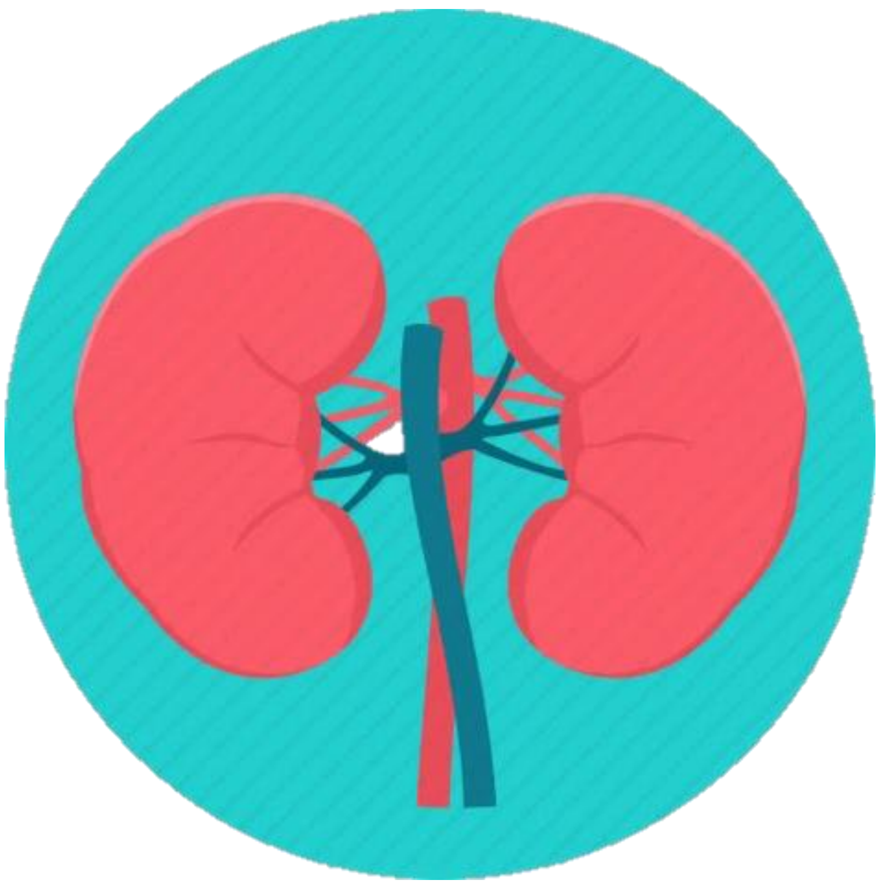
Lecture (8)

Urine Concentration



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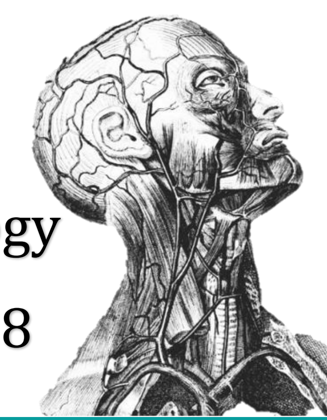


Physiology

MED438

ECF Osmolarity

- Maintaining normal and constant concentration of solutes and electrolytes in the ECF is **important** for normal cellular function
- Concentration of solutes in ECF = osmolarity = **300 mOsm/L**

$$Osmolarity = \frac{Amount\ of\ solute}{Volume\ of\ ECF\ (water)}$$

- Determinant of osmolarity is amount of **water,** since amount **solute** excreted daily is normally the same (approximately 600 mOsm)
- To maintain constant osmolarity water must be balanced were:

Input = Output

Water intake:

- Fluid ingested = 2.1 L
- Fluid metabolism = 0.2 L

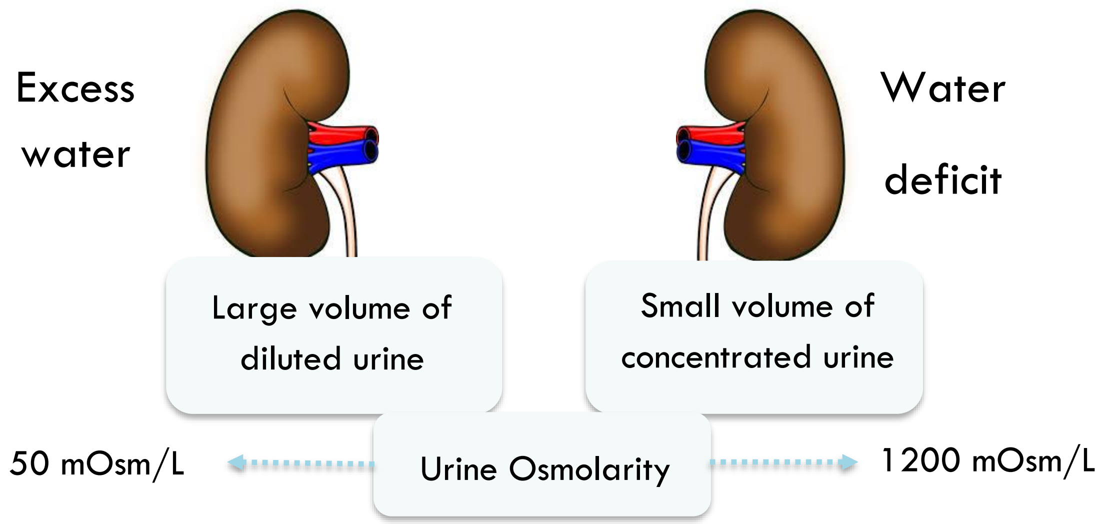
Total = 2.3 L

Water loss:

- Insensible loss = 0.7 L
- Sweat = 0.1 L
- Feces = 0.1 L
- **Urine = 1.4 L**

Total = 2.3 L

- The kidneys regulate water balance by changing urine concentration



Obligatory Urine Volume

- **Obligatory urine volume** is the minimal amount of urine that must be excreted to get rid of body waste products
- A 70-kg average person need to excrete around 600 mOsm of solutes

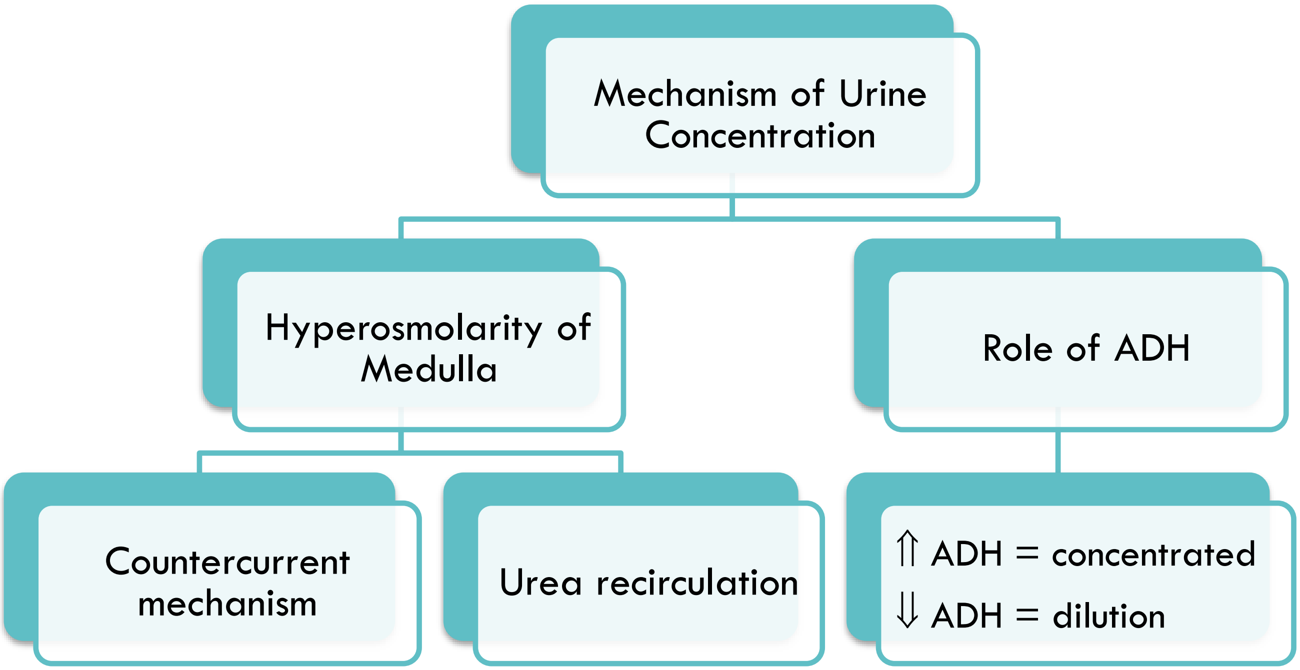
$$Obligatory\ Urine\ Volume = \frac{600\ mOsm/day\ \text{(amount of sol.)}}{1200\ mOsm/L\ \text{(max urine conc.)}} = 0.5\ L/day$$

Mechanism of Urine Concentration

- The **countercurrent system** is a system in which the inflow runs parallel and in close proximity but opposite to the outflow (like in loop of Henle & vasa recta)
- This system allows the outgoing fluid to balance the incoming fluid
- While the loop of Henle reabsorb 20% of the salt/water in tubular fluid, its primary function is to determine urine concentration using:

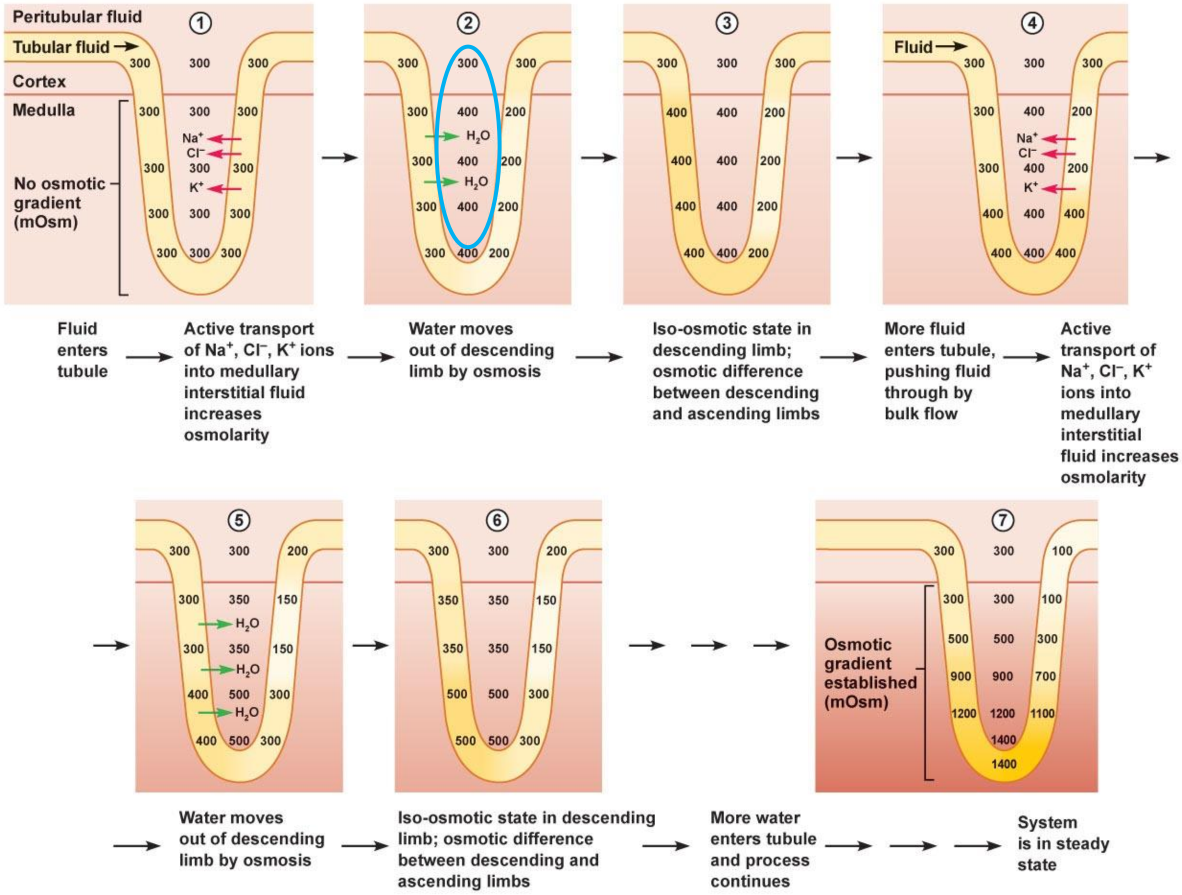
Countercurrent multiplier system

- While the collecting ducts is where urine concentration is determined



Countercurrent Multiplier System

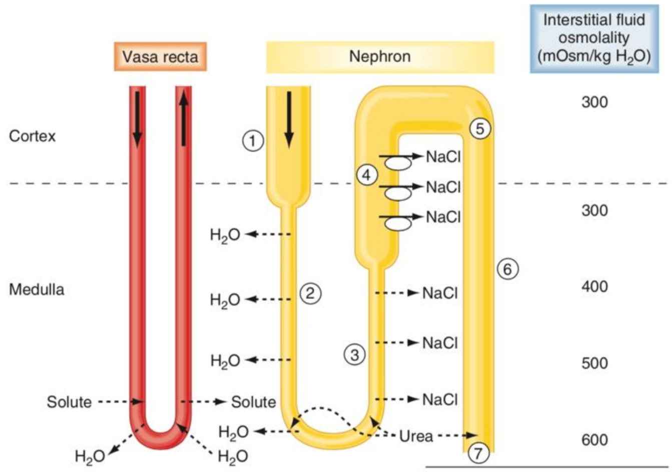
- As we know the renal medulla is hyperosmotic*
- Normal osmolarity is 300 mOsm
- The deepest point in the medulla reached 1200 mOsm



- NaCl is reabsorbed into the interstitium in the ascending loop of Henle, which will increase the interstitial osmolarity. This will stimulate water reabsorption in the descending loop of Henle, which will again cause the ascending part to reabsorb more solute until they reach an osmolarity of 1200 mOsm
- This is called the **countercurrent multiplier system** (opposite + multiply Osm)
- This system produces a diluted urine of **100 mOsm** at the end
- If the body is dehydrated ADH is released to promote H_2O reabsorption in the collecting ducts which will increase the osmolarity up to 1200 mOsm.

Concentrating segment = DLH   Diluting segment = thick ALH

Dilution vs Concentration

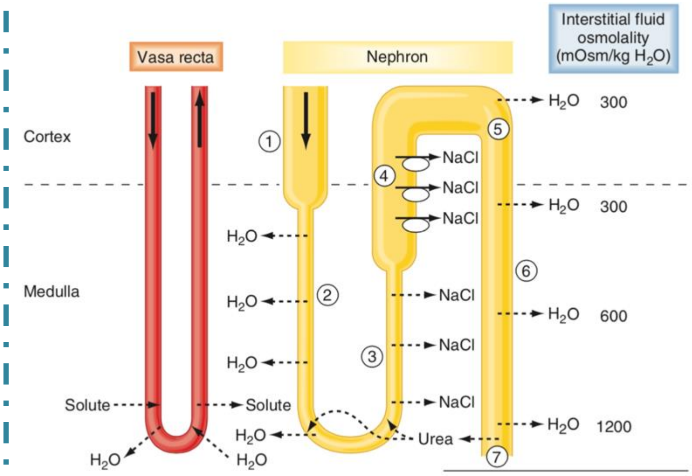


Urine Dilution

- No or very low ADH
- No water reabsorption

Occurs in 7 steps:

1. Isoosmotic PCT = 300 mOsm
2. Water reabsoption in thin descending loop of Henle
   → solutes are impermeable
3. Passive NaCl reabsoption in thin ascending loop of Henle
   → Water is impermeable
4. Active NaCl reabsorption in thick ascending loop of Henle (100 mOsm)
5. NaCl reabsorption in collecting ducts (CD) (decrease Osm from 100 to 50)
6. NO water reabsorption in CD
7. Urine concentrate = **50 mOsm/kg**



Urine Concentration

- High ADH
- Water reabsorption

Occurs in 7 steps:

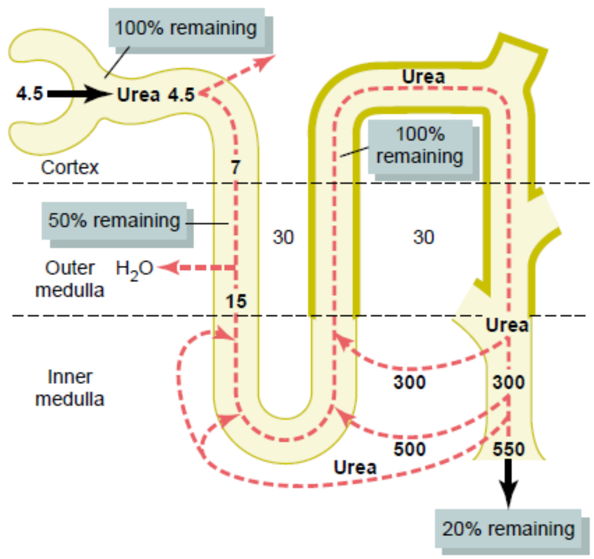
1 → 4 same as dilution

5. ADH causes water reabsoprtion in CD and increase in Osm to 300 mOsm
6. Water reabsorption by ADH in CD
7. Urine concentrate = **1200 mOsm/kg**
   → NaCl accounts for 600 mOsm
   → Urea accounts for 600 mOsm

- Urea equilibrate for the water reabsoprtion by tranporting to the interstitium to balance the interstitial osmolarity

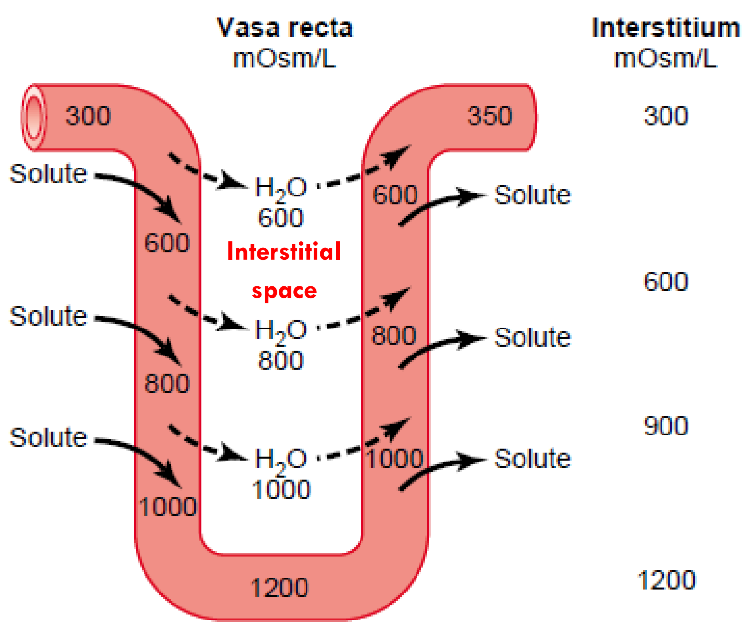
Urea Recirculation

- Urea recycling is essential in creating the longitudinal osmotic gradient and the countercurrent system
- Urea will go from the lower CD into the interstitium to increase osmolarity to be reabsorbed back in the loop of Henle
- A person on a protein free diet cannot concentrate urine due to lack of urea



Vasa Recta

- The vasa recta act as a **countercurrent exchanger**
- Which has the effect of recycling the solutes utilized in the countercurrent multiplier system
- Walls are permeable to H_2O, NaCl & Urea
  Descending: urea transporters, aquaporins (water channels)
  Ascending: fenestrated capillary
- Colloid p. > Interstitial fluid p. which pulls in and recycles NaCl & H_2O



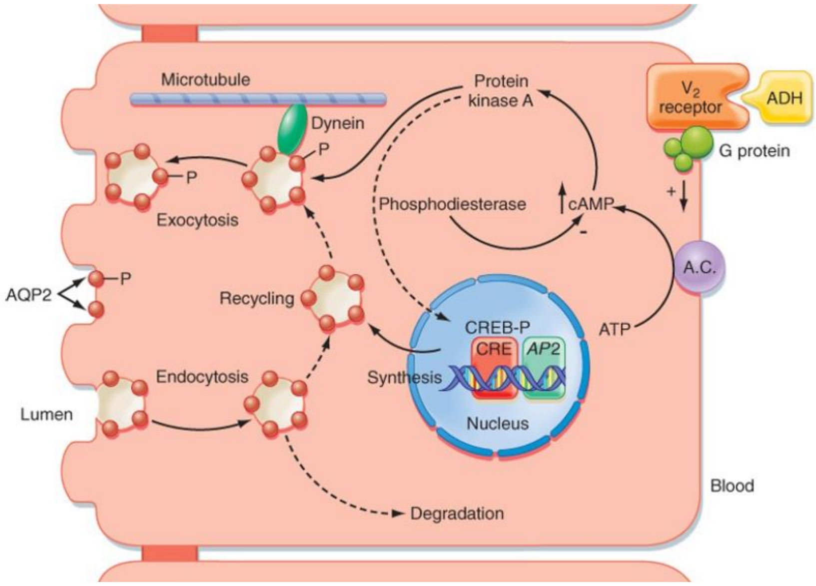
Why doesn't the blood flow in the medullary region wash the hyperosmolarity gradient?

1. Vasa recta acts as a counter-exchanger

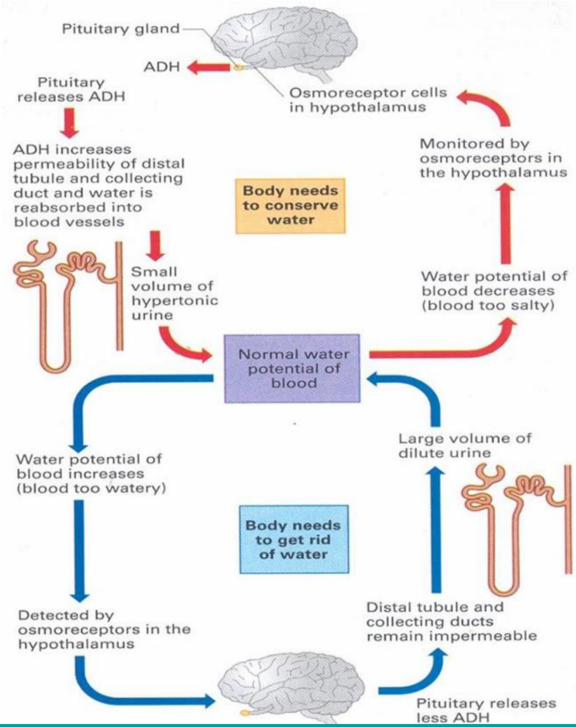
2. Medullary blood flow is very slow (5% of RBF) otherwise it would wash out the medullary hyperosmolarity completely

Stimulants and Action of ADH

- **ADH** is released from the posterior pituitary gland through 2 stimulants
  1. **Osmotic changes:** 1% change can stimulate ADH release **(very important)**
  2. **Hemodynamic changes:** 5-10% BP/BV decrease will stimulate ADH release
- After ADH is released it goes to the principal cells in the CD and late DCT



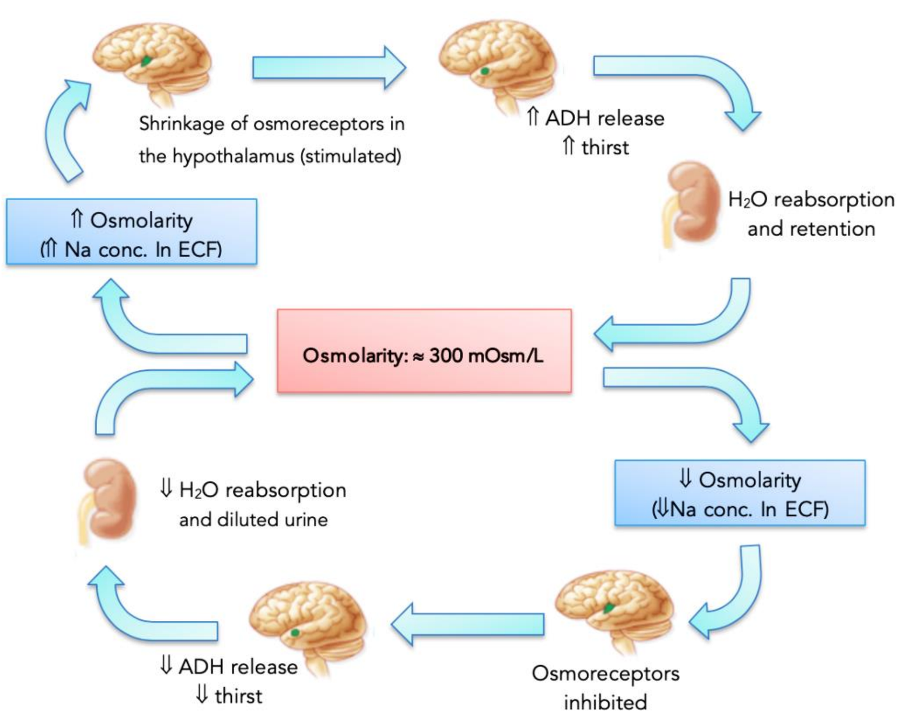
- ADH activates G_s-coupled protein which activates adenylyl cyclase (AC)
- AC will convert ATP to cAMP which will activate protein kinase A
- This will phosphorylase dynein which will exocytose (release) vesicles containing aquaporins II (H₂O channels) which will reabsorb water



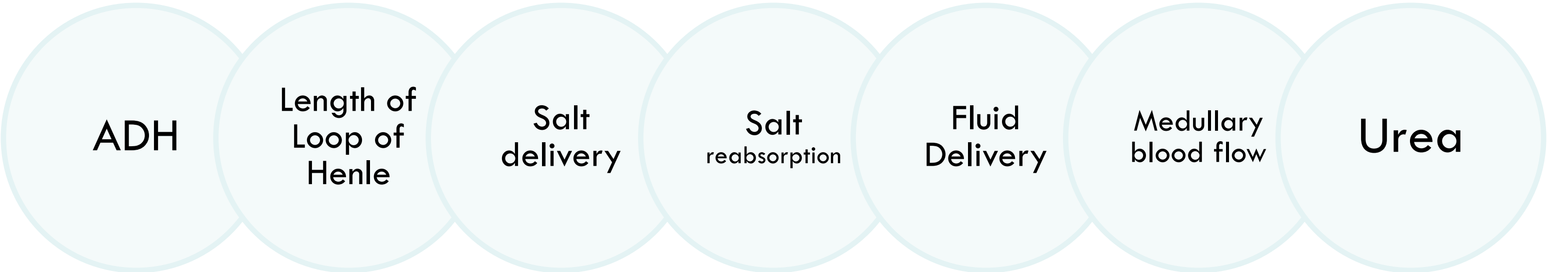
Control of ADH Secretion and Thirst

Regulation of ADH Secretion	
Increase ADH	Decrease ADH
○ **⇑ Plasma osmolarity** ○ **⇓ Blood volume** ○ **⇓ Blood pressure** ○ **Nausea** ○ **Hypoxia** ○ **Angiotensin II** **Drugs** ○ **Morphine** ○ **Nicotine** ○ **Cyclophosphamide**	○ ⇓ Plasma osmolarity ○ ⇑ Blood volume ○ ⇑ Blood pressure ○ ANP Drugs ○ Alcohol ○ Clonidine (Antihypertensive Drug) ○ Haloperidol (Dopamine Blocker)
Control of Thirst	
Increase Thirst	Decrease Thirst
○ **⇑ Osmolarity** ○ **⇓ Blood volume** ○ **⇓ Blood pressure** ○ **⇑ Angiotensin** ○ **Dryness of mouth**	○ ⇓ Osmolarity ○ ⇑ Blood volume ○ ⇑ Blood pressure ○ ⇓ Angiotensin II ○ Gastric distension

Regulation of Water Balance



Factors Affecting Urine Concentration



1. **ADH**
   - It increases in the permeability of DCT, CT, & CD for water
   - It increases the permeability of medullary CD for urea
2. **Length of the loop of Henle:**
   - Longer loop → more effective in concentrating urine
   - New born → shorter loop → less effective in concentrating urine
3. **Delivery of salt to ALH** (ascending loop of Henle)**:**
   - Due to decrease in GFR (e.g. hemorrhage) → less delivery of salt to ALH
   - Decreasing countercurrent system → decreasing urine concentration
4. **Reabsorption of salt out of ALH:**
   - Diuretic drugs (Lasix) prevents NaCl reabsorption from thick ALH
   - Decreasing salt reabsorption in ALH → decrease in osmotic gradient
   - Decreasing countercurrent system → decreasing urine concentration
5. **Delivery of fluid to medullary CT and CD:**
   - Max urinary concentration occurs when little fluid enters CT & CD
   - Increased fluid to CT & CD → decreasing urine concentration
6. **Medullary blood flow:**
   - High Medullary BF will wash-out the hyperosmolar gradient
7. **Urea:**
   - Urea recycling is essential for the countercurrent system

Water Diuresis vs Osmotic Diuresis

	Water	Osmotic
Definition	Increased urine flow rate (No change in urine excretion of solutes)	Increased urine flow and solutes excretion
Causes	• Excessive hydration • Lack of ADH • Defect in ADH receptors in Distal segment of nephron (Nephrogenic Diabetes Insipidus)	• Increase in plasma glucose • Increase in plasma solutes • Diuretic drugs (e.g. Lasix)
Process	Decreased water reabsorption in **distal** segment of nephron	Decreased solutes and water reabsorption in PCT or LOH (leading to decrease Reabsorbtion distally)
Urine volume	High excretion of pure water	High excretion of solutes which pulls water with it
Urine osmolality	Decreased <plasma osmolality	Decreased >plasma osmolality
Water excretion	20 ml/min (15% of water) only distal part is affected	>20 ml/min All segments are affected
ADH effect	Stop diuresis Except in nephrogenic DI	No effect

Disorder in Concentrating Urine

Disorders

Central Diabetes Insipidus

- inability to produce ADH
- low specific gravity (diluted urine)
- Polyuria (⇑ urine) & Polydipsia (⇑ thirst)

Nephrogenic Diabetes Insipidus

- Inability to respond to ADH
- Mutation in V2/AQP2 receptors
- Polyuria (⇑ urine) & Polydipsia (⇑ thirst)

Diabetes Mellitus

- High urine specific gravity
- Concentrated urine
- Osmotic diuresis

SIADH

- High ADH → water retention
- ECF → hypo-osmotic
- Urine → Hyper-osmotic

Quiz

1. **Which part of the nephron is impermeable to water?**

   A. Descending loop of Henle
   B. Proximal convoluted tubules
   C. Thick ascending loop of Henle
   D. Late distal convoluted tubules

2. **Which of the following best describes diabetes insipidus?**

   A. Decreased renin release
   B. Decreased plasma osmolality
   C. Increased urine concentration
   D. Increased urine volume

3. **A person lost in the desert for 24 hrs. Which of the following will happen?**

   A. Inhibition of ADH
   B. Increased water permeability
   C. Decreased solutes excretion
   D. Urine dilution

4. **What is the main function of the countercurrent exchanger system?**

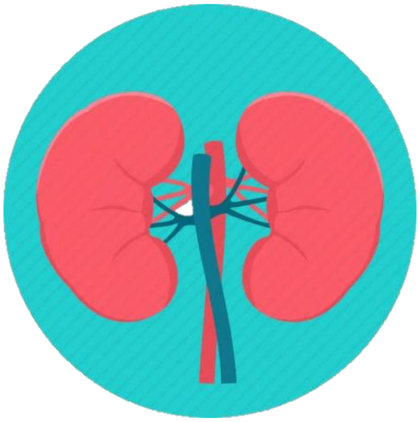
   A. Create osmotic gradient
   B. Maintain osmotic gradient
   C. Increase hyperosmolarity of medulla
   D. decrease hyperosmolarity of medulla

5. **What is the main diluting segment in the nephron?**

   A. Ascending loop of Henle
   B. Descending loop of Henle
   C. Proximal convoluted tubules
   D. Collecting tubules

Answers: C, D, B, B, A

Thank You



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