King Saud University

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Urine Concentration & Dilution

Lecture 8

RENAL BLOCK

PHYSIOLOGY TEAM 437

Editing file

Objectives:

by the end of this lecture you will be able to:

- At the end of this session, students should be able to:
- Identify and describe that the loop of Henle is referred to as countercurrent multiplier and the vasa recta as countercurrent exchanger systems in concentrating and diluting urine.
- Explain what happens to osmolarity of tubular fluid in the various segments of the loop of Henle when concentrated urine is being produced.
- Explain the factors that determine the ability of loop of Henle to make a concentrated medullary gradient.
- Differentiate between water diuresis and osmotic diuresis.
- Appreciate clinical correlates of diabetes mellitus and diabetes insipidus.

OVERVIEW

Renal Regulation of Body Fluids

By regulating the extracellular fluid

- Osmolarity
  - Regulated by H_2O
- Volume
  - Regulated by Na^+

Discussed in the previous lecture <3

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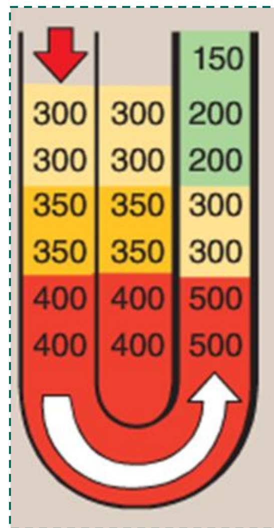
Countercurrent System:

- A system in which inflow runs parallel and in close proximity but opposite to the outflow.
- The operation of such a system allows the outgoing fluid to heat the incoming fluid.



Mechanism for urine concentration/dilution

- While the loop of Henle reabsorbs another 20% of the salt/water in tubular fluid, primary function is to determine osmolarity of urine (i.e. whether concentrated or diluted) using **countercurrent multiplier system.**
- While collecting duct is where urine concentration is determined, osmolarity of interstitial fluid in medulla must be high and osmolarity of tubular fluid must be low
- Countercurrent multiplier system achieves this.

How the Kidney Excrete Dilute Urine?

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[Urine concentration and dilution, Duration 14:43 mins]

- Dilution (low or no ADH):
- Reabsorb solute don't absorb water

1) Isosmotic fluid from PCT

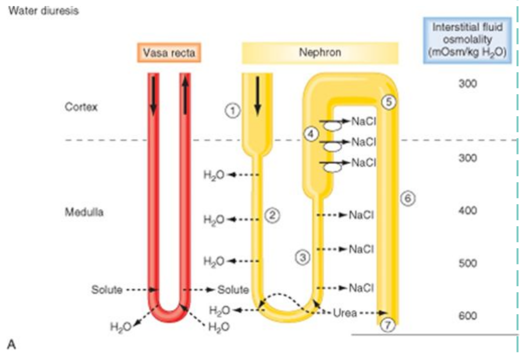
2) Thin descending limb permeable to water, less for NaCl water reabsorbed, tubule osmolality = medulla (i.e. high)

3) Thin ascending limb impermeable to water, permeable to NaCl (passive). Tubule volume unchanged, ↓ [NaCl].

4) TAL impermeable to water, NaCl actively reabsorbed (diluting segment of nephron). Diluting tubule fluid 150 mOsm/kg water

5) Collecting duct reabsorb NaCl

- osmolality, may reach 50 mOsm/kg water.



Remember descending part is permeable to water while ascending part is permeable to salt.

Concentration of urine (ADH dependent):

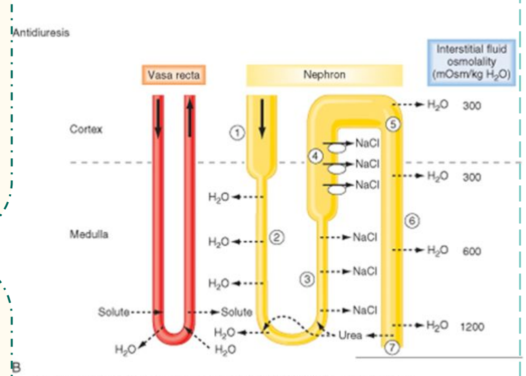
- 1-4 same as dilution
- Reabsorbed NaCl in loop of Henle → osmolality of interstitium
- Generated by **Countercurrent Multiplication**

5) Fluid reaching CD hypo-osmotic.

- ADH causes water to diffuse out up to a max of 300 mOsm/kg water.

6) Osmolality of medullary tissue high up to 1200 mOsm/kg water

- due to NaCl (accounts for 600)
- urea (accounts for 600)
- early CD impermeable to urea
- ADH allows water reabsorption passively



Koeppen & Stanton: Berne and Levy Physiology, 6th Edition.

ADH works on medullary segment of CD enhancing reabsorption of urea. Which moves to interstitium increasing osmolarity of interstitium

How the kidney excrete concentrated urine?

- When ADH levels high urea levels in medullary CD & interstitium equilibrate
- ADH mostly affects water reabsorption in the cortical collecting duct
- **Even in the presence of high ADH most water is absorbed in the PCT**

Forming a Concentrated Urine requires:

[Urine concentration, Duration 4:52 mins]

1.High levels of ADH.

2.Hyperosmotic renal medulla.

A. Countercurrent mechanism.

B. Urea recirculation.

IF around the body has an osmolarity of ≈ 300 mOsm/L..

How did the renal medullary interstitium become hyperosmotic?

Countercurrent Multiplier Mechanism

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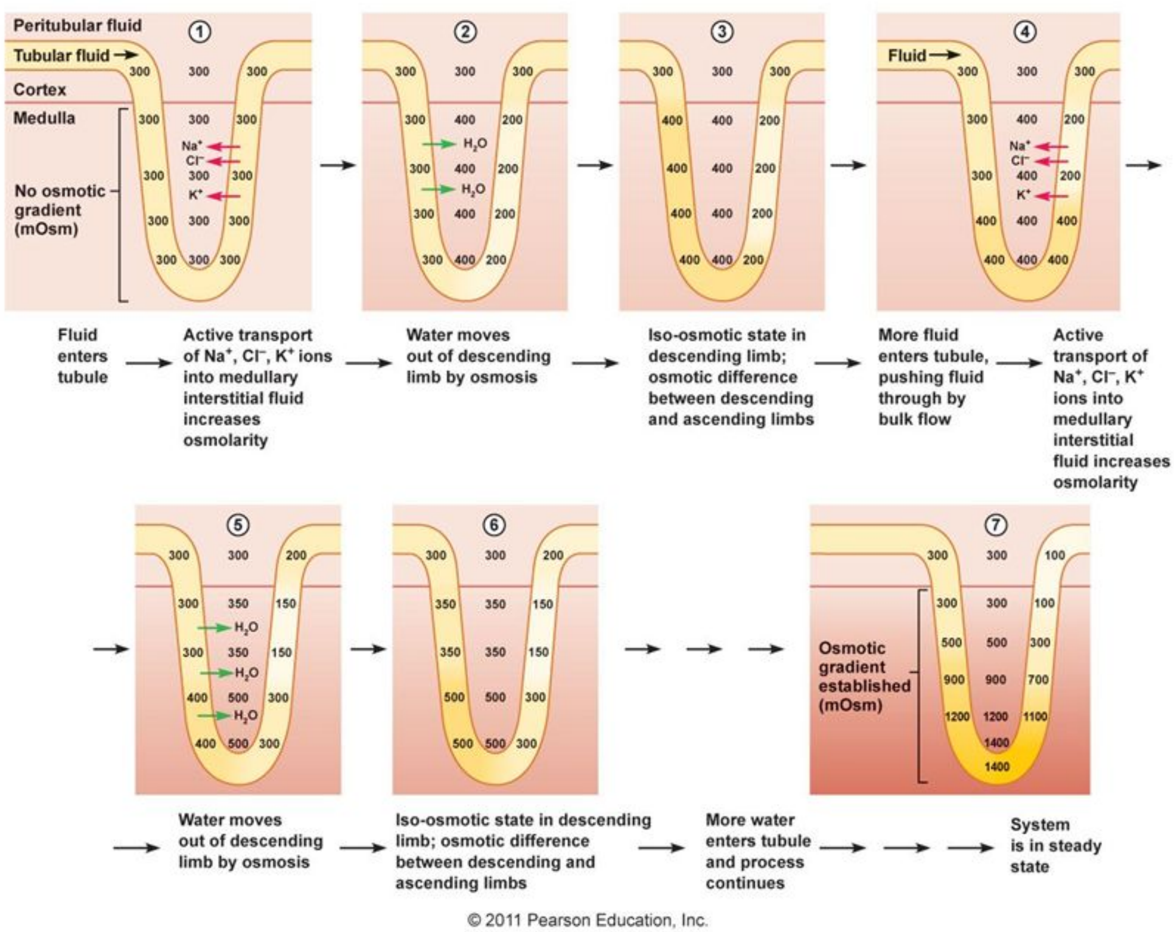

Recirculation of Urea

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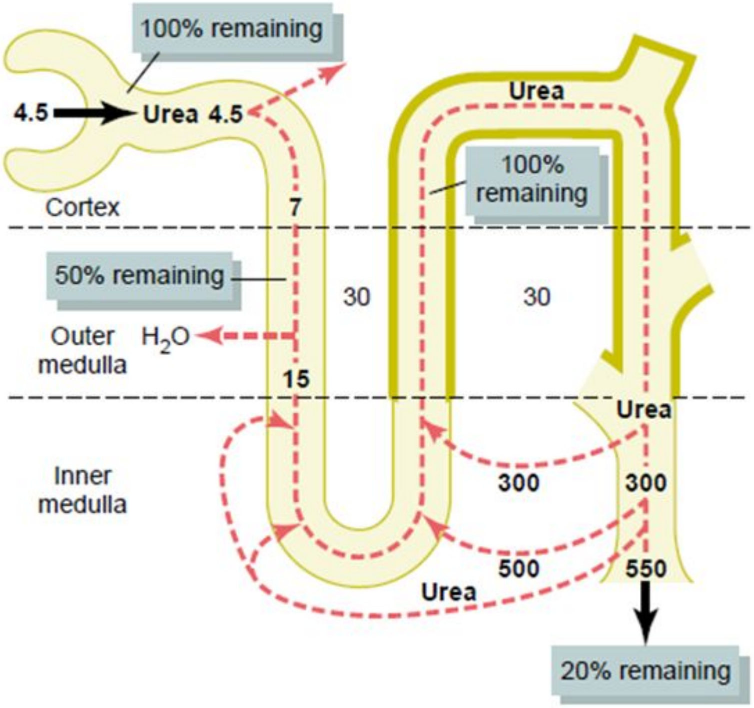

[Role of urea in kidney Pt. 1, Duration 2:58 mins]

[Role of urea in kidney Pt. 2, Duration 3:03 mins]

The Vasa Recta

- **Why doesn't the blood flowing through the vasa recta into the renal medulla wash out the medullary hyperosmotic gradient?**

1.Medullary blood flow is low (<5%) of renal blood flow.

2.The vasa recta serve as countercurrent exchangers.

3-Recycles NaCl in Medulla

- Transports H_2O from interstitial fluid.

Descending limb
- Urea transporters
- Aquaporin proteins (H_2O channels)

Ascending limb
- Fenestrated capillaries.

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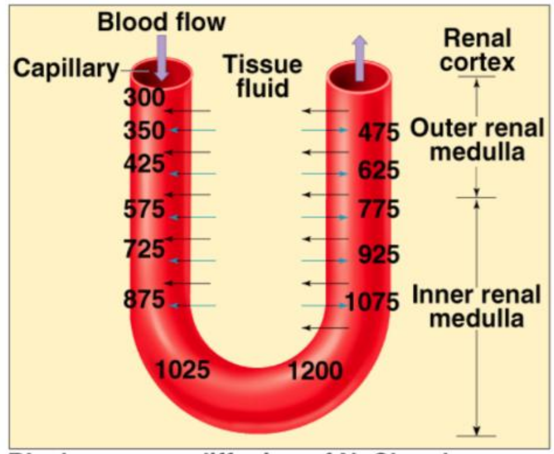
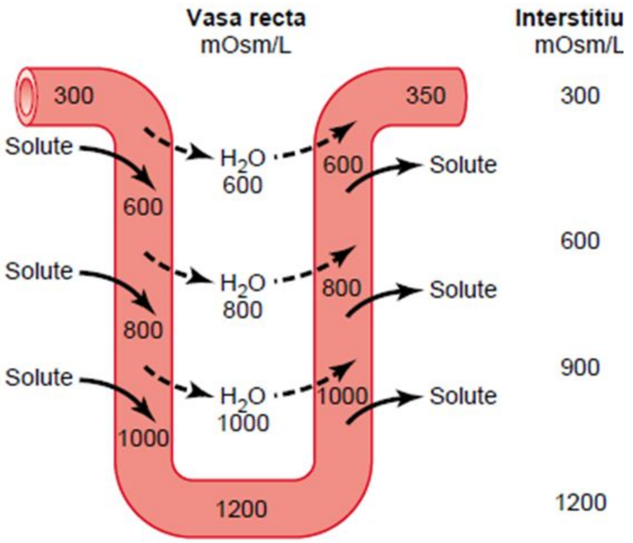
The Vasa Recta

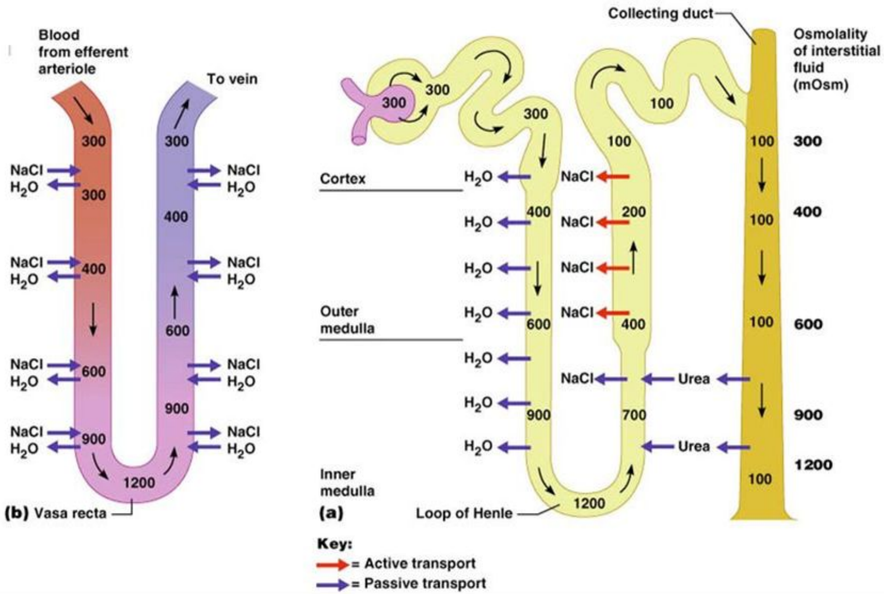
- Vasa recta maintains hypertonicity by countercurrent exchange.
- NaCl and urea diffuse into descending limb and diffuse back into medullary tissue fluid.
- Walls are permeable to H_2o, NaCl and urea.
- Colloid osmotic pressure in vasa recta > interstitial fluid.



Black arrows = diffusion of NaCl and urea
Blue arrows = movement of water by osmosis

The Vasa Recta Countercurrent exchanger





Factors affecting urine concentration

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ADH	causes an increase in permeability of DCT, CT, and CD for water. It also increase the permeability of medullary CD to urea.
Length of the loop of Henle	The longer the loop of Henle, the greater the countercurrent multiplication effect and more urine concentration. - The new born baby having shorter loop of Henle can not concentrate as same as the adult.
Delivery of salt to ALH	- Due to a decrease in GFR (Hemorrhage) the filter load of solute is decreased. - This leads to a decrease in the delivery of salt to ALH resulting in decreased reabsorption of salt from ALH. - Thus there is decreased addition of salts to the medullary ISF, leading to decreased medullary longitudinal osmotic gradient and decreased urine concentration.
Reabsorption of salt	Diuretic drugs (Lasix) prevents NaCl reabsorption from thick ALH, leading to decreased addition of salts to the medullary ISF, decreased medullary longitudinal osmotic gradient and finally decreased urine concentration.
Delivery of fluid to medullary CT and CD	- Maximum urine concentration occurs when only a small amount of fluid enters the medullary CT and CD. - Even during an osmotic diuresis, the increased fluid volume delivered to the medullary CT and CD leads to wash out of medullary longitudinal osmotic gradient and cause decreased urine concentration.

Factors affecting urine concentration Cont.

Medullary blood flow

- Normally very low blood flow (about 5% of total RBF) to the medulla.
- Increased blood flow to the medulla may cause wash out of the medullary longitudinal osmotic gradient, decreased effectiveness of the countercurrent exchange system and decreased urine concentration.

Urea

- Urea recycling contributes significantly to the medullary longitudinal osmotic gradient and is essential for the countercurrent system.
- A person on a protein free diet loses the ability to concentrate urine due to lack of urea in the medulla.

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ECF osmolarity

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- Maintaining a constant concentration of solutes & electrolytes in the ECF is important for normal cellular function.
- The concentration of solutes in the ECF = ***osmolarity.***
- Normal ECF osmolarity ≈ ***300 mOsm/L***

A. What determines the osmolarity of ECF?
  a. Osmolarity = Amount of solute/Volume of ECF.
  b. Volume of ECF= water.

Water Balance

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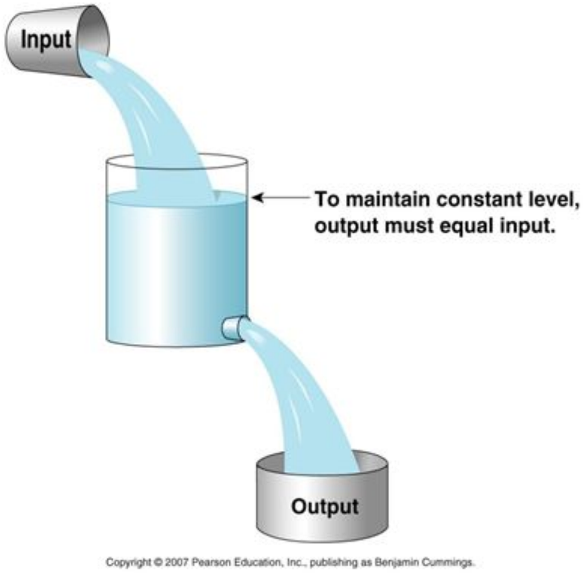


Water intake:

- **Fluids ingested (2100 ml).**
- **From metabolism (200ml).**

Daily loss:

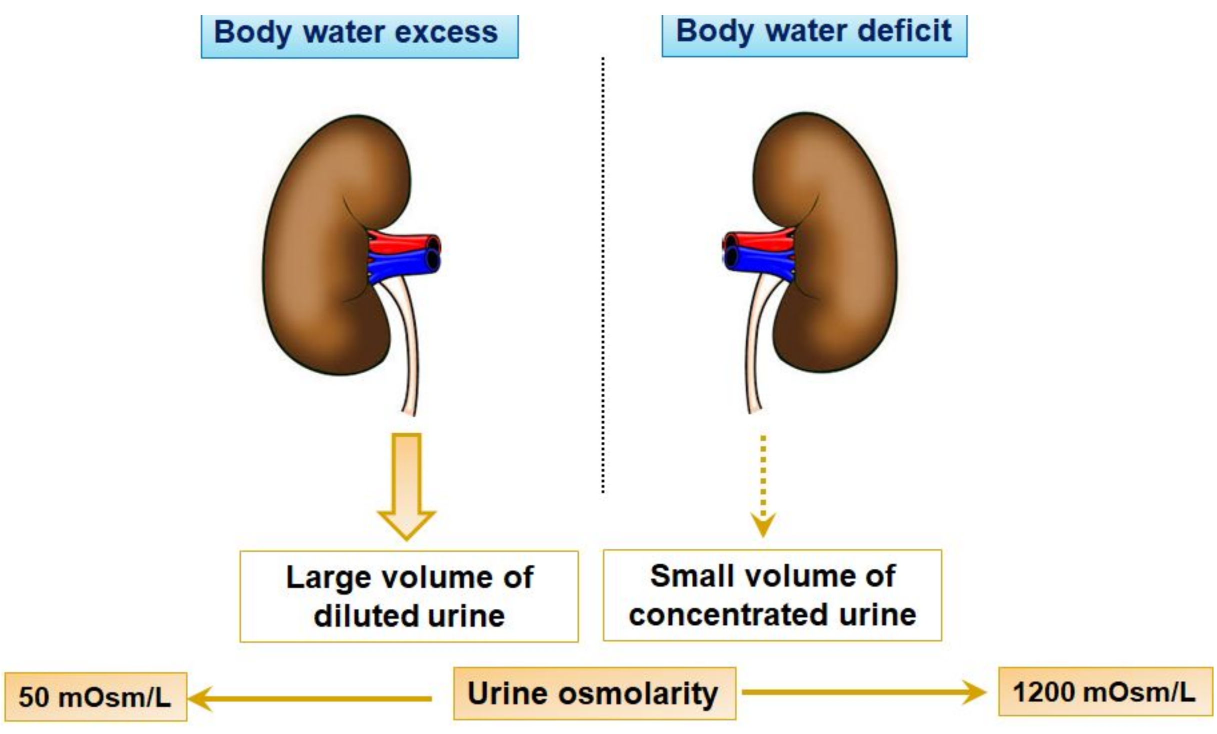
- **Insensible loss (700 ml).**
- **Sweat (100 ml).**
- **Feces (100 ml).**
- **Urine (1400 ml).**

Total intake = 2300 ml

Input = output

Total loss = 2300 ml

Regulation of H2O by the Kidney



H_2O Handling by the Kidney

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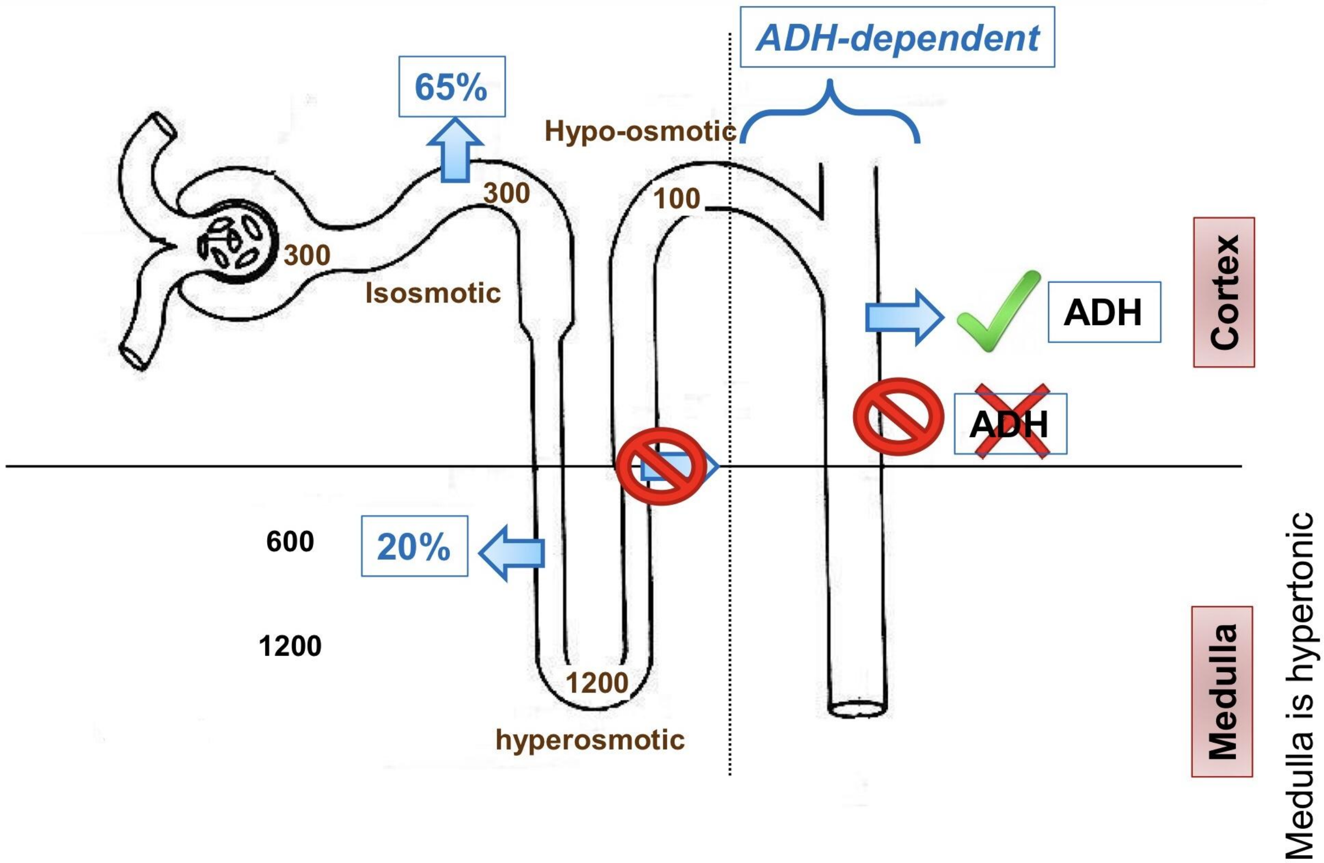

Obligatory urine volume:

- The minimal volume of urine that must be excreted to rid the body of waste products of metabolism.
- A 70-Kg human needs to excrete 600 mOsm of solutes per day.
- ***What is the obligatory urine volume?***

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

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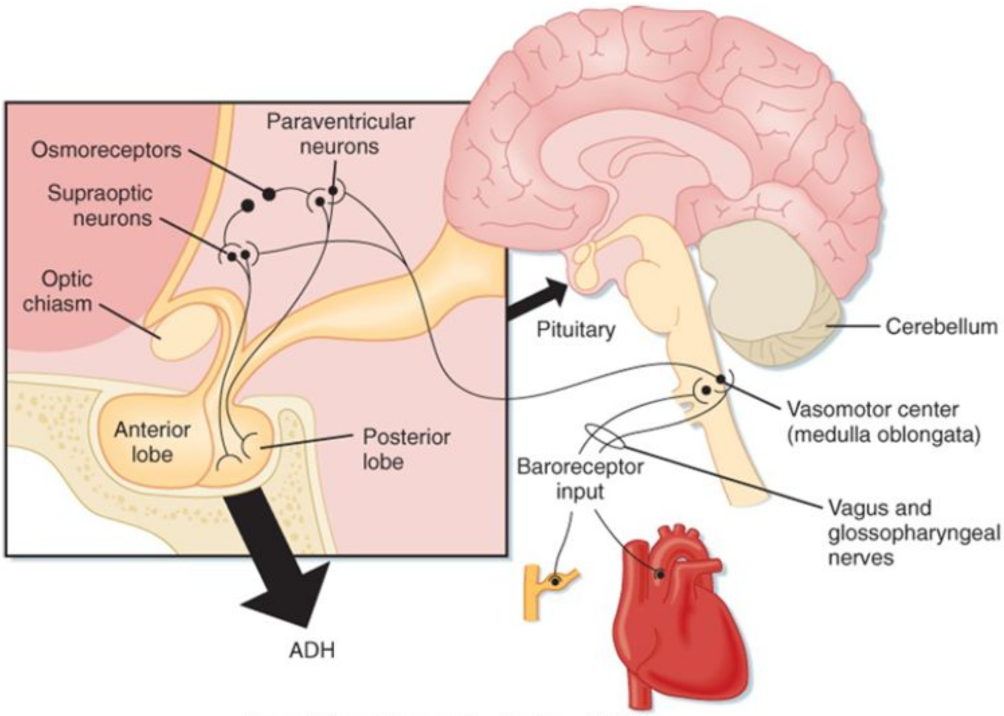
Regulation of ECF osmolarity

Antidiuretic Hormone (ADH):



Stimulants for ADH Secretion:

- ***Osmotic:*** (most important)
  - Osmolarity of ECF.
  - 1% change in osmolarity can alter ADH secretion significantly.
- ***Hemodynamic:***
  - Volume & pressure in the vascular system.
  - 5-10% decrease in BP or BV is required before ADH secretion is stimulated.

Water Balance

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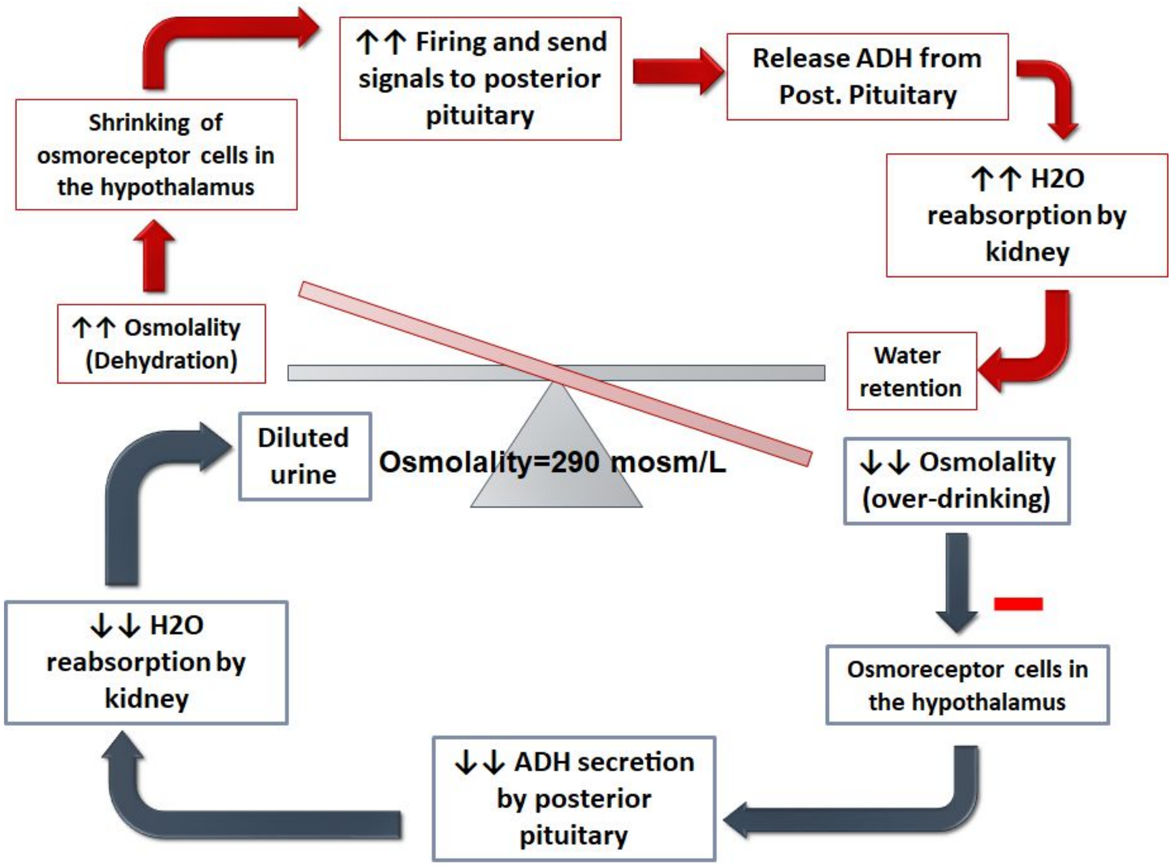
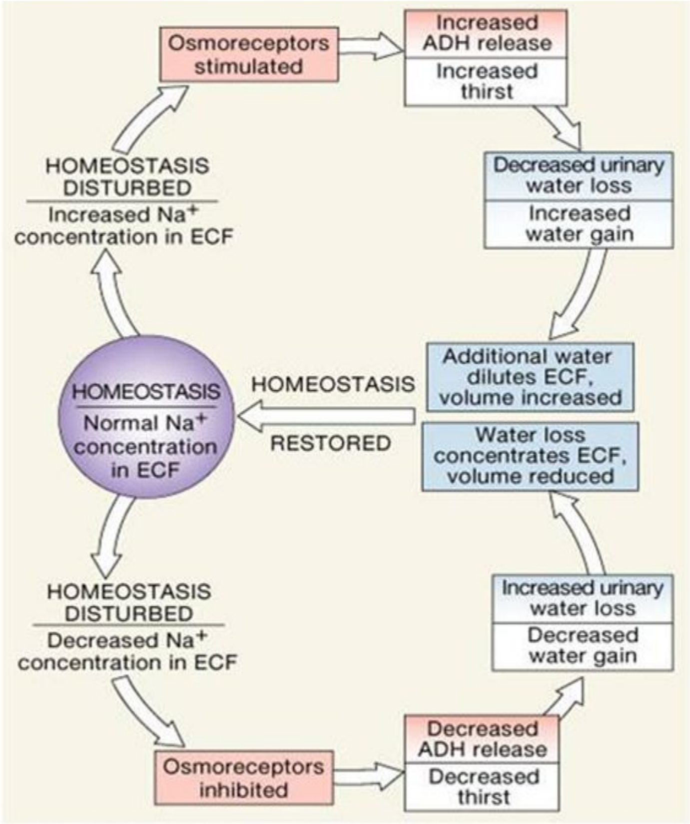


Feedback Mechanisms Involved in Regulation of Water Balance



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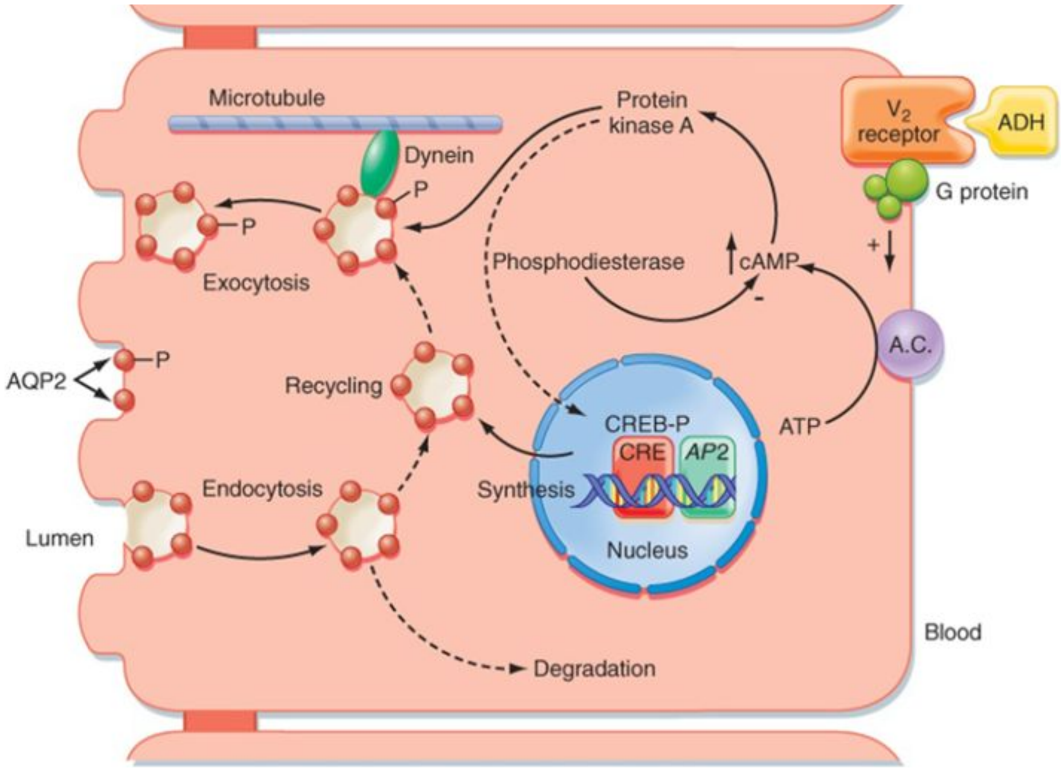
Factors That Can Alter ADH Secretion

Increase ADH	Decrease ADH
Nausea	ANP
Hypoxia	-
Angiotensin II	-
• Drugs: ◦ Morphine. ◦ Nicotine.	• Drugs: ◦ Alcohol.

ADH Mechanism of Action



Control of ADH Secretion and Thirst

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Regulation of ADH Secretion

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

Control of Thirst

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

Water Diuresis vs Osmotic Diuresis:

Water diuresis	Osmotic diuresis
Increased urine flow rate (No change in urine excretion of solutes).	Increase urine flow rate as well as the excretion of solutes.
Causes: - Excess ingestion of water - Lack of ADH - Defect in ADH receptors in Distal segment of nephron (nephrogenic Diabetes Insipidus)	Causes: - Increase plasma glucose level (DM) - Increase level of poorly reabsorbed solutes/ anions - Diuretic drugs (Lasix)
Diuresis is mainly due to decrease in water reabsorption in distal segment of nephron. No change to the water reabsorbed proximally.	Diuresis is mainly due to decrease reabsorption of solute in PCT or LOH. Decrease solute reabsorption results in decrease in water reabsorption proximally as well as distally.
Increase urine volume results from increased excretion of pure water	Increase urine volume results from increased excretion of osmotically active solutes which pulls water with it.
Urine osmolality falls far below plasma osmolality.	Urine osmolality falls but remains above plasma osmolality.
Only about 15% filtered load of water reaching distal segments may remain unabsorbed and excreted in urine (maximum urine volume 20 ml/min).	Due to decreased water reabsorption in all segments of nephron, a much greater fraction of filtered water may be excreted volume more than 20 ml/min.
ADH administration will stop diuresis if it is due to lack of ADH. ADH administration will not be effective in Nephrogenic Diabetes Insipidus.	ADH administration will not stop diuresis.

Disorders Of Urinary Concentrating Ability

ONLY in male slides

Diabetes mellitus
High specific gravity urine.
Due to excretion of Glucose

Abnormalities in ADH secretion

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Excessive ADH effect
"SIADH"
↓
- High ADH levels.
- Water retention.
- ECF hypo-osmotic
- Urine hyperosmotic

No ADH effect

Central diabetes insipidus

- Cause: inability to produce or release ADH from posterior pituitary.
- Urine: low fixed specific gravity (diluted urine).
- Polyuria.
- Polydipsia.

Nephrogenic diabetes insipidus

- Cause: Mutations in V2 receptors or AQP2.
- Cannot respond to ADH.
- Polyuria
- Polydipsia.

Quiz

1- Osmolarity of interstitial fluid in collecting duct must be high and osmolarity of tubular fluid must be low?

A. True.

B. False.

2- When the active ion pump of the thick ascending limb on the loop of Henle, it'll reduces the concentration inside the tubule, and raises the interstitial concentration, this pump establishes a 200-mOsm/L concentration gradient between the tubular fluid and the interstitial fluid, this scene happen in step 3 of Steps Involved in Causing Hyperosmotic Renal Medullary Interstitium?

A.True.

B. False.

3- The travel of urine to be diluted starts from proximal convoluted tubule which is carry isosmotic urine, then goes to thin AL which is permeable to water only, then to the thick AL, then end to the collecting ducts to reabsorb NaCl, and decrease the osmolarity until it reaches 50 mOsm/kg?

A. True.

B. False.

4- As the loop of Henle become longer as it work become lesser, because of the long period that the urine going to take until reach the collecting duct?

A. True. .

B. False.

5- loop of henle reabsorbed 03% of water and salt?

A. True.

B. False.

6- Thick ascending limb is impermeable to water, but permeable to sodium chloride passively?

A. True.

B. False.

7- The thick AL is the diluted segment of nephron?

A. True.

B. False.

8- The fluid in the collection duct is isosmotic?

A. True. .

B. False.

9- ADH causes an increase in permeability of DCT, CT, and CD for NaCl?

A. True. .

B. False.

10- In the new born baby the length of loop of henle increase their concentrate urine?

A. True. .

B. False.

11- When the urine flow rate increased, but there's no change in urine excretion of solutes, this's describe the osmotic diuresis?

A. True.

B. False.

1- B 2- B 3- B 4- B 5- B 6- B 7- A 8- B 9- B 10- B 11- B

Thank you for checking our work

Male Team:

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