



INCREASE IN WATER INTAKE





ATRIAL NATRIURETIC PEPTIDE (ANP)

- INCREASE GLOMERULAR FILTRATION
- INHIBIT NA^+ REABSORPTION.
- INCREASE IN CAPILLARY PERMEABILITY LEADING TO EXTRAVASATION OF FLUID AND A DECLINE IN BLOOD PRESSURE.
- RELAX VASCULAR SMOOTH MUSCLE IN ARTERIOLES AND VENULES
- THESE PEPTIDES ALSO INHIBIT RENIN SECRETION

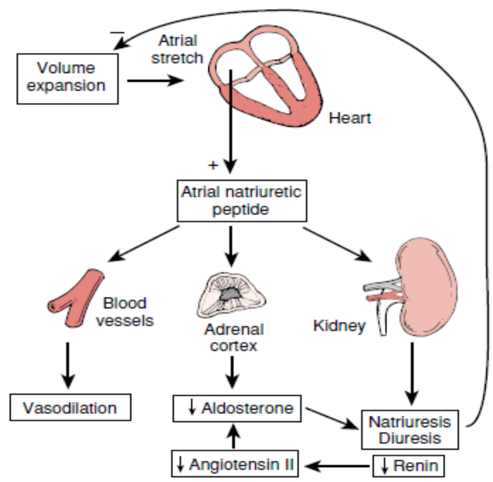


FIGURE 24.10 **Atrial natriuretic peptide and its actions.** ANP release from the cardiac atria is stimulated by blood volume expansion, which stretches the atria. ANP produces effects that bring blood volume back toward normal, such as increased Na^+ excretion.

GLOMERULOTUBULAR BALANCE

An increase in GFR causes an increase in the reabsorption of solutes to keep the percentage of the solute reabsorbed constant

When the GFR is high, there is a relatively large increase in the oncotic pressure of the plasma leaving the glomeruli via the efferent arterioles and hence in their capillary branches This increases the reabsorption of Na+ from the tubule