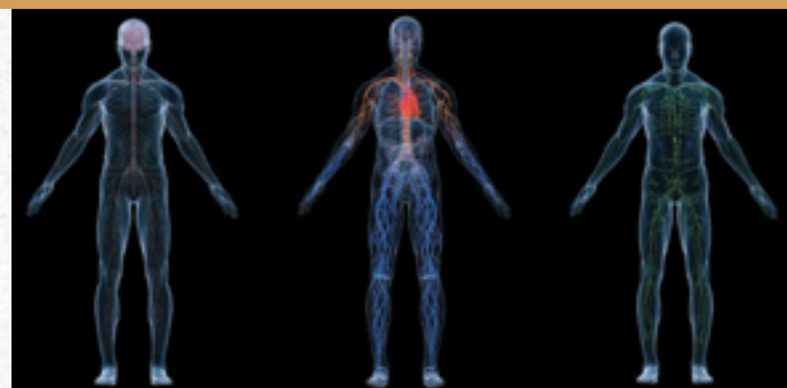
UNIT V

GUYTON AND HALL *Textbook of*

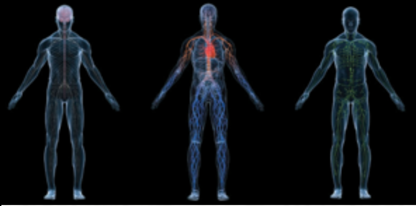
Medical Physiology

TWELFTH EDITION



Chapter 28:

Urine Concentration and Dilution; Regulation of Extracellular Fluid Osmolarity and Sodium Concentration



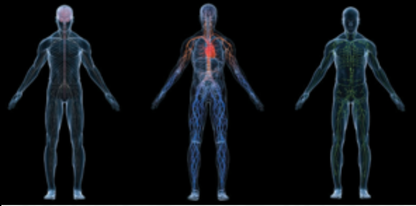
Control of Extracellular Osmolarity (NaCl Concentration)

- ADH
- Thirst

→ ADH -Thirst Osmoreceptor System

Mechanism:

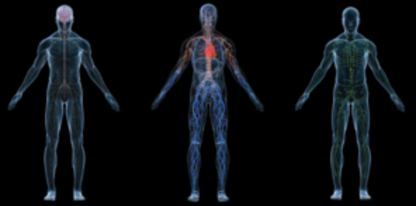
increased extracellular osmolarity (NaCl) stimulates ADH release, which increases H_2O reabsorption, and stimulates thirst (intake of water)



Concentration and Dilution of the Urine

- Maximal urine concentration
  = 1200 - 1400 mOsm / L
  (specific gravity ~ 1.030)

- Minimal urine concentration
  = 50 - 70 mOsm / L
  (specific gravity ~ 1.003)



Water diuresis in a human after ingestion of 1 liter of water.

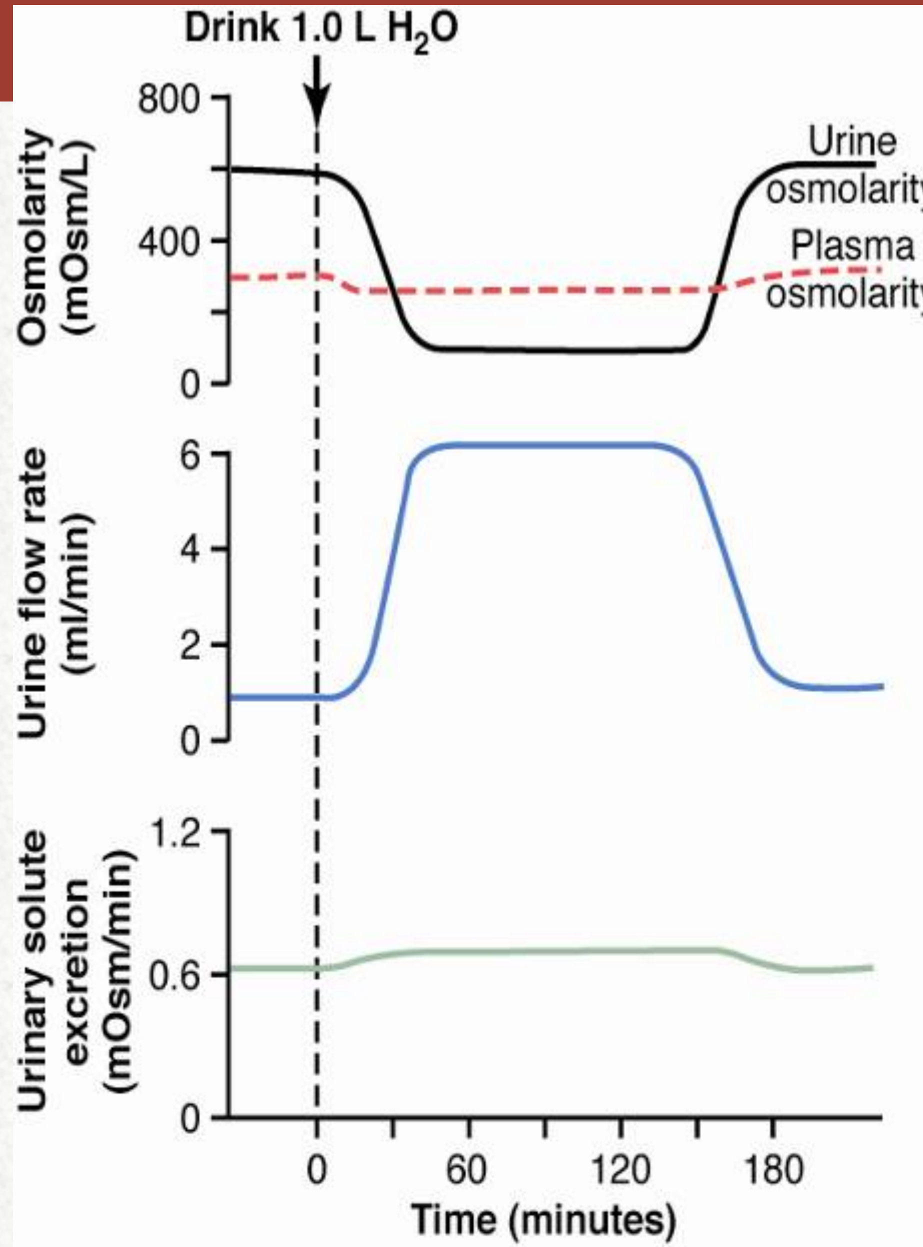


Figure 28-1

Formation of a dilute urine

- Continue electrolyte reabsorption
- Decrease water reabsorption

Mechanism:

Decreased ADH release

and reduced water

permeability in distal and

collecting

tubules

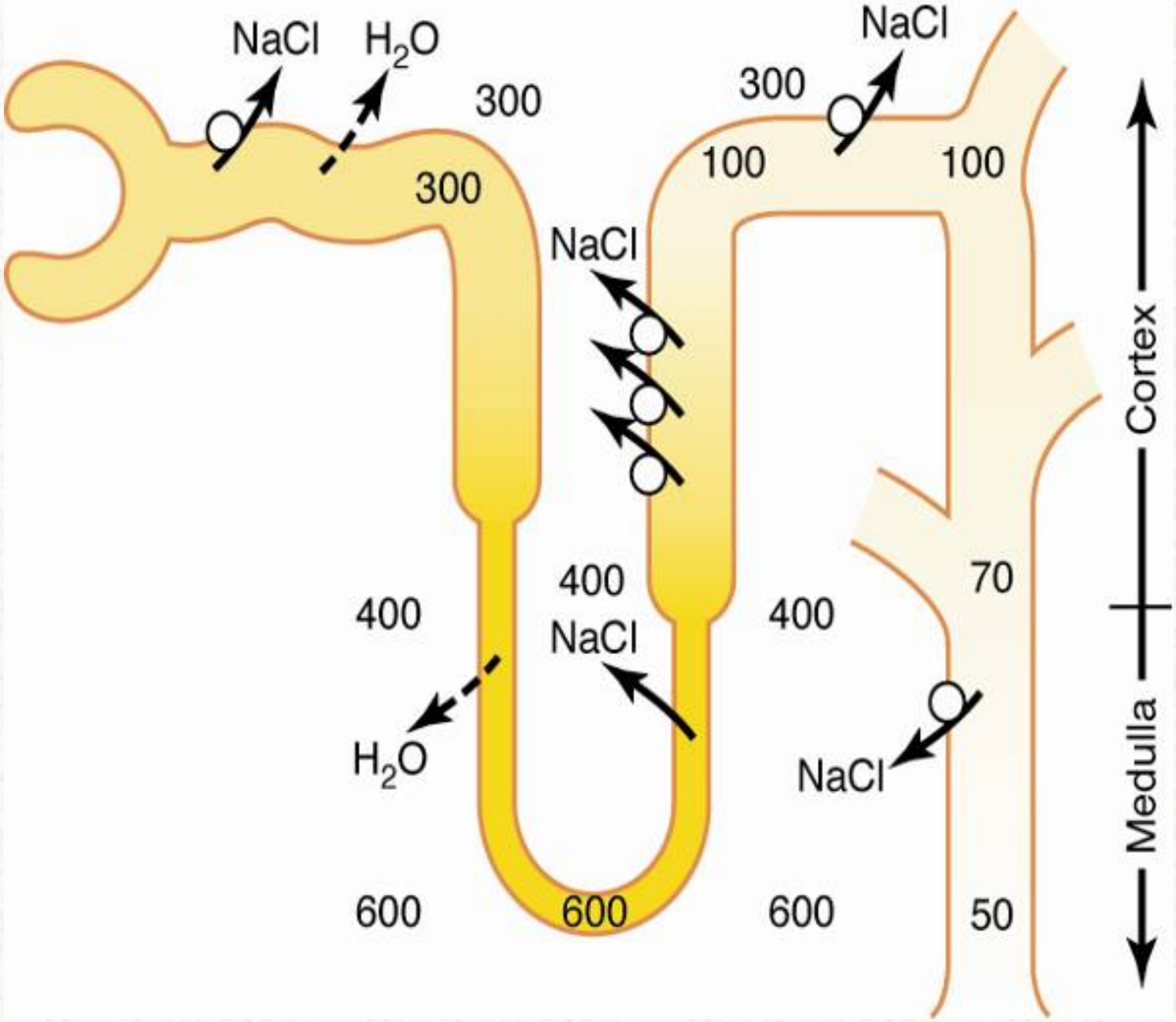


Figure 28-2

Relationship between urine osmolarity and specific gravity

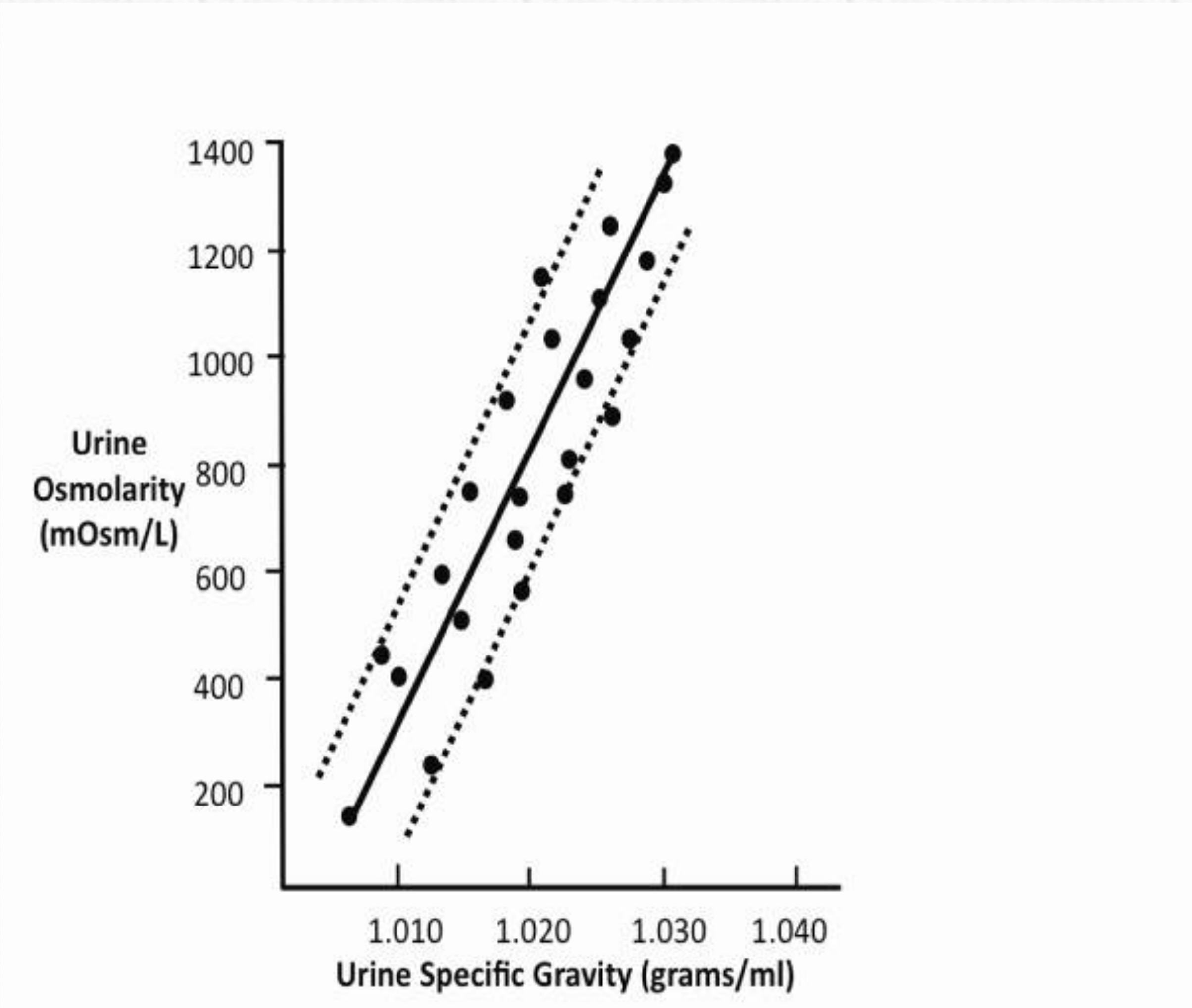
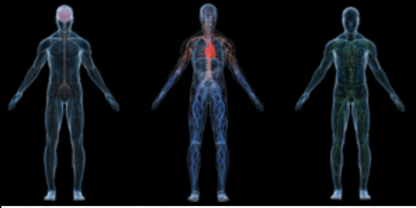


Figure 28-3

Influenced by

- glucose in urine
- protein in urine
- antibiotics
- radiocontrast media

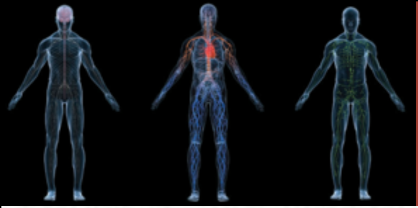


Formation of a Concentrated Urine

- Continue electrolyte reabsorption
- Increase water reabsorption

Mechanism :

- Increased ADH release which increases water permeability in distal and collecting tubules
- High osmolarity of renal medulla
- Countercurrent flow of tubular fluid



Formation of a Concentrated Urine when antidiuretic hormone (ADH) are high.

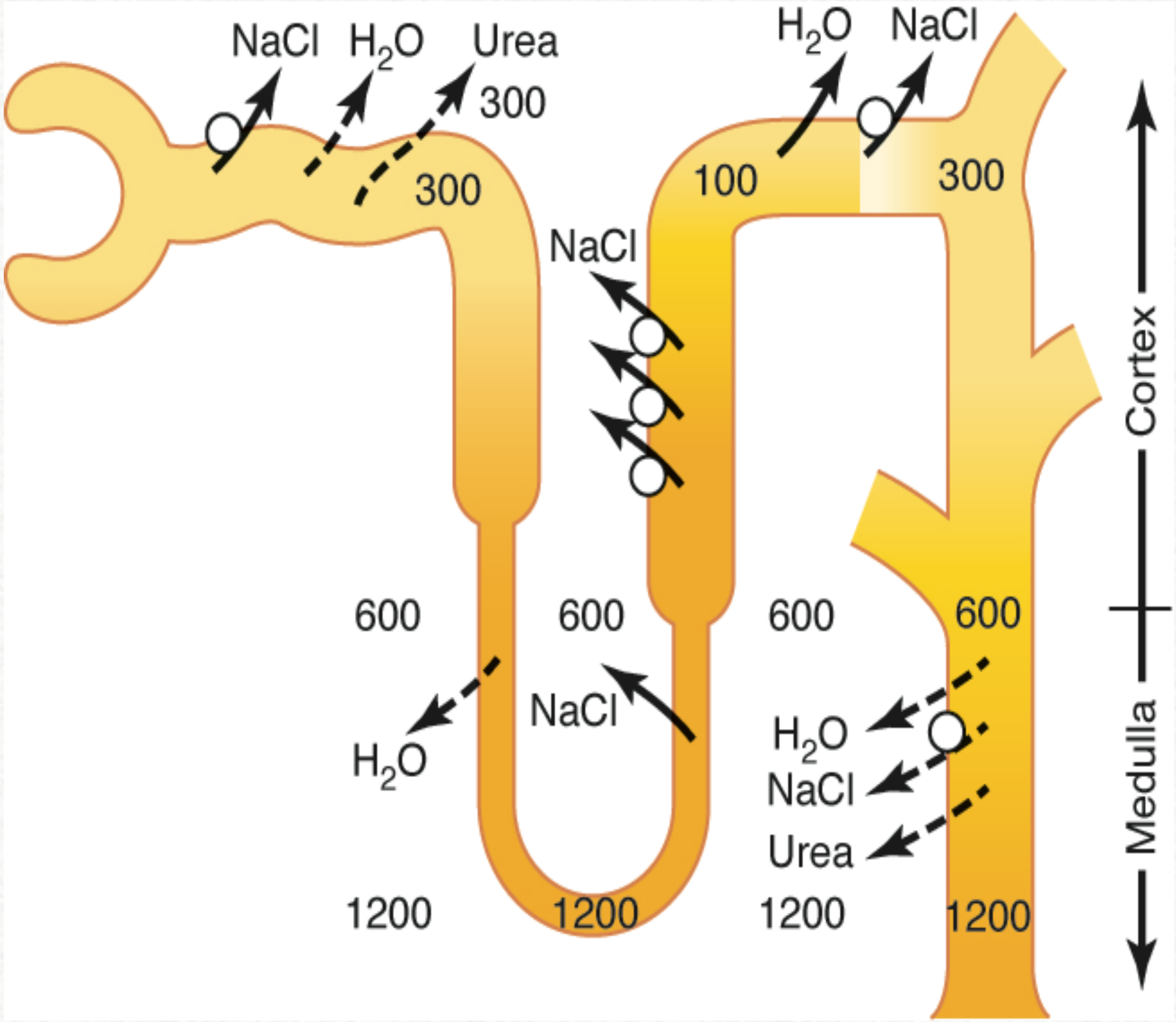
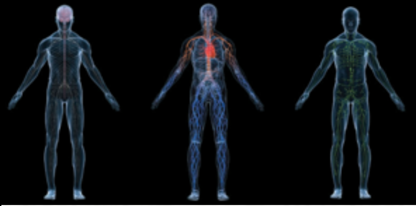


Figure 28-4



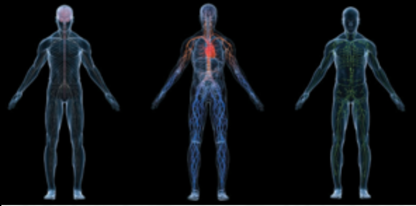
Obligatory Urine Volume

The minimum urine volume in which the excreted solute can be dissolved and excreted

Example:

If the max. urine osmolarity is 1200 mOsm/L, and 600 mOsm of solute must be excreted each day to maintain electrolyte balance, the obligatory urine volume is:

$$\frac{600 \text{ mOsm/d}}{1200 \text{ mOsm/L}} = 0.5 \text{ L/day}$$



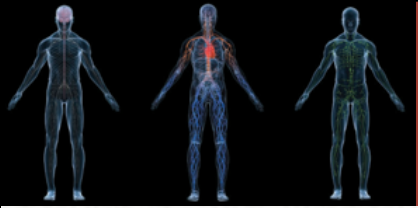
Obligatory Urine Volume

In renal disease the obligatory urine volume may be increased due to impaired urine concentrating ability

Example:

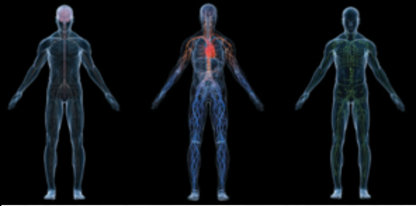
- If the max. urine osmolarity = 300 mOsm/L,
- If 600 mOsm of solute must be excreted each day to maintain electrolyte balance
- obligatory urine volume = ?

$$\frac{600 \text{ mOsm/d}}{300 \text{ mOsm/L}} = 2.0 \text{ L/day}$$



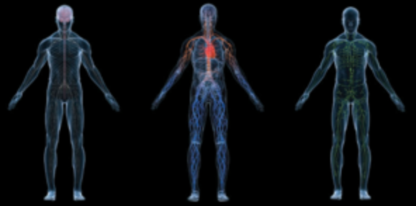
Factors That Contribute to Buildup of Solute in Renal Medulla - Countercurrent Multiplier

- Active transport of Na^+, Cl^-, K^+ and other ions from thick ascending loop of Henle into medullary interstitium
- Active transport of ions from medullary collecting ducts into interstitium
- Passive diffusion of urea from medullary collecting ducts into interstitium
- Diffusion of only small amounts of water into medullary interstitium



Summary of Tubule Characteristics

Tubule Segment	Active NaCl Transport	Permeability H_2O	Permeability NaCl	Permeability Urea
Proximal	++	+++	+	+
Thin Desc.	0	+++	+	+
Thin Ascen.	0	0	+	+
Thick Ascen.	+++	0	0	0
Distal	+	+ADH	0	0
Cortical Coll.	+	+ADH	0	0
Inner Medullary Coll.	+	+ADH	0	+++



Countercurrent multiplier system in the loop of Henle.

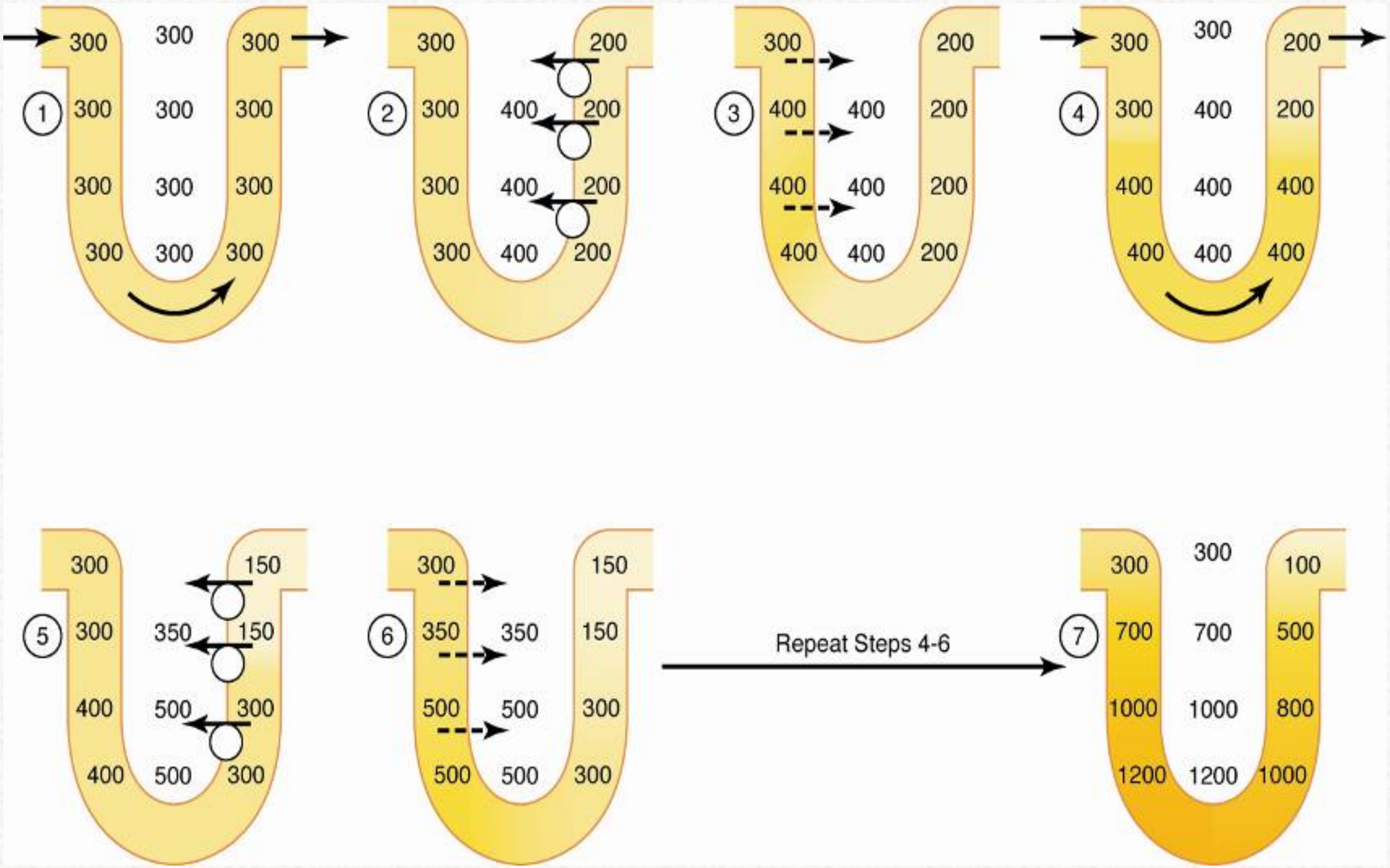
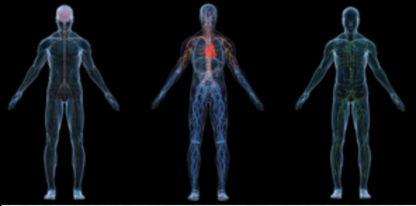


Figure 28-4



Net Effects of Countercurrent Multiplier

1. More solute than water is added to the renal medulla. i.e solutes are “trapped” in the renal medulla
2. Fluid in the ascending loop is diluted
3. Most of the water reabsorption occurs in the cortex (i.e. in the proximal tubule and in the distal convoluted tubule) rather than in the medulla
4. Horizontal gradient of solute concentration established by the active pumping of NaCl is “multiplied” by countercurrent flow of fluid.

Recirculation of urea absorbed from medullary collecting duct into interstitial fluid.

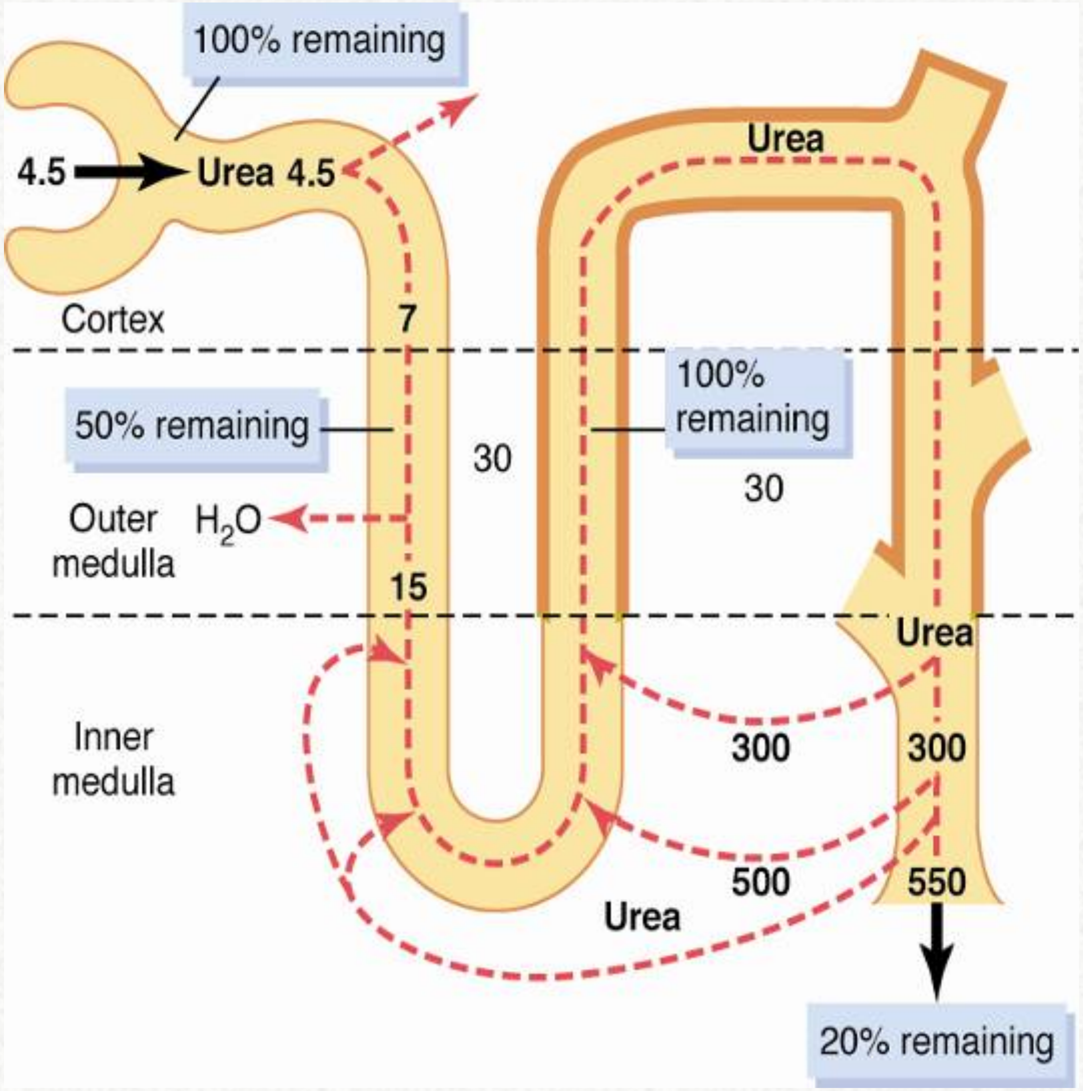


Figure 28-5

Urea Recirculation

- Urea is passively reabsorbed in proximal tubule (~ 50% of filtered load is reabsorbed)
- In the presence of ADH, water is reabsorbed in distal and collecting tubules, concentrating urea in these parts of the nephron
- The inner medullary collecting tubule is highly permeable to urea, which diffuses into the medullary interstitium
- ADH increases urea permeability of medullary collecting tubule by activating urea transporters (UT-1)

The Vasa Recta Preserve Hyperosmolarity of Renal Medulla

- The vasa recta serve as countercurrent exchangers

- Vasa recta blood flow is low (only 1-2 % of total renal blood flow)

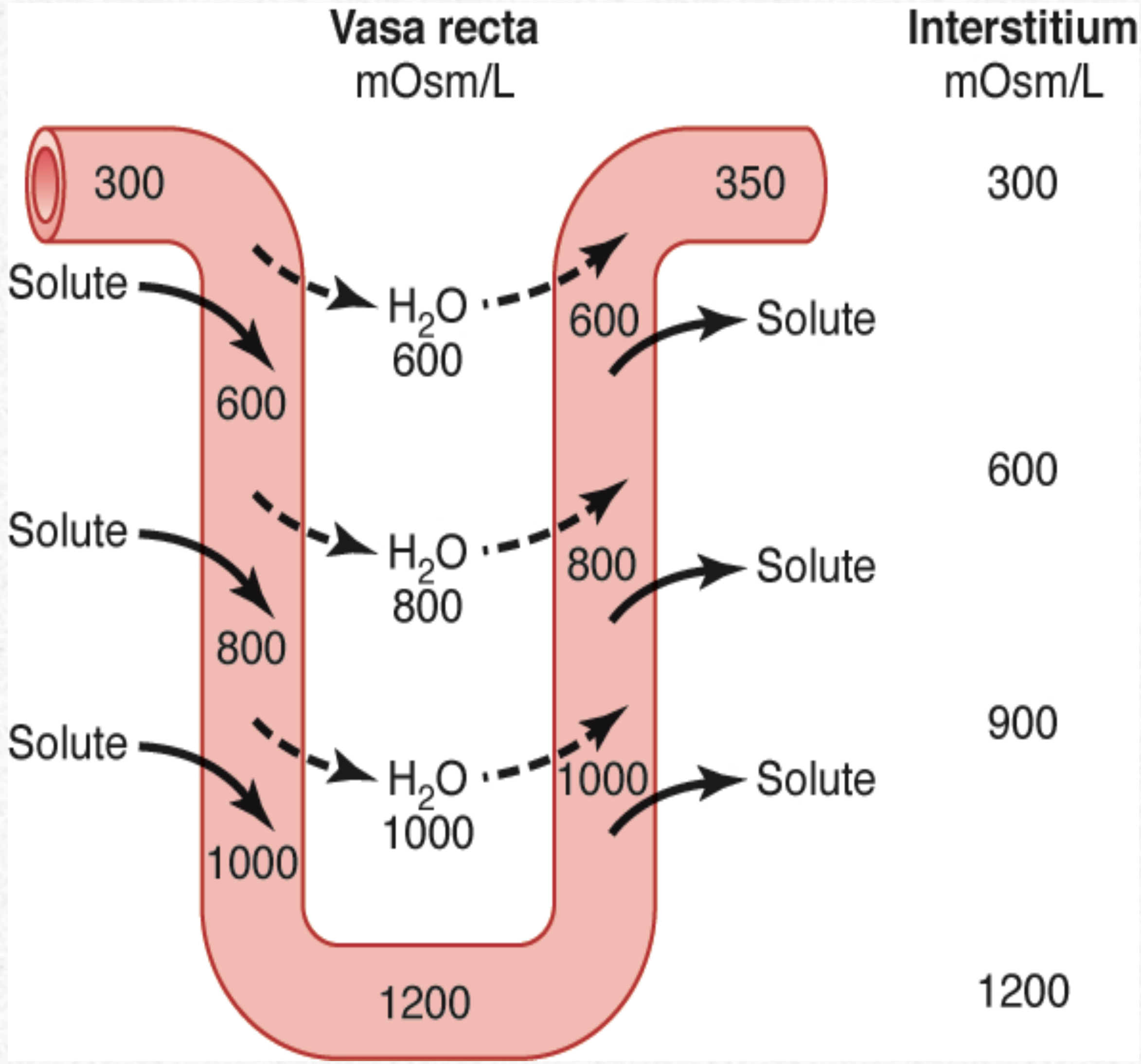


Figure 28-7

Changes in osmolarity of the tubular fluid

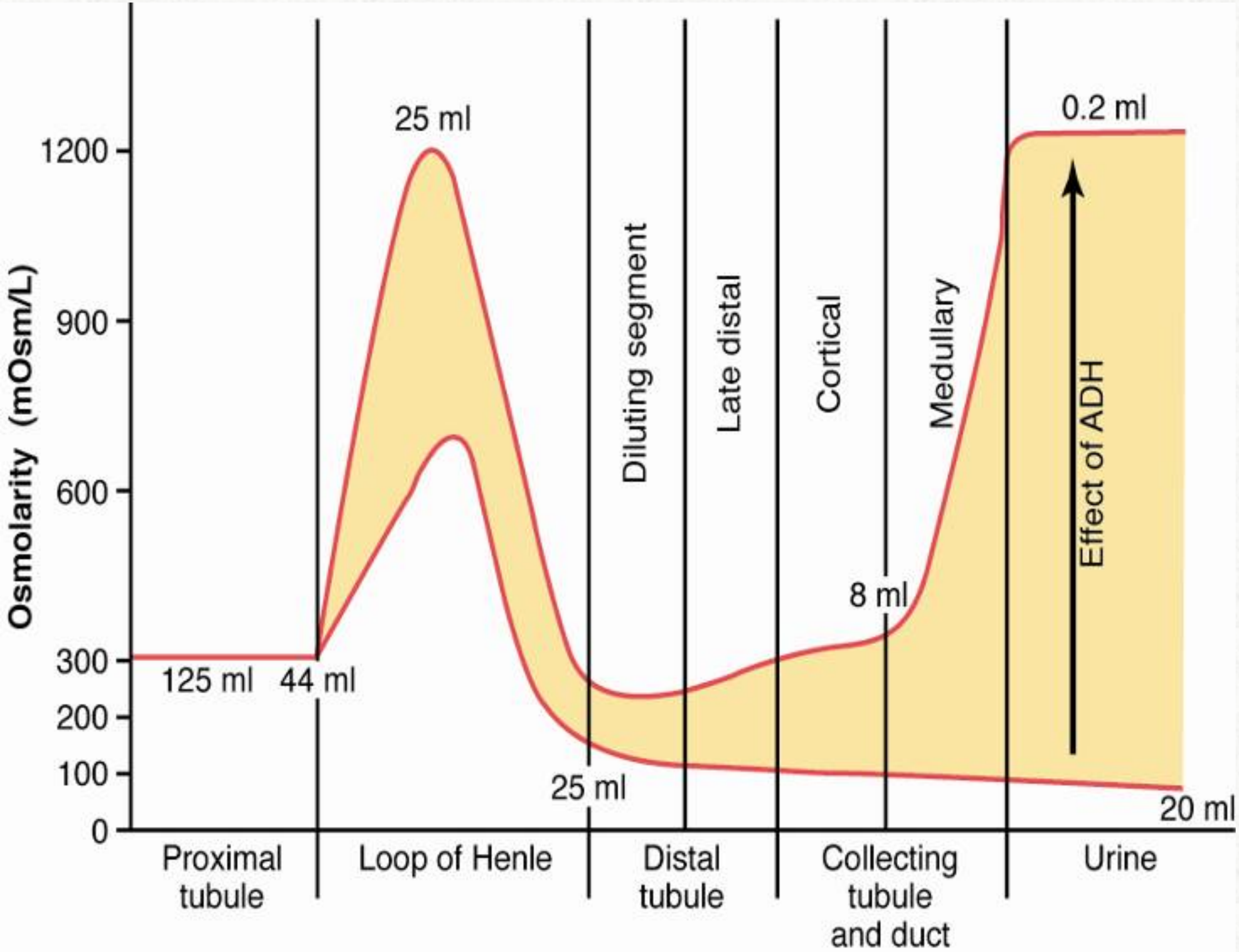
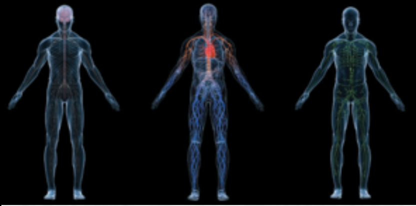
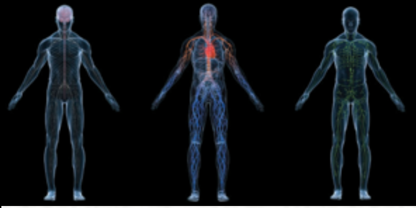


Figure 28-8



Summary of water reabsorption and osmolarity in different parts of the tubule

- Proximal Tubule: 65 % reabsorption, isosmotic
- Desc. loop: 15 % reasorption, osmolarity increases
- Asc. loop: 0 % reabsorption, osmolarity decreases
- Early distal: 0 % reabsorption, osmolarity decreases
- Late distal and coll. tubules: ADH dependent water reabsorption and tubular osmolarity
- Medullary coll. ducts: ADH dependent water reabsorption and tubular osmolarity



“Free” Water Clearance (C_{H_2O}) (rate of solute-free water excretion)

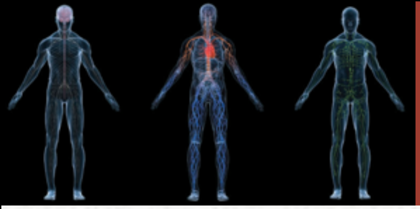
$$CH_2O = V - \frac{Uosm \times V}{Posm}$$

where:

Uosm = urine osmolarity
V = urine flow rate
P = plasma osmolarity

If: Uosm < Posm, CH_2O = +

If: Uosm > Posm, CH2O = -



Question

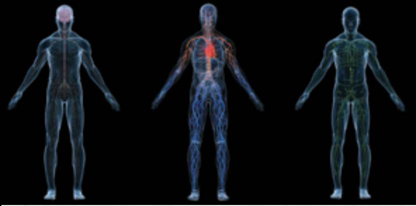
Given the following data, calculate " free water" clearance :

urine flow rate = 6.0 ml/min

urine osmolarity = 150 mOsm /L

plasma osmolarity = 300 mOsm / L

Is free water clearance in this example positive or negative ?



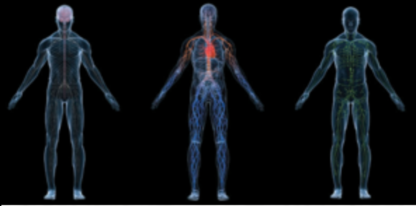
Answer

$$C_{H_2O} = V - \frac{Uosm \times V}{Posm}$$

$$= 6.0 - \frac{(150 \times 6)}{300}$$

$$= 6.0 - 3.0$$

$$= +3.0 \text{ ml / min (positive)}$$



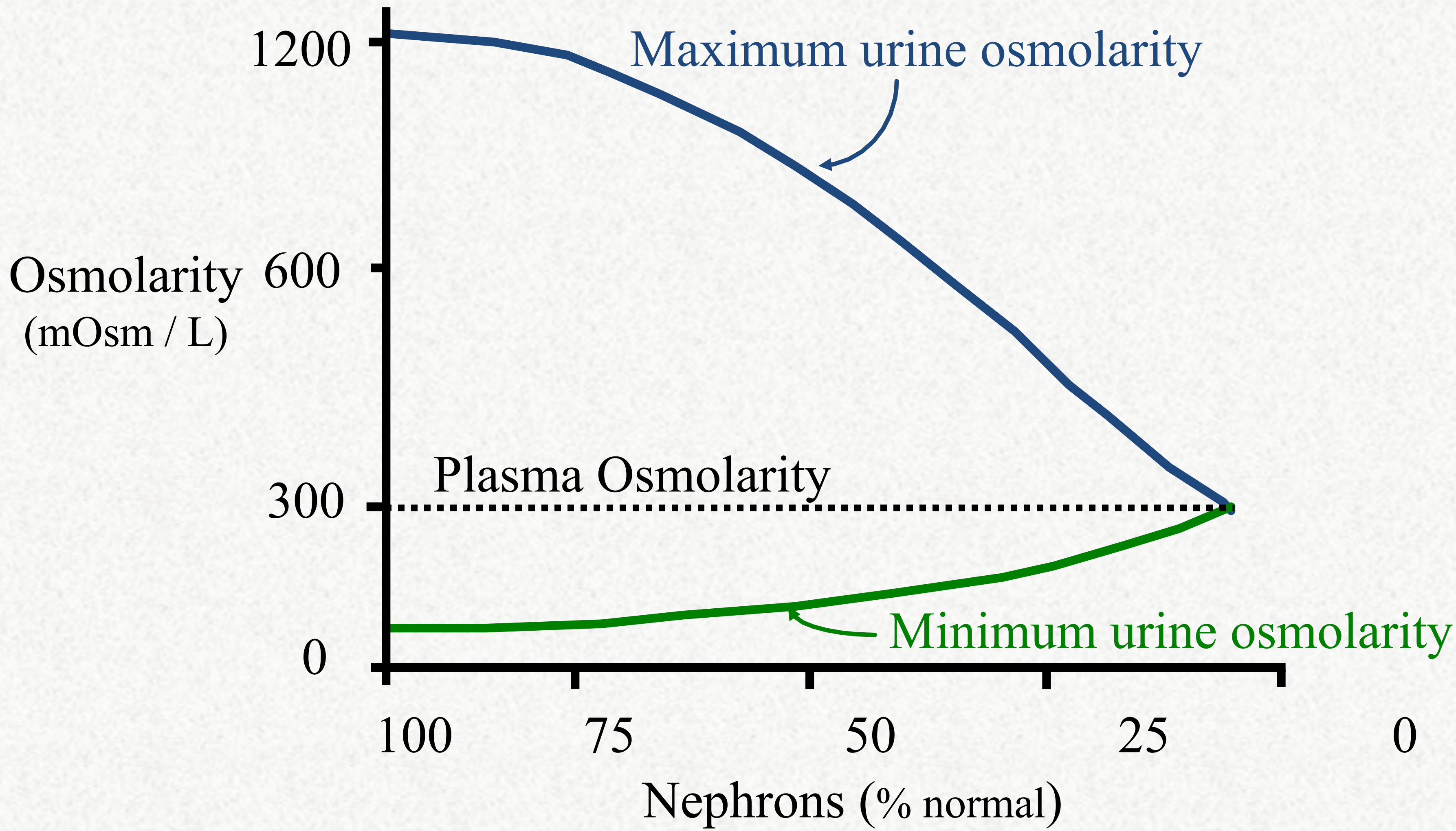
Disorders of Urine Concentrating Ability

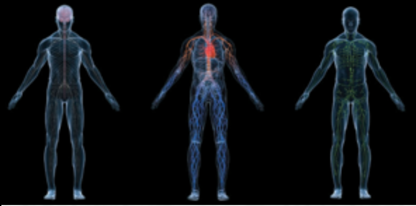
- Failure to produce ADH :
  "Central" diabetes insipidus

- Failure to respond to ADH:
  "nephrogenic" diabetes insipidus

  - impaired loop NaCl reabs. (loop diuretics)
  - drug induced renal damage: lithium, analgesics
  - malnutrition (decreased urea concentration)
  - kidney disease: pyelonephritis, hydronephrosis, chronic renal failure

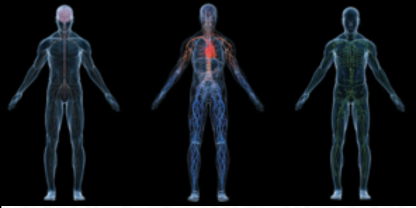
Development of Isosthenuria With Nephron Loss in Chronic Renal Failure (inability to concentrate or dilute the urine)





Total Renal Excretion and Excretion Per Nephron in Renal Failure

	Normal	75 % loss of nephrons
Number of nephrons	2,000,000	500,000
Total GFR (ml/min	125	40
GFR per nephron (nl/min)	62.5	80
Total Urine flow rate (ml/min)	1.5	1.5
Volume excreted per nephron (nl/min)	0.75	3.0



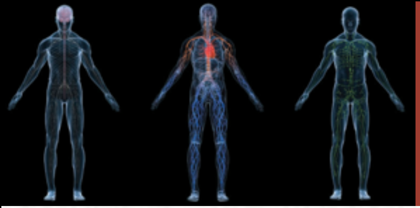
Control of Extracellular Osmolarity (NaCl Concentration)

- ADH
- Thirst

→ ADH -Thirst Osmoreceptor System

Mechanism:

increased extracellular osmolarity (NaCl) stimulates ADH release, which increases H_2O reabsorption, and stimulates thirst (intake of water)



Osmoreceptor–antidiuretic hormone (ADH) feedback mechanism for regulating extracellular fluid osmolarity.

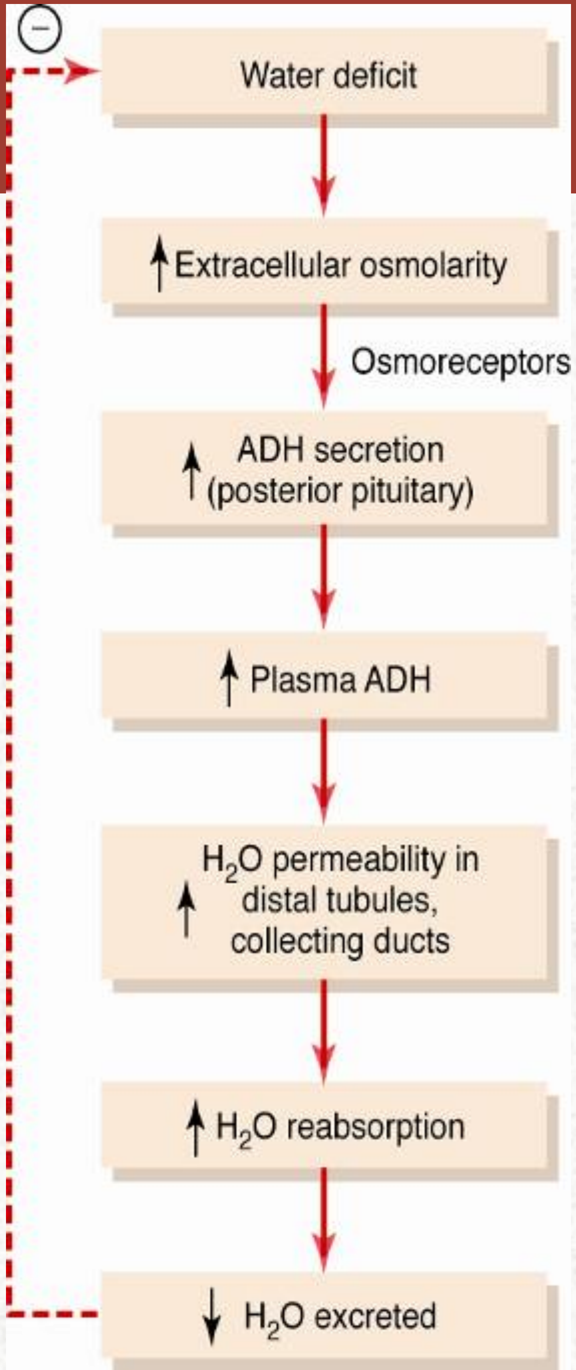
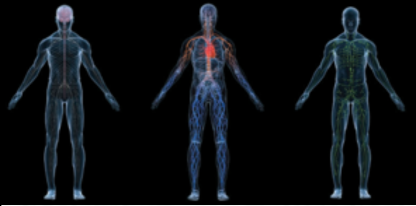


Figure 28-9



ADH synthesis in the magnocellular neurons of hypothalamus, release by the posterior pituitary, and action on the kidneys

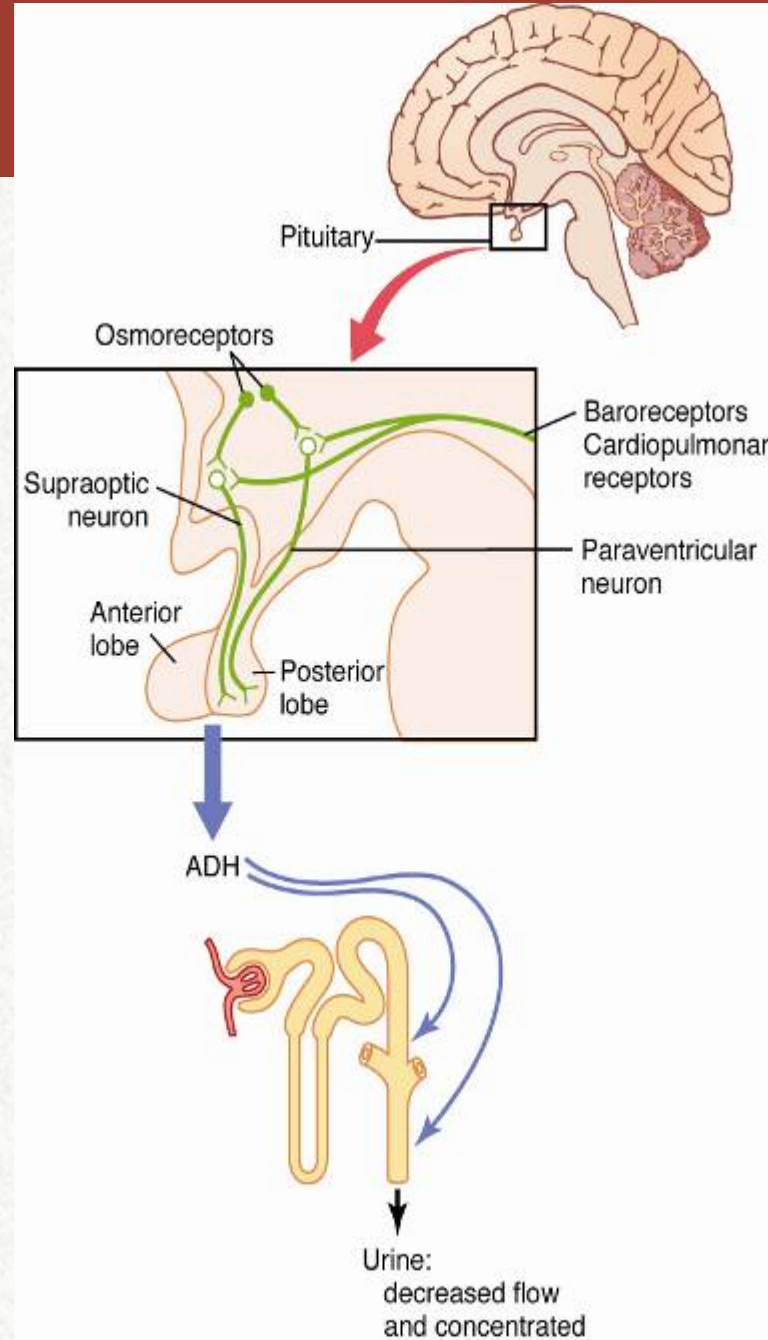
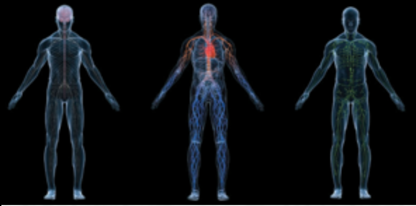
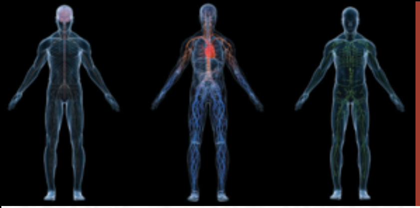


Figure 28-10



Stimuli for ADH Secretion

- Increased osmolarity
- Decreased blood volume (cardiopulmonary reflexes)
- Decreased blood pressure (arterial baroreceptors)
- Other stimuli :
  - input from cerebral cortex (e.g. fear)
  - angiotensin II
  - nausea
  - nicotine
  - morphine



The effect of increased plasma osmolarity or decreased blood volume.

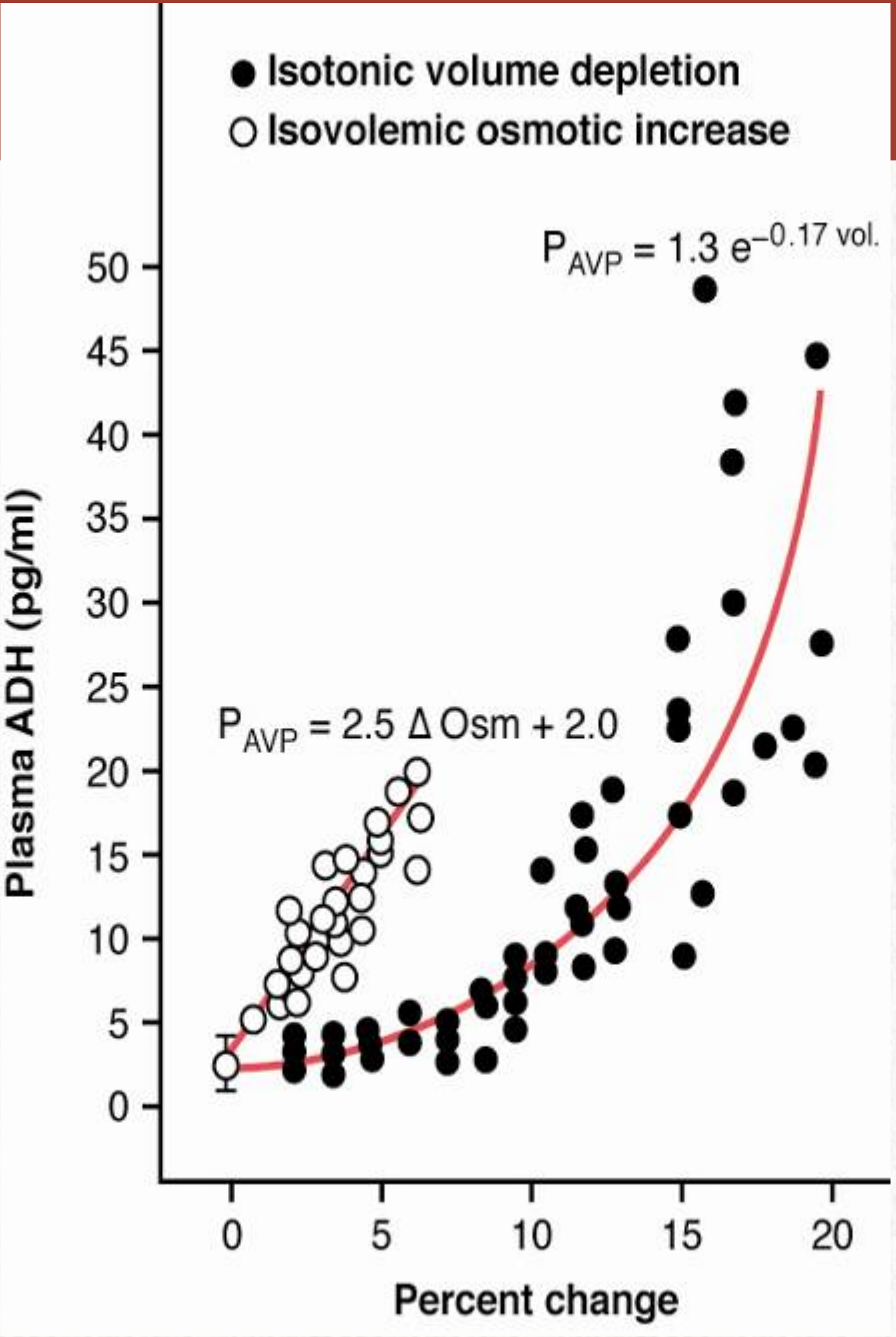
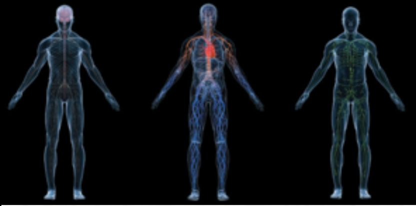
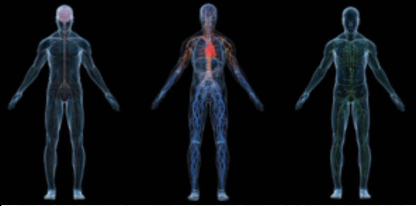


Figure 28-11



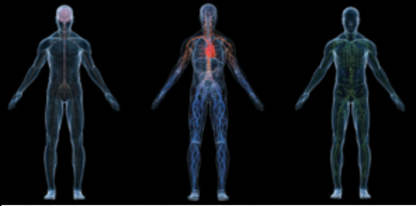
Factors That Decrease ADH Secretion

- Decreased osmolarity
- Increased blood volume (cardiopulmonary reflexes)
- Increased blood pressure (arterial baroreceptors)
- Other factors :
  - alcohol
  - clonidine (antihypertensive drug)
  - haloperidol (antipsychotic, Tourette’s)



Stimuli for Thirst

- Increased osmolarity
- Decreased blood volume
  (cardiopulmonary reflexes)
- Decreased blood pressure
  (arterial baroreceptors)
- Increased angiotensin II
- Other stimuli:
  - dryness of mouth



Factors That Decrease Thirst

- Decreased osmolarity
- Increased blood volume
  (cardiopulmonary reflexes)
- Increased blood pressure
  (arterial baroreceptors)
- Decreased angiotensin II
- Other stimuli:
  -Gastric distention