
In The Name Of God

C H A P T E R 2 9

- **Urine concentration and dilution, regulation of extracellular fluid osmolarity and sodium concentration**

هدف کلی جلسه: تغلیظ و رقیق سازی ادرار، تنظیم اسمولالیته مایع خارج سلولی و غلظت سدیم

اهداف ویژه جلسه
در پایان دانشجو قادر باشد:

- نحوه رقیق سازی و تغلیظ ادرار توسط کلیه ها جهت تنظیم حجم مایعات بدن را شرح دهد
- نقش هیپراسمولاریته مدولای کلیه در تغلیظ ادرار و نحوه بوجود آمدن آنرا توضیح دهد
- نقش ADH در تنظیم حجم و نحوه آزاد شدن آنرا شرح دهد
- محل های مختلف اثر ADH و اثر آن در هر محل را توضیح دهد
- نقش اوره در تغلیظ ادرار و چرخش مجدد آنرا در کلیه توضیح دهد
- نحوه اثر اجزای سیستم رنین – آنژیوتانسین را در تنظم آب و الکترولیتها توضیح دهد
- مکانیسم اسمورسپتور- ADH و تشنگی را در کنترل حجم و اسمولاریته مایعات خارج سلولی شرح دهد

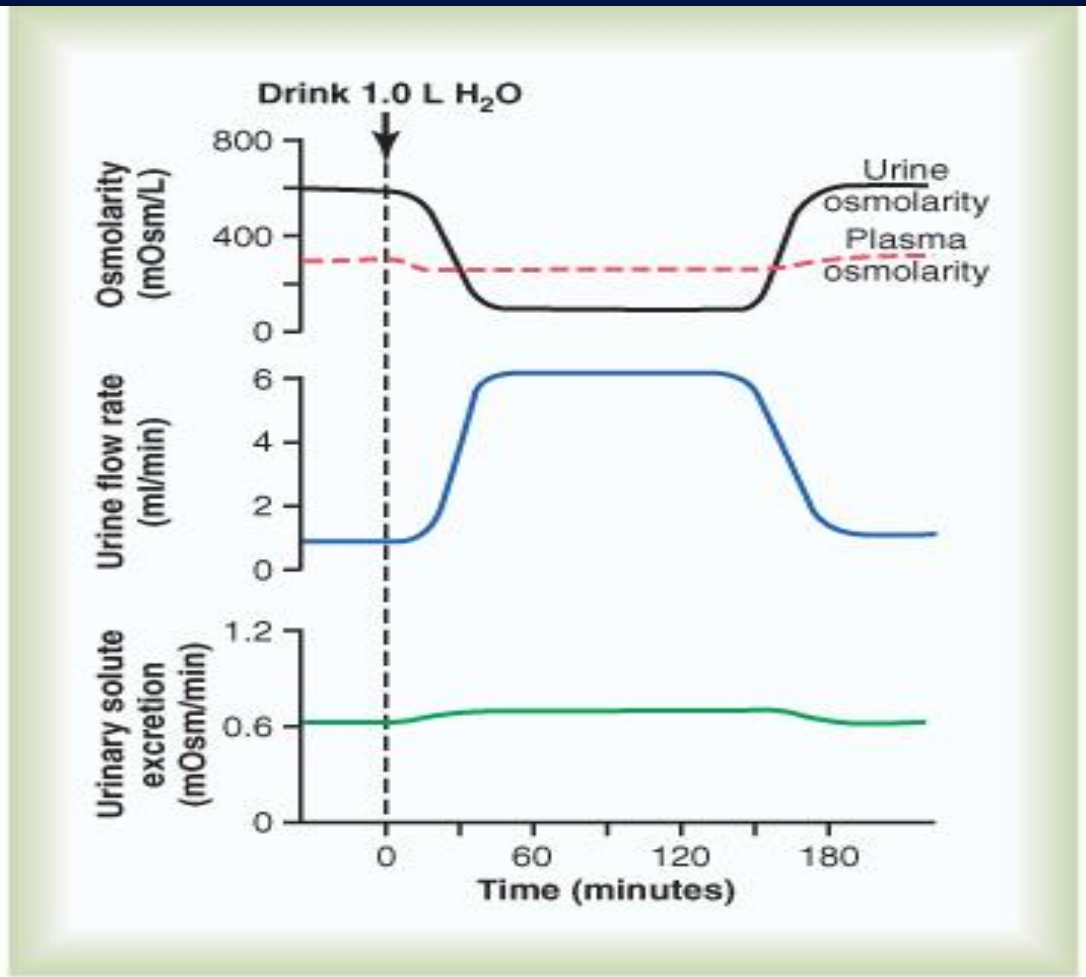
- The Kidneys Excrete Excess Water by Forming a Dilute Urine

-Independent regulation of water excretion from solutes

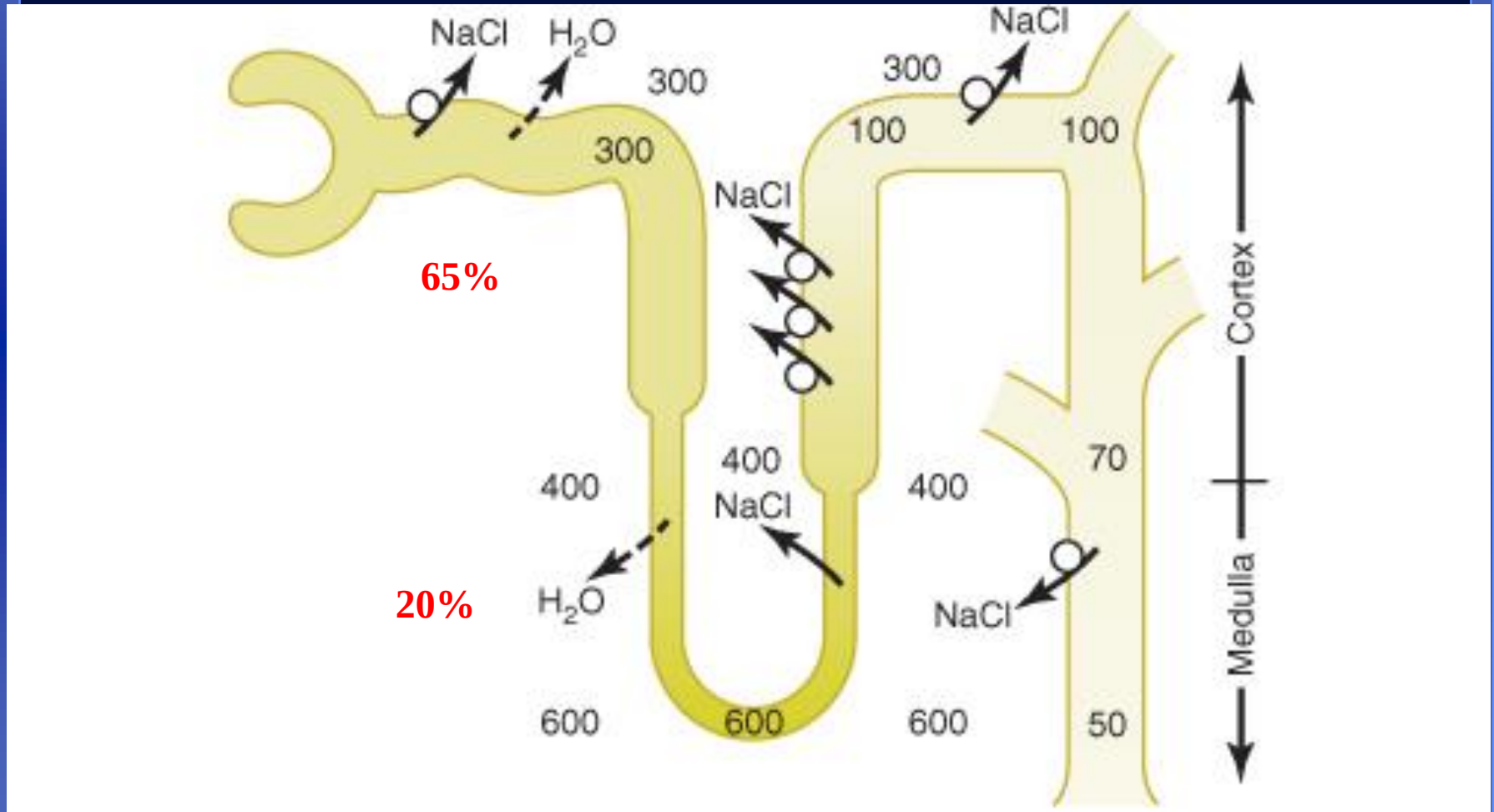
- ADH Controls Urine Concentration

- Renal Mechanisms for Excreting a Dilute Urine

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



Formation of a dilute urine when ADH levels are very low



Therefore in total:

-Tubular Fluid Remains Isosmotic in the Proximal Tubule

-Tubular Fluid Becomes Dilute in the Ascending Loop of Henle

-Tubular Fluid in Distal and Collecting Tubules Is Further Diluted in the Absence of ADH

- The Kidneys Conserve Water by Excreting a Concentrated Urine (1400 mosm)

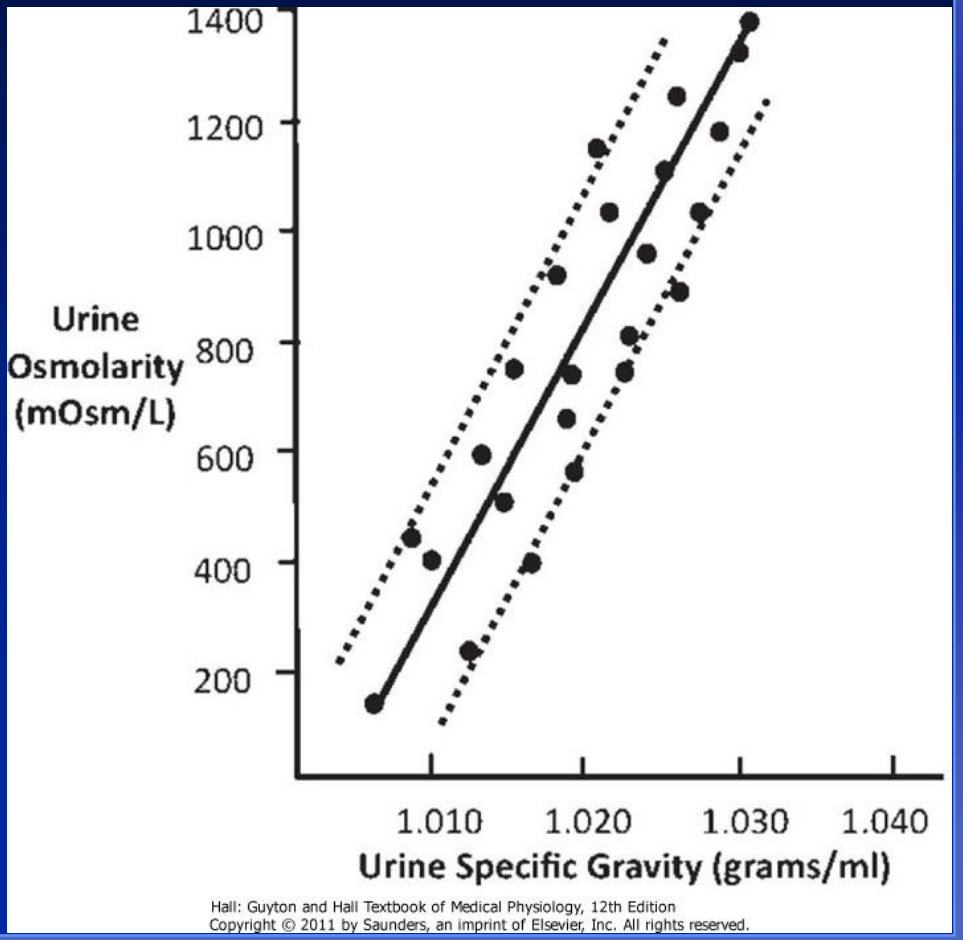
-Obligatory Urine Volume

= amount of excreted solutes / maximum concentrating ability

- why severe dehydration occurs if one attempts to drink seawater

Specific Gravity of Urine

- The weight of a volume of solution divided by the weight of an equal volume of distilled water (1.002-1.028)



- Requirements for Excreting a Concentrated Urine

-High ADH Level

-Hyperosmotic Renal Medulla

- Countercurrent Mechanism Produces a Hyperosmotic Renal Medullary Interstitium

The major factors that contribute to the buildup of solute concentration into the renal medulla

1. Active transport of sodium ions and co-transport of potassium, chloride and other ions in TAL

2. Active transport of ions from the collecting ducts into the medullary interstitium

3. Facilitated diffusion of large amounts of urea from the inner medullary collecting ducts

4. Diffusion of only small amounts of water

- Special Characteristics of Loop of Henle That Cause Solutes to Be Trapped in the Renal Medulla

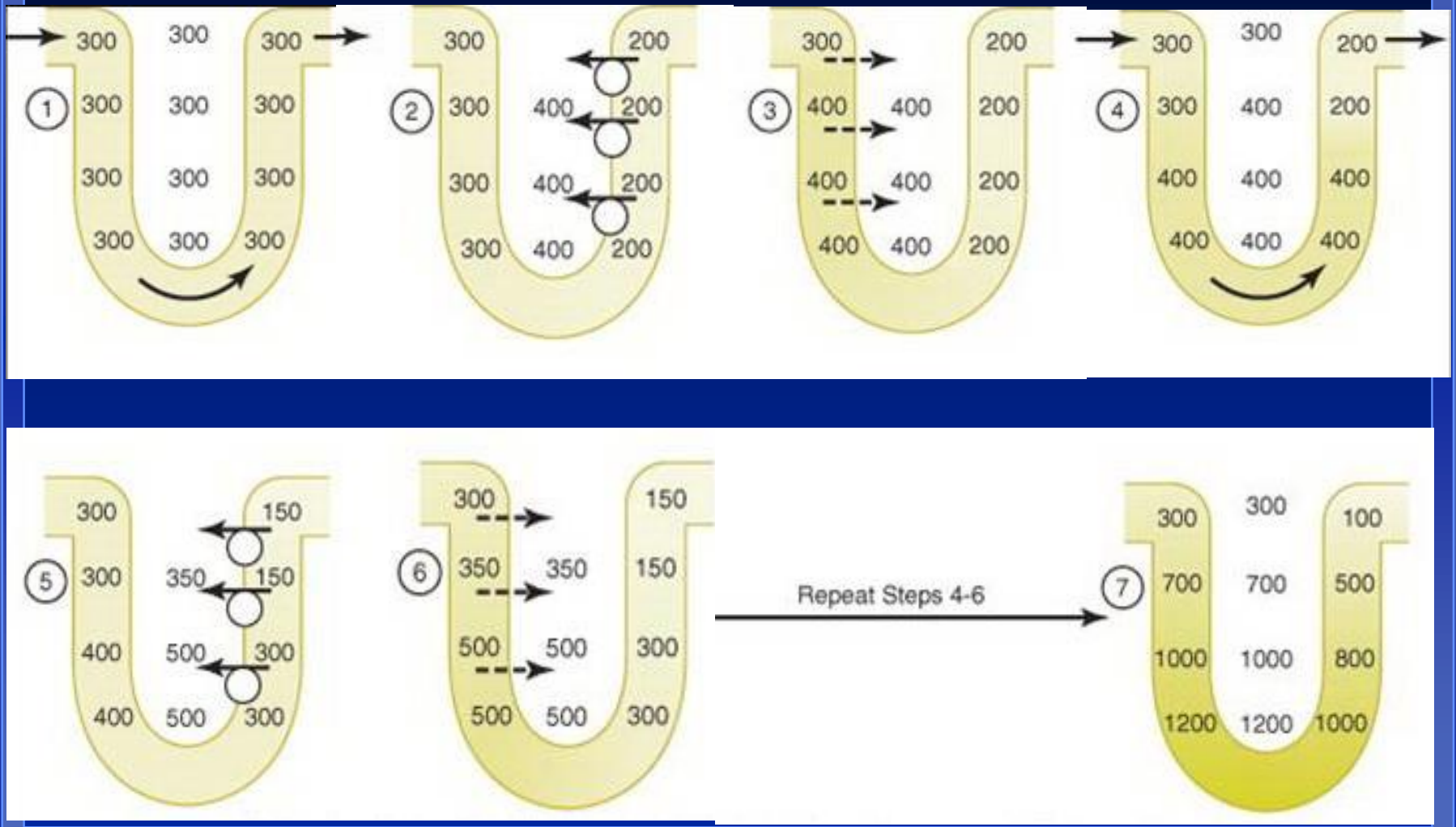
Summary of Tubule Characteristics—Urine Concentration

	Active NaCl Transport	Permeability		
		H_2O	NaCl	Urea
Proximal tubule	++	++	+	+
Thin descending limb	0	++	+	+
Thin ascending limb	0	0	+	+
Thick ascending limb	++	0	0	0
Distal tubule	+	+ADH	0	0
Cortical collecting tubule	+	+ADH	0	0
Inner medullary collecting duct	+	+ADH	0	++ADH

The most important cause of the high medullary osmolarity is active transport of sodium and cotransport of potassium, chloride, and other ions from TAL

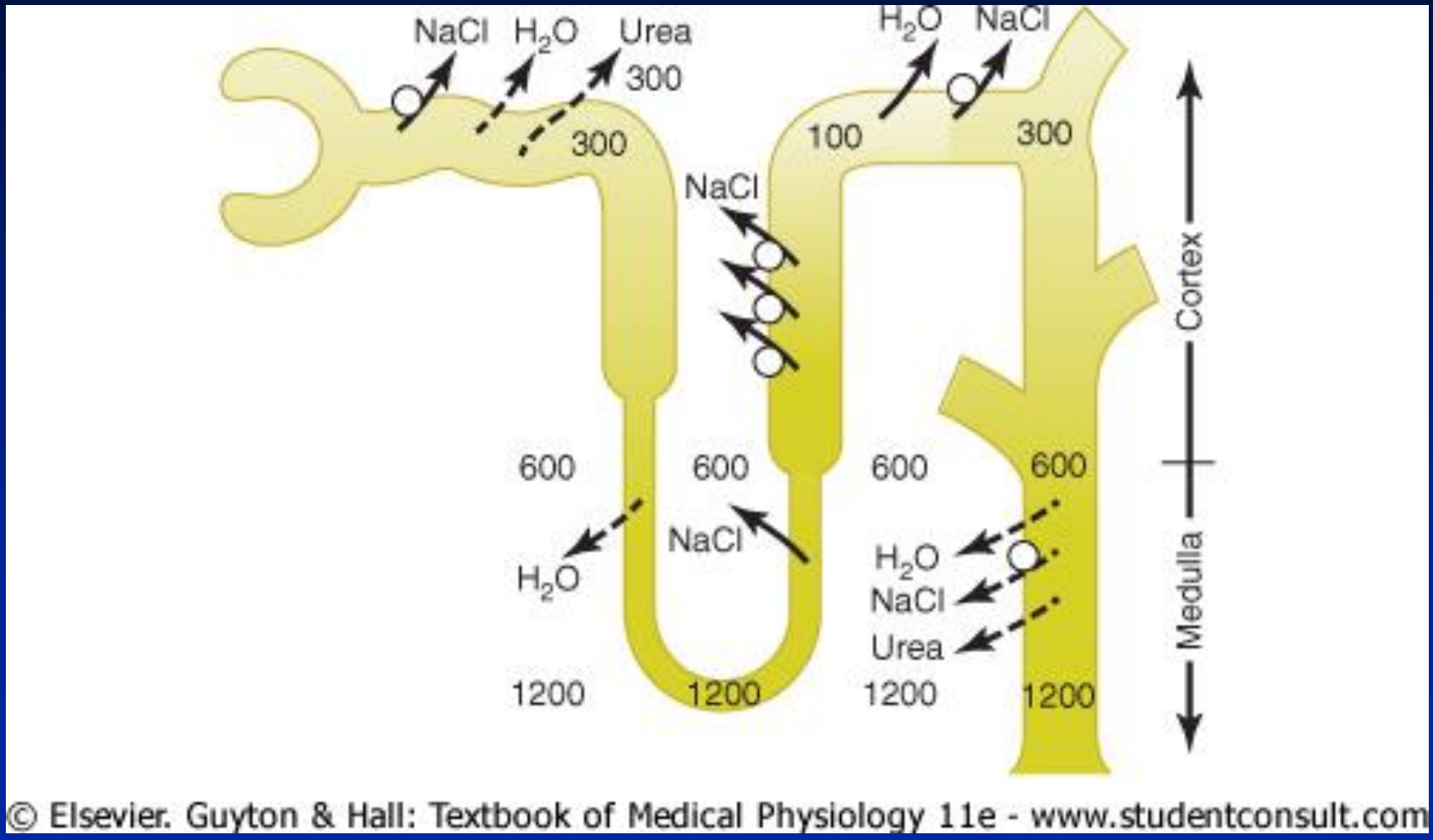
- Steps Involved in Causing Hyperosmotic Renal Medullary Interstitium (200 mOsm)

Countercurrent multiplier system in the loop of henle for producing a hyperosmotic renal medulla



- Role of Distal Tubule and Collecting Ducts in Excreting a Concentrated Urine

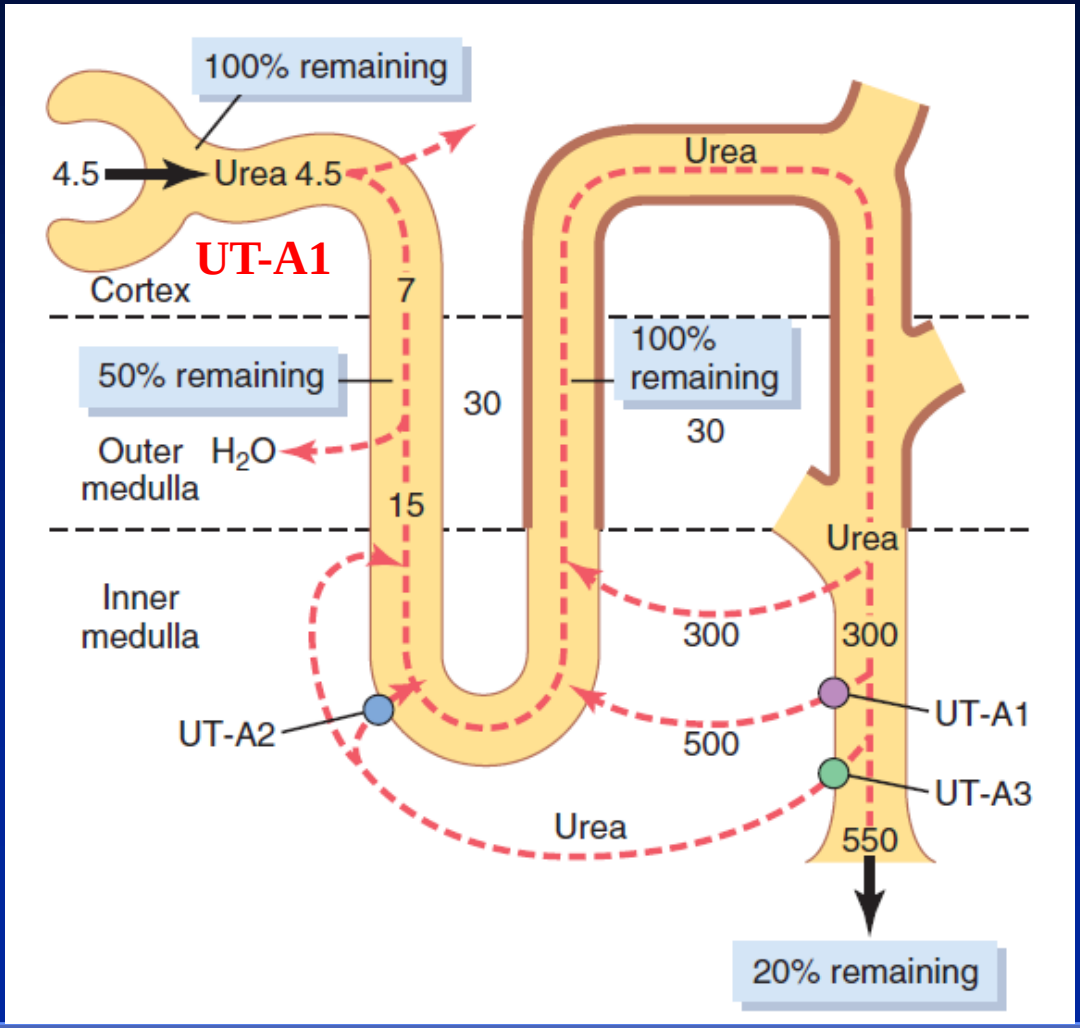
Formation of a concentrated urine when ADH levels are high (role of ADH?)



- **Urea Contributes to Hyperosmotic Renal Medullary Interstitium and to a concentrated Urine (40%)**

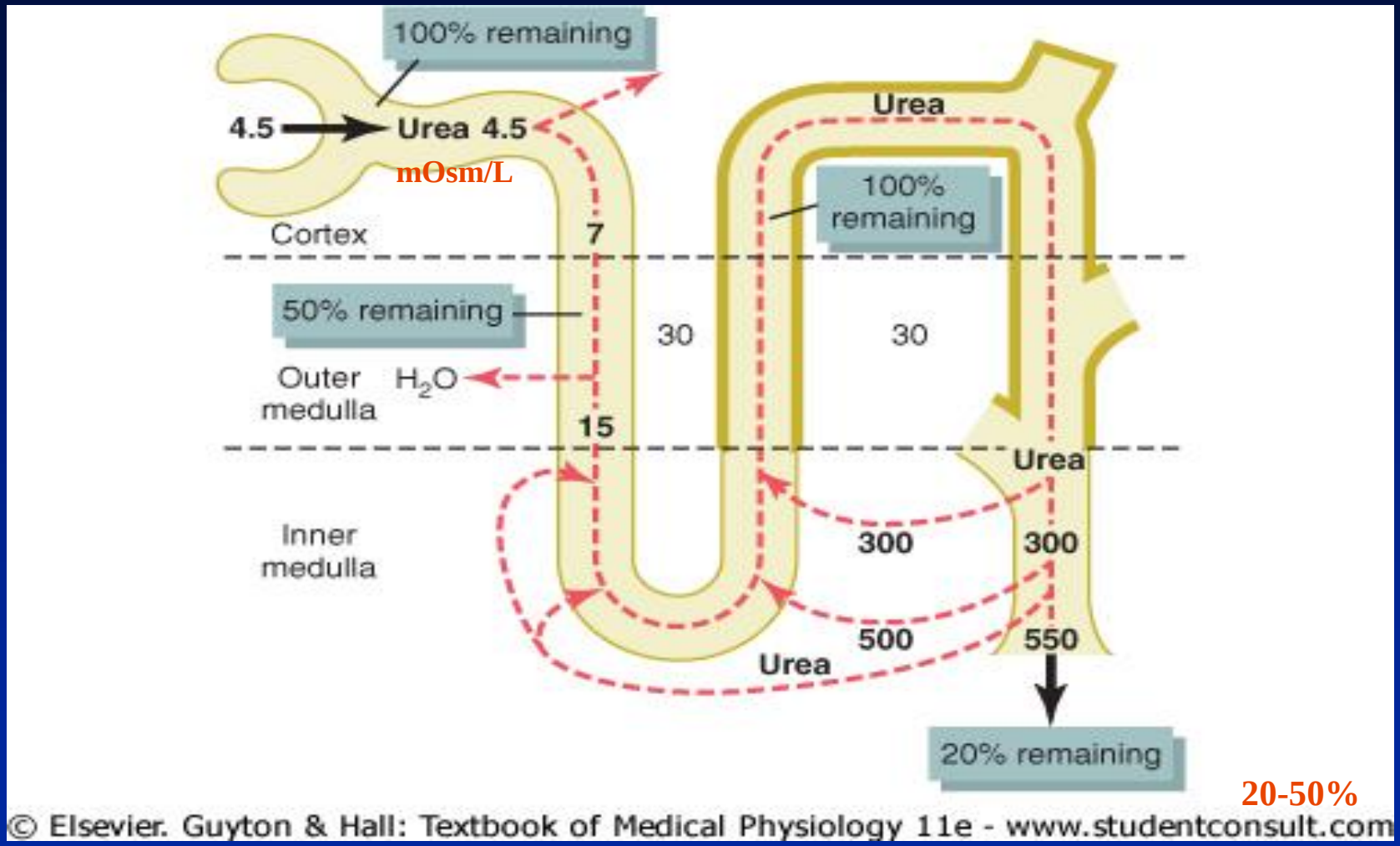
*** UT-A1 and UT-A3 receptors in IMCD**

The mechanism for reabsorption of urea into the renal medulla

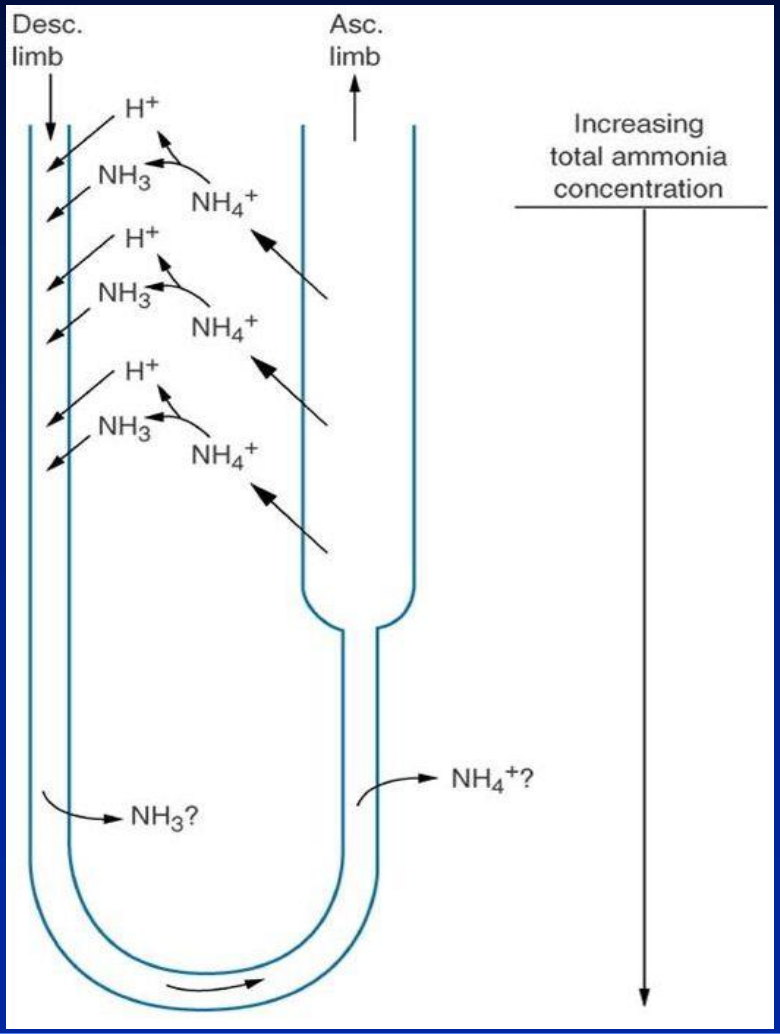


- **Recirculation of Urea from Collecting Duct to Loop of Henle Contributes to Hyperosmotic Renal Medulla**

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



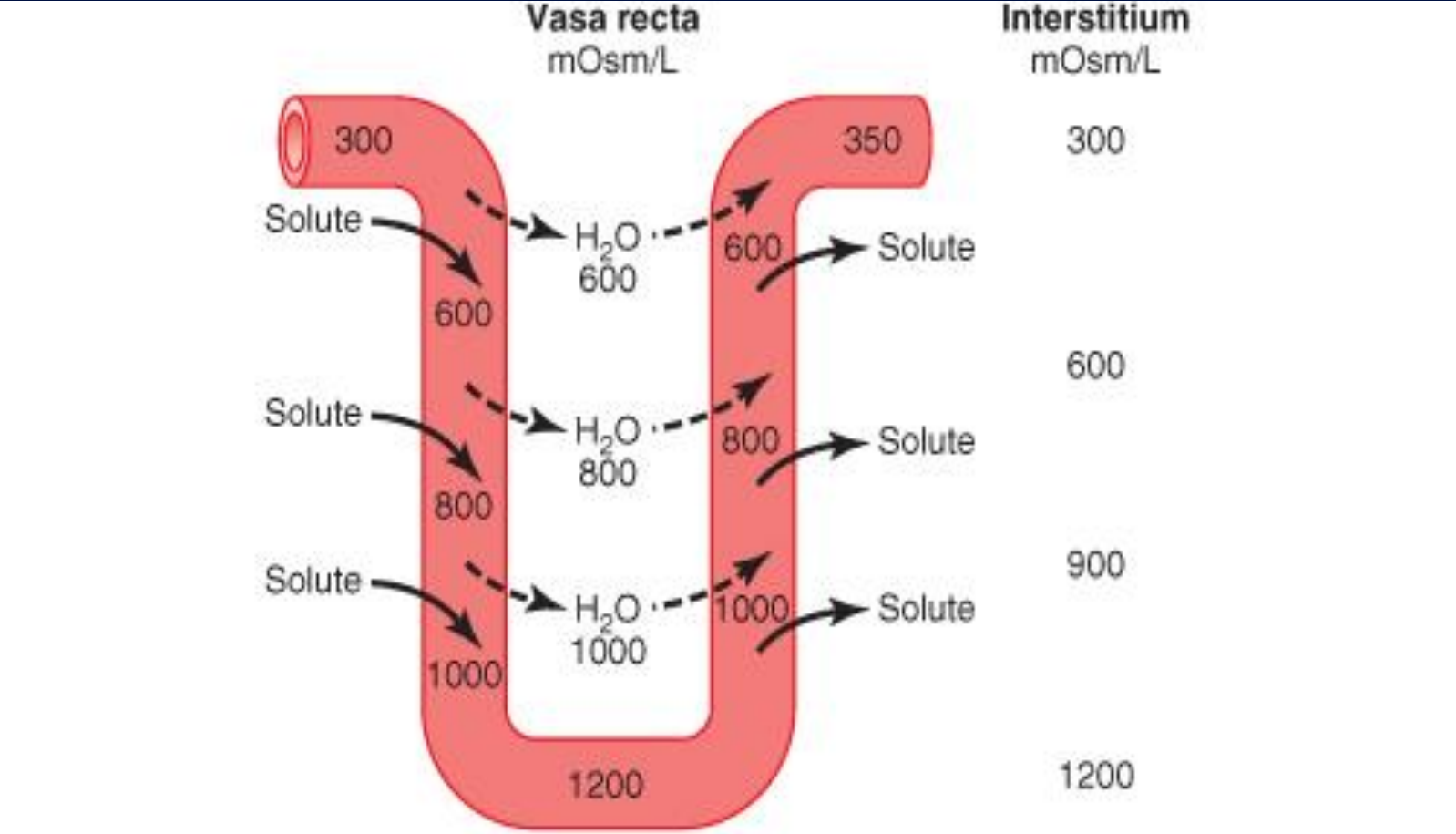
Countercurrent multiplier for NH_4



- Countercurrent Exchange in the Vasa Recta Preserves Hyperosmolarity of the Renal Medulla

1. *The medullary blood flow is low*
2. *The vasa recta serve as countercurrent exchangers*

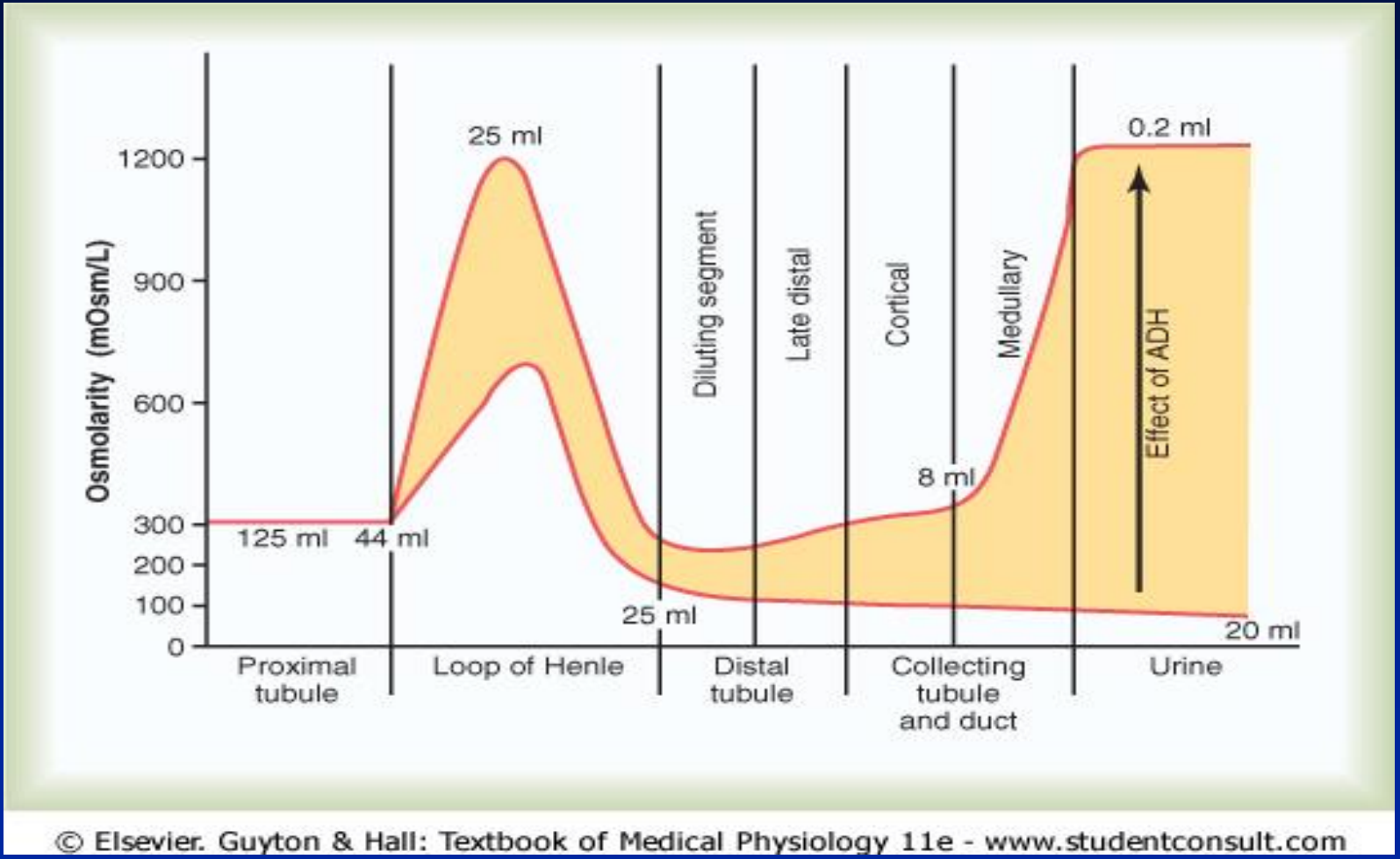
Countercurrent exchange in the vasa recta



- Increased Medullary Blood Flow or Blood Pressure Can Reduce Urine Concentrating Ability

- Summary of Urine Concentrating Mechanism and Changes in Osmolarity in Different Segments of the Tubules

Changes in osmolarity of the tubular fluid as it passes through the different tubular segments in the presence and absence of ADH



Quantifying Renal Urine Concentration and Dilution: "Free Water" and Osmolar Clearances

$$C_{osm} = \frac{U_{osm} \times V}{P_{osm}}$$

- Relative Rates at Which Solutes and Water Are Excreted Can Be Assessed Using the Concept of "Free-Water Clearance"

$$C_{H_2O} = V - C_{osm} = V - \frac{(U_{osm} \times V)}{(P_{osm})}$$

Disorders of Urinary Concentrating Ability

- Failure to Produce ADH: “Central” Diabetes Insipidus
- Inability of the Kidneys to Respond to ADH: “Nephrogenic” Diabetes Insipidus

- Control of Extracellular Fluid Osmolarity and Sodium Concentration

- Estimating Plasma Osmolarity from Plasma Sodium Concentration

- $P_{osm} = 2.1 \times [Na^+]_p$

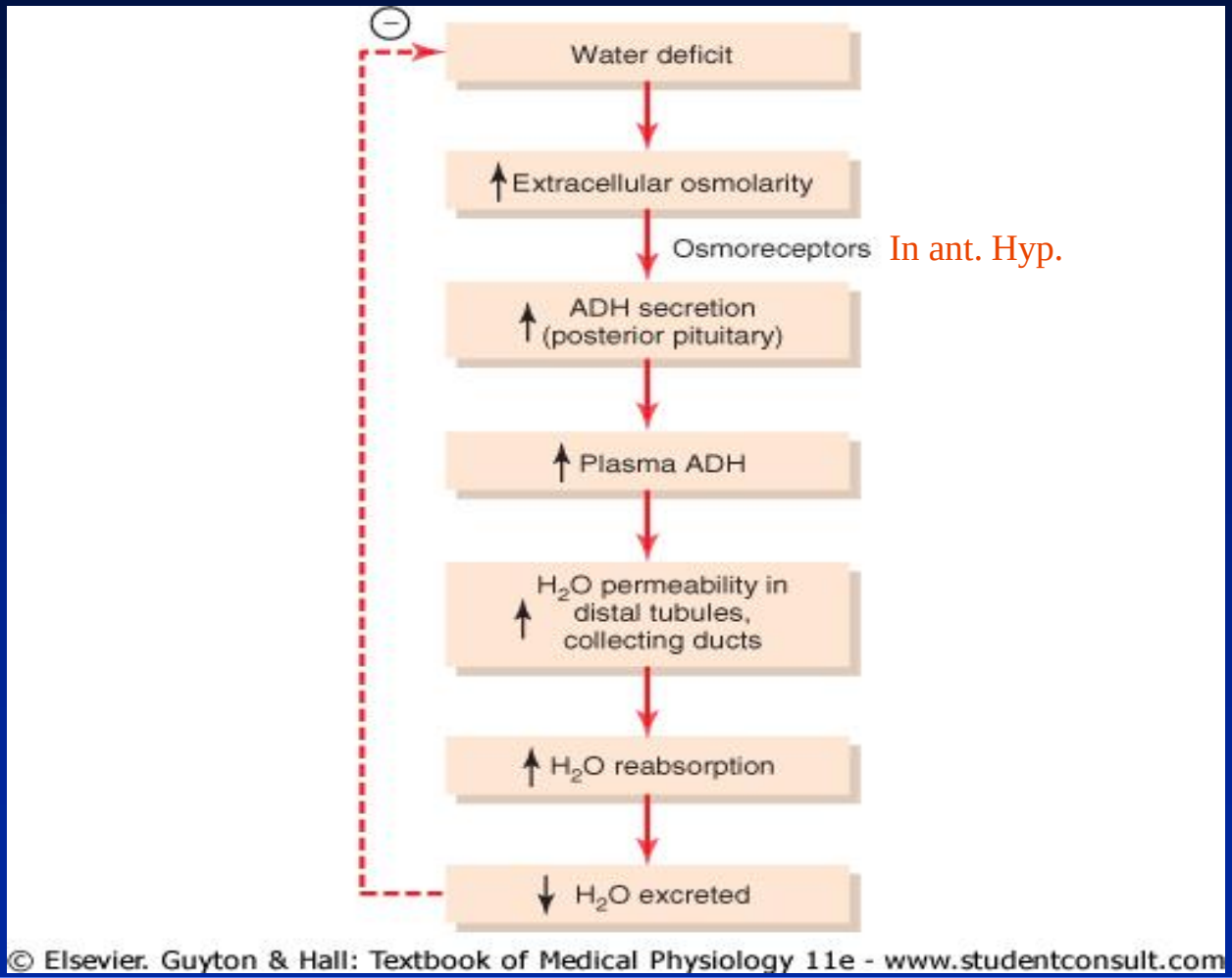
- $P_{osm} = 2[Na^+]_p + \frac{[Glucose]_p}{18} + \frac{[Urea]_p}{2.8}$

Two primary systems for regulating the concentration of sodium and osmolarity of extracellular fluid

(1) the osmoreceptor-ADH system

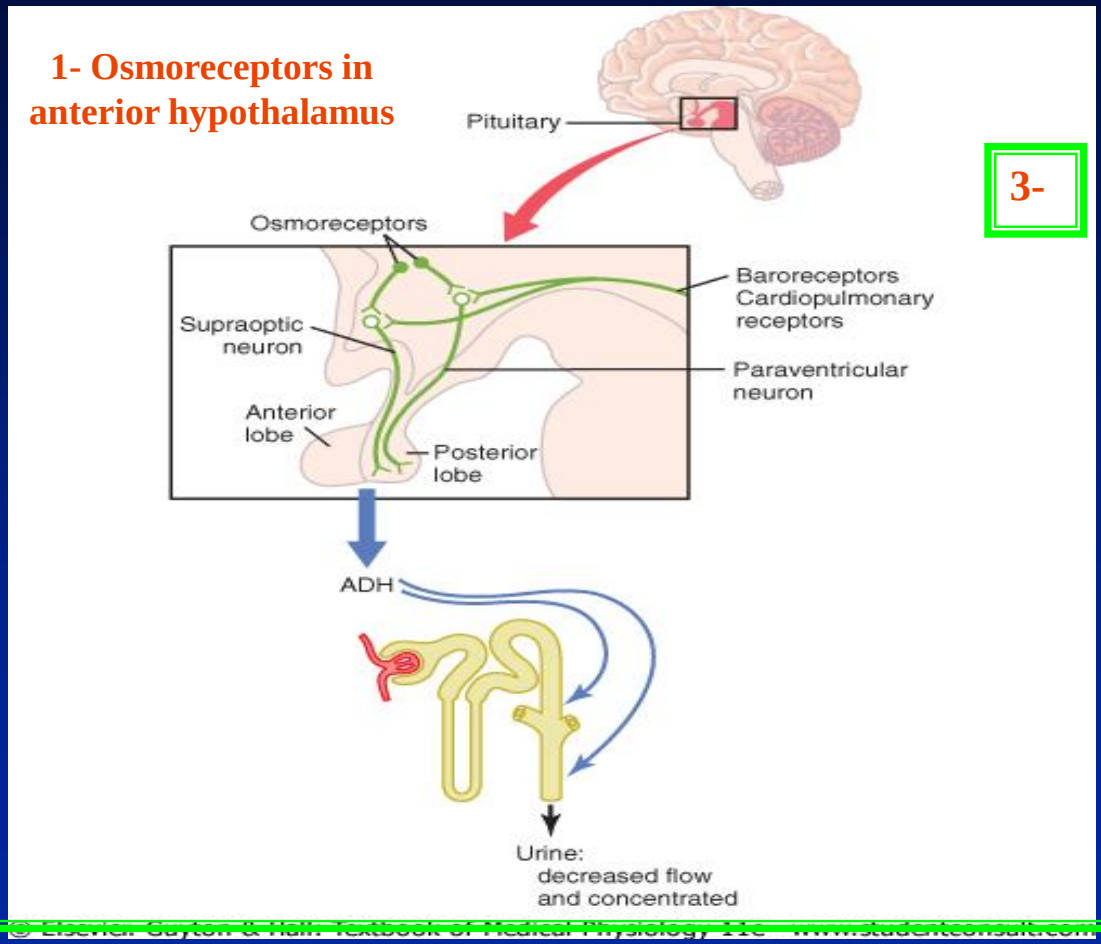
(2) the thirst mechanism

Osmoreceptor- ADH feedback mechanism for regulating ECF osmolarity in response to a water deficit



- ADH Synthesis in Supraoptic and Paraventricular Nuclei of the Hypothalamus and ADH Release from the Posterior Pituitary

Neuroanatomy of the hypothalamus, where ADH is synthesized, and posterior pituitary gland, where ADH is released

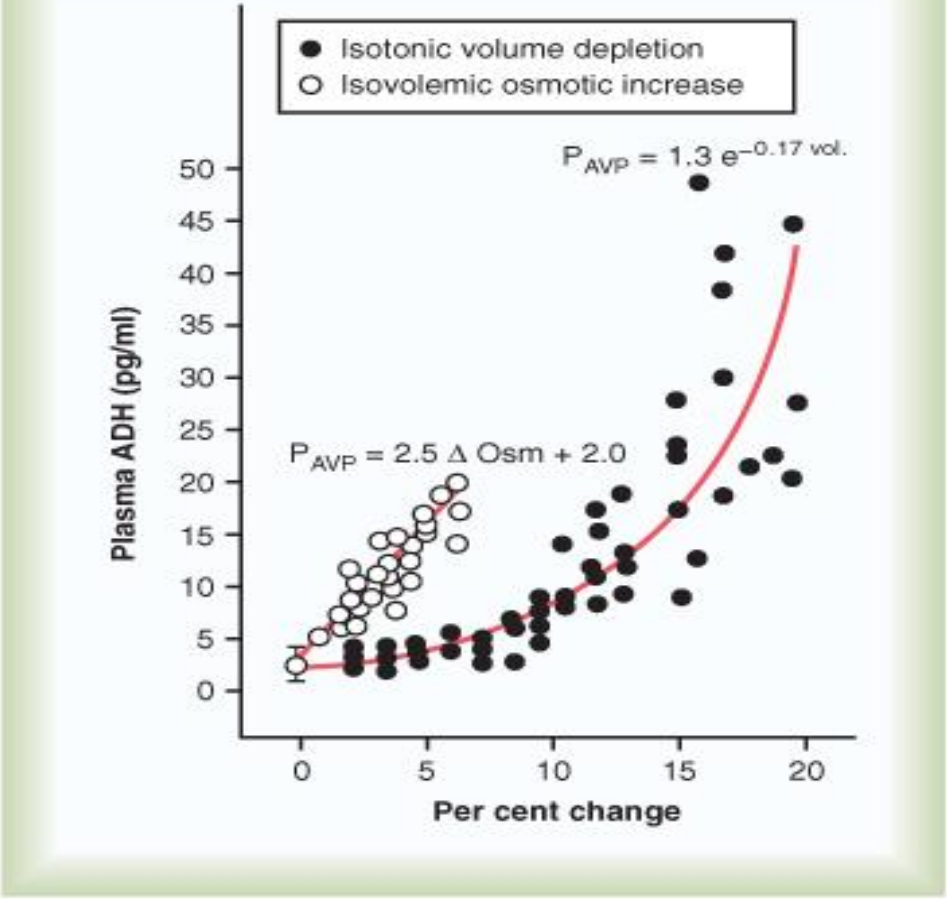


2- Anteroventral region of the third ventricle (AV3V) : subfornical organ & organum vasculosum of the lamina terminalis

- Cardiovascular Reflex Stimulation of ADH Release by Decreased Arterial Pressure and/or Decreased Blood Volume

- Quantitative Importance of Cardiovascular Reflexes and Osmolarity in Stimulating ADH Secretion

The effect of increased plasma osmolarity or decreased blood volume on the level of plasma ADH



Other Stimuli for ADH Secretion -Regulation of ADH Secretion

Increase ADH	Decrease ADH
↑ Plasma osmolarity	↓ Plasma osmolarity
↓ Blood volume	↑ Blood volume
↓ Blood pressure	↑ Blood pressure
Nausea	
Hypoxia	
Drugs:	Drugs:
Morphine	Alcohol
Nicotine	Clonidine (antihypertensive drug)
Cyclophosphamide	Haloperidol (dopamine blocker)

- Role of Thirst in Controlling Extracellular Fluid Osmolarity and Sodium Concentration

- Central Nervous System Centers for Thirst
  - AV3V
  - Anterolateral area of preoptic nuclei

Stimuli for Thirst

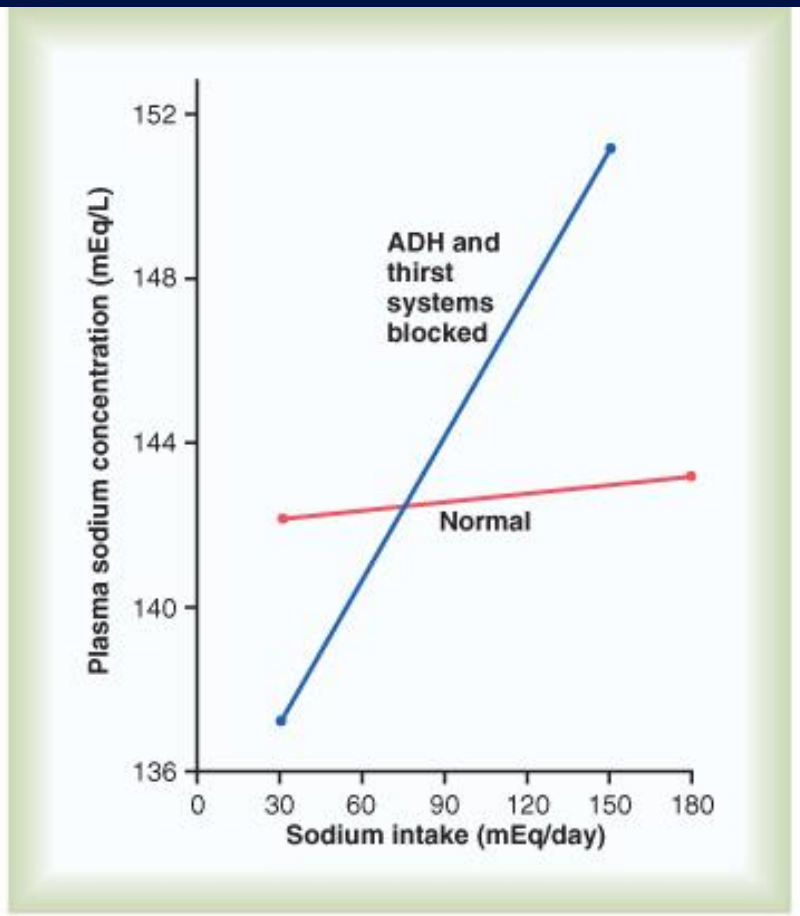
Increase Thirst	Decrease Thirst
↑ Osmolarity	↓ Osmolarity
↓ Blood volume	↑ Blood volume
↓ Blood pressure	↑ Blood pressure
↑ Angiotensin	↓ Angiotensin II
Dryness of mouth	Gastric distention

- Threshold for Osmolar Stimulus of Drinking

  (2 meq/L)

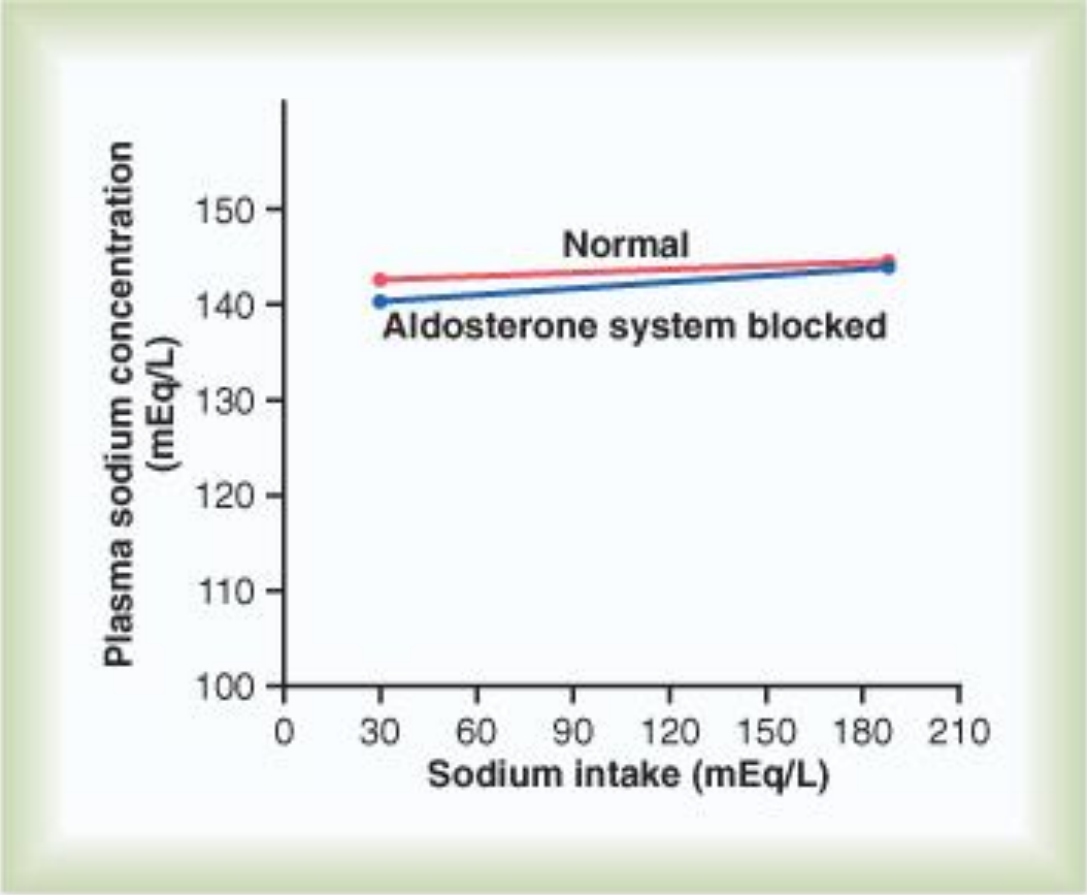
- Integrated Responses of Osmoreceptor-ADH and Thirst Mechanisms in Controlling Extracellular Fluid Osmolarity and Sodium Concentration

Effect of large changes in sodium intake on extracellular fluid sodium concentration under normal conditions and after blockade of ADH and thirst feedback systems



- Role of Angiotensin II and Aldosterone in Controlling Extracellular Fluid Osmolarity and Sodium Concentration

Effect of large changes in Na^+ intake on ECF sodium concentration under normal conditions and after blockade of aldosterone system



- Salt-Appetite Mechanism for Controlling Extracellular Fluid Sodium Concentration and Volume

- two primary stimuli that increase salt appetite:

(1) decreased extracellular fluid sodium concentration

(2) decreased blood volume or blood pressure

- Its center: AV3V


Thanks for your attention