MED439
KING SAUD UNIVERSITY

Physiology Team 439

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PHYSIOLOGY

MECHANISMS FOR CONCENTRATING & DILUTING URINE

Objectives:

- 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.

Black: in male AND female slides
Red : important
Pink: in female slides only
Blue: in male slides only
Green: Notes
Gray: extra information

Editing file

ECF Osmolarity

- 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**
- Why it's important to keep osmolarity constant (300)? because it will affect the cell if it's NOT constant:
  -If the cell in Hypotonic solution —> the cell will **Swell**.
  -If the cell in Hypertonic solution —> the cell will **Shrink.**
- The osmolarity of ECF determined by : $Osmolarity = \frac{Amount\ of\ solute}{Volume\ of\ ECF\ (water)}$
- **Water reabsorption is a passive process that occurs through the whole nephron. It is of 2 types: 1- Obligatory. 2- Facultative.**

Water Balance

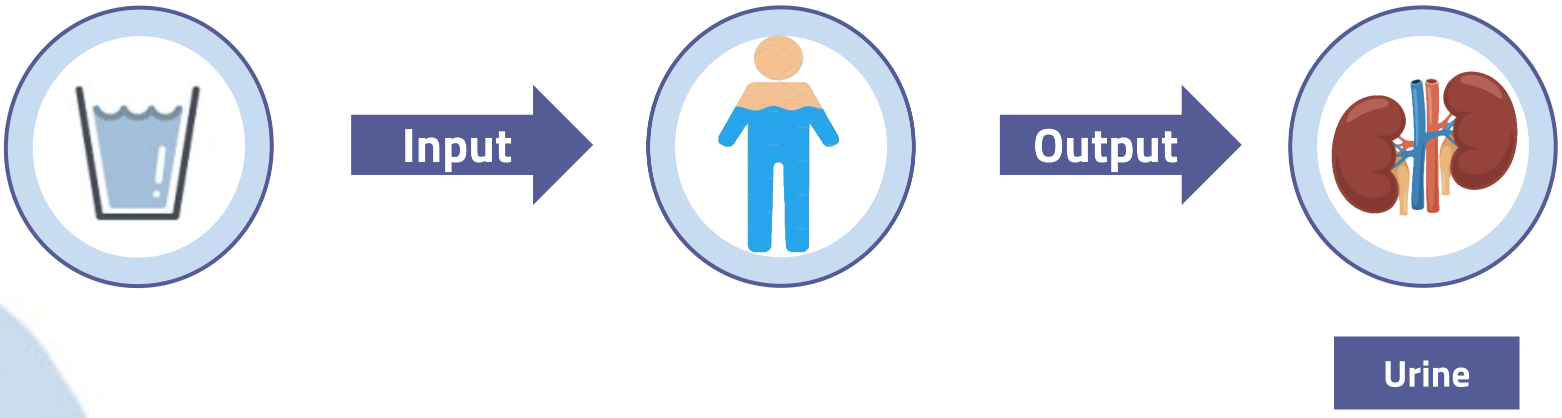
Input = output

Water intake:
Mainly Fluids ingested (2100 ml).
From metabolism (200ml)

Total intake= 2300ml

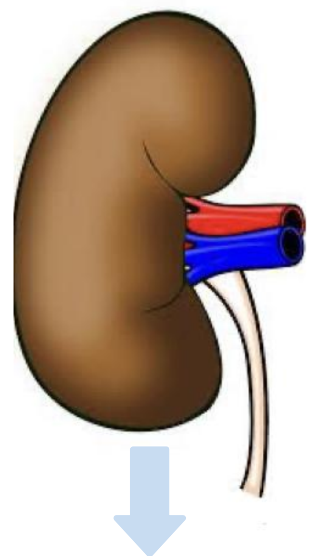
Daily loss:
Insensible loss (700 ml).
Sweat (100 ml).
Feces (100 ml).
Mainly Urine (1400 ml).

Total loss = 2300 ml



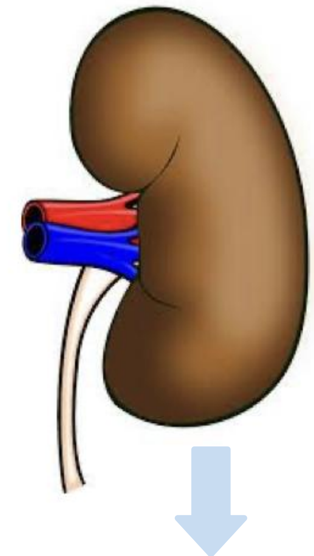
Regulation of H2O by the Kidney

Body water excess



Large volume of diluted urine

Body water deficit



Small volume of concentrated urine

Urine osmolarity

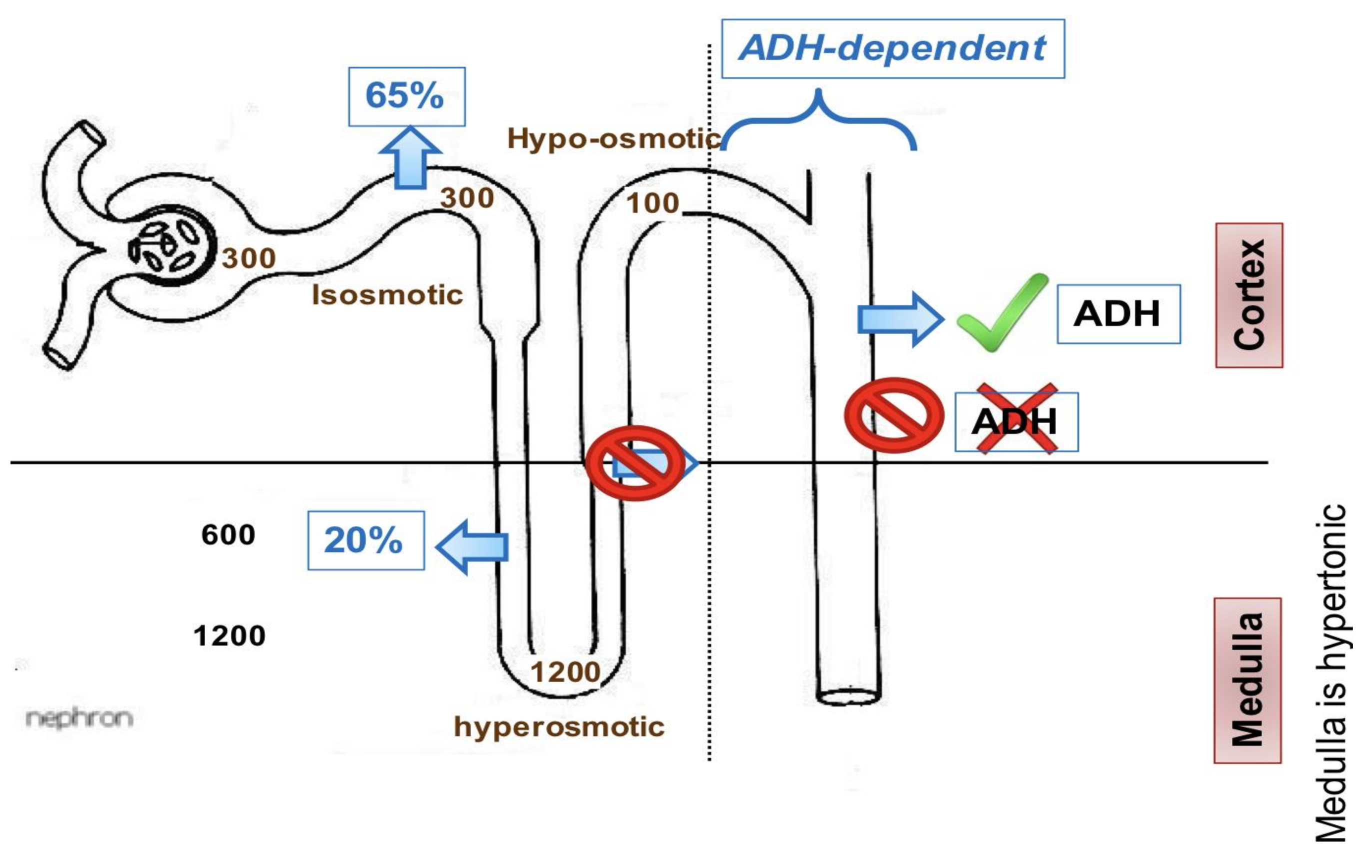
50 mOsm/L

The most diluted urine the human can excrete.

1200 mOsm/L

The Maximum concentrated urine the human can excrete.

H2O Handling by the Kidney



What happens to the osmolarity of tubular filtrate?
Explanations in the slide no.6.

In boys' slides

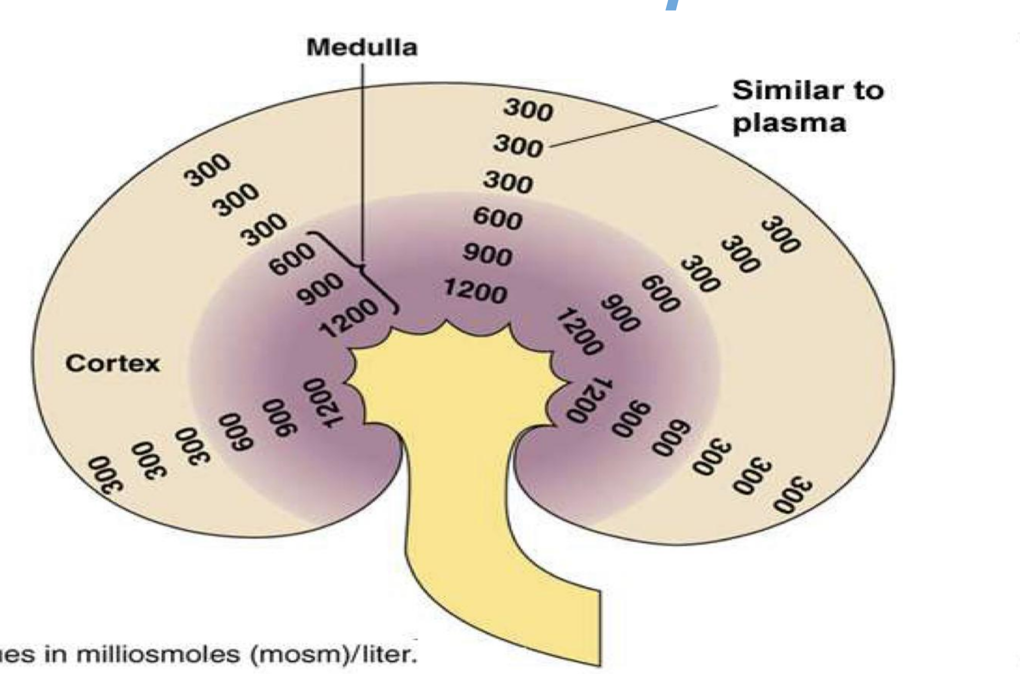
Water transport along the nephron

Segment	% filtered load Mechanism	Mechanism of H_2O reabsorption	Hormones that regulate H_2O
Proximal tubule	65	Passive	None
Descending loop of Henle —Early DCT	15 - 20	Passive	None
Ascending loop of Henle & Early Distal tubule	0	No water reabsorption	None
Late distal tubule & collecting duct	5-14	Passive	ADH

Water Reabsorption in PCT

- 65% of filtered water is reabsorbed in PCT.
- Extrusion of Na+ from the renal cell to peritubular space Increase osmolality of peritubular space Drags water by osmosis.
- Filtrate remains iso-osmotic (Equal quantity of water & solute are absorbed).

Hyperosmotic medullary interstitium

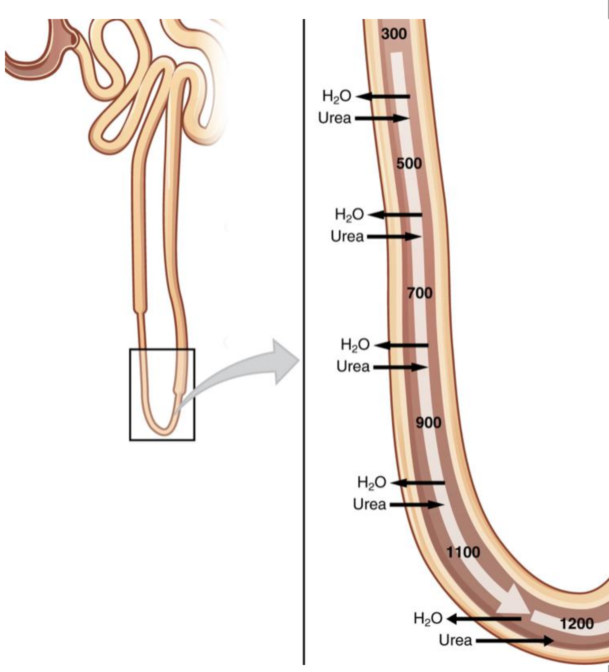


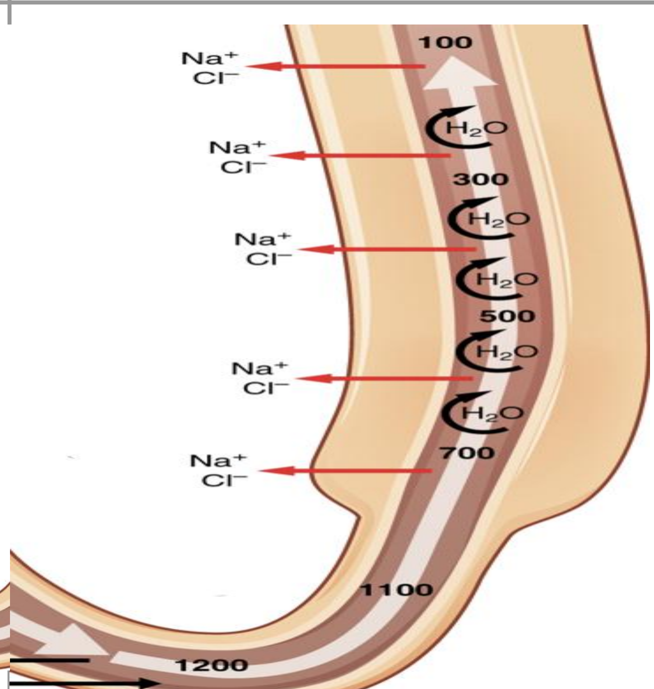
ll values in milliosmoles (mosm)/liter.

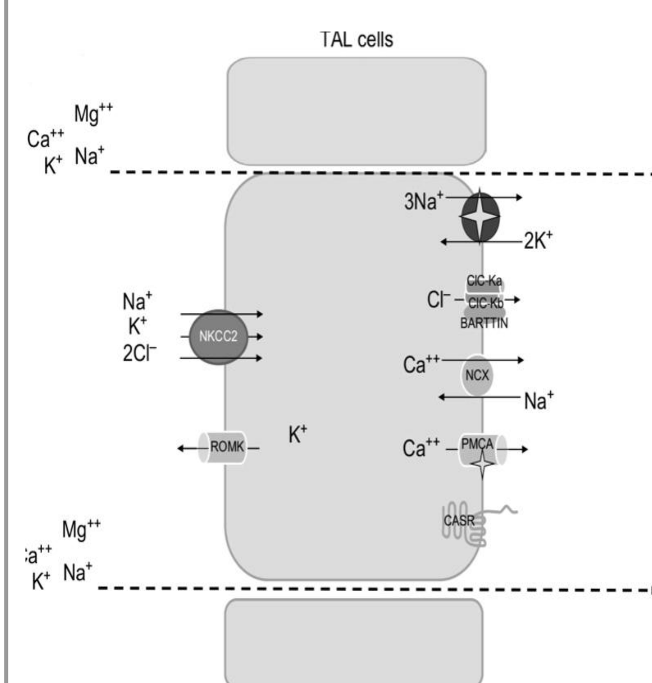
In boys' slides but explained by girls' Dr

The Loop of Henle

Thin descending loop	"Diluting segments (LoH+DCT)" Thin ascending loop	Thick ascending limb
Major function = H_2O reabsorption. -**At start of descending loop** osmolarity is same as plasma (~300 mOsm) . **-At end of descending loop** osmolarity= **1200 mOsm** -**Not permeable** to solute reabsorption.	-No **H_2O** reabsorption. -Increases solute reabsorption (mainly NaCl) . -This part of the loop is very **permeable** to **Na^+** and **Cl^-.** - **Passive** diffusion out of tubule. -As NaCl diffuses **out** of the tubule, the fluid becomes more dilute due to the movement of only solutes and not the **H_2O** .	-Reabsorption of NaCl from tubule to interstitial fluid is active (**requiring energy**). -Na+ , K+ , $2Cl^-$ cotransport causes movement of these **ions into cells from tubular lumen.** -Na+ is actively transported out of cell via **Na+,K+ ATPase activity.** -Cl^- increases in cell due to the cotransporter (**Na+,K+,$2Cl^-$ cotransport**). Therefore Cl^- moves out of cell passively through Cl- channels and K+,Cl- cotransport. -NaCl reabsorption acts to **dilute urine**. -Osmolarity at the end of **thick ascending** limb is near 100 mOsm and is dilute compared to plasma ,which is ~**300 mOsm.**







More details in next slides..

Explanation...

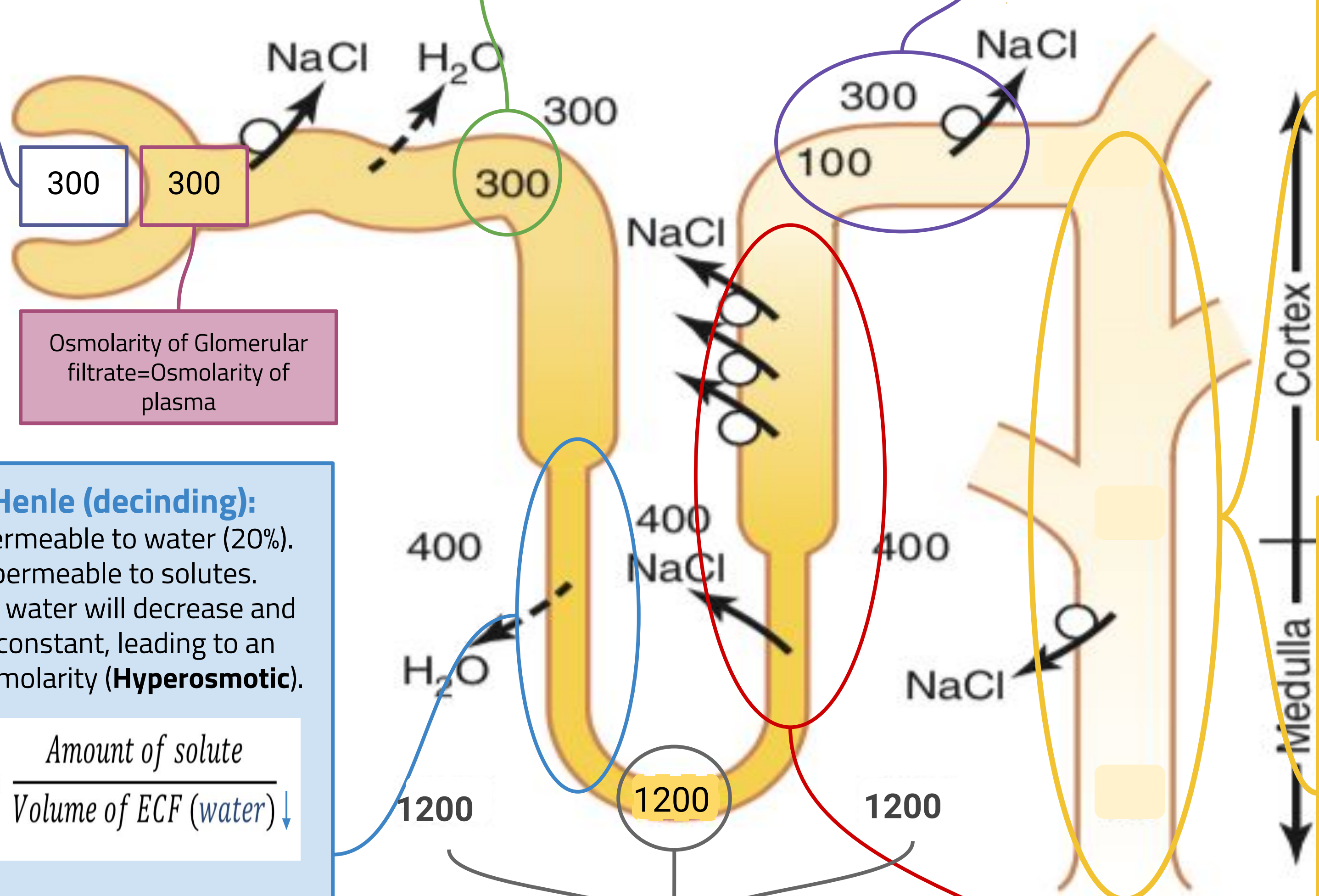
fluid Osmolarity through out every segment of the Nephron

Important point

If the volume of ECF ↑ the Osmolarity will ↓
If the amount of solutes ↑ the Osmolarity ↑

START FROM HERE

Osmolarity of plasma



Osmolarity of Glomerular filtrate=Osmolarity of plasma

Proximal tubule:

As fluid flows through the proximal tubule, solutes and water are reabsorbed **equally**, so there will be no change in Osmolarity **(Isosmotic)**.

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

Early distal tubule:

dilution continues. NaCl is reabsorbed by the Na+-Cl- cotransporter, but the cells are impermeable to water.

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

Late tubule +collecting duct:

If ADH is absent:

1-water will not be Reabsorbed.

2- Solutes will still be Reabsorbed.

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

The failure to reabsorb water and the continued reabsorption of solutes lead to a large volume of dilute urine. minimum is 50 mOsm/L

If ADH is present:

1-water will be Reabsorbed.

2- Solutes will still be Reabsorbed.

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

Which will lead to the formation of concentrated Urine. Maximum is 1200 mOsm/L

Loop of Henle (decinding):

❖ It is permeable to water (20%).

❖ Impermeable to solutes.

Which means water will decrease and solutes are constant, leading to an increase in Osmolarity (**Hyperosmotic**).

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

Explanation: As fluid passes down the descending loop of Henle, water is reabsorbed by osmosis and the tubular fluid reaches equilibrium with the surrounding interstitial fluid of the renal medulla, which is very hypertonic, about two to four times the osmolarity of the original glomerular filtrate. Therefore, the tubular fluid becomes more concentrated as it flows into the inner medulla.

It becomes 600mOsm/L if ADH is absent, because urine recirculation won't occur.

Ascending loop of Henle:

❖ Impermeable to water, **even if ADH is present**

❖ Permeable to solutes.

Which means water is constant and solutes are decreasing, leading to a decrease in Osmolarity **(Hypoosmotic)**. Therefore, the fluid becomes more diluted, as it flows up the ascending loop of Henle into the early distal tubule. as the osmolarity decrease progressively to about 100mOsm/L.

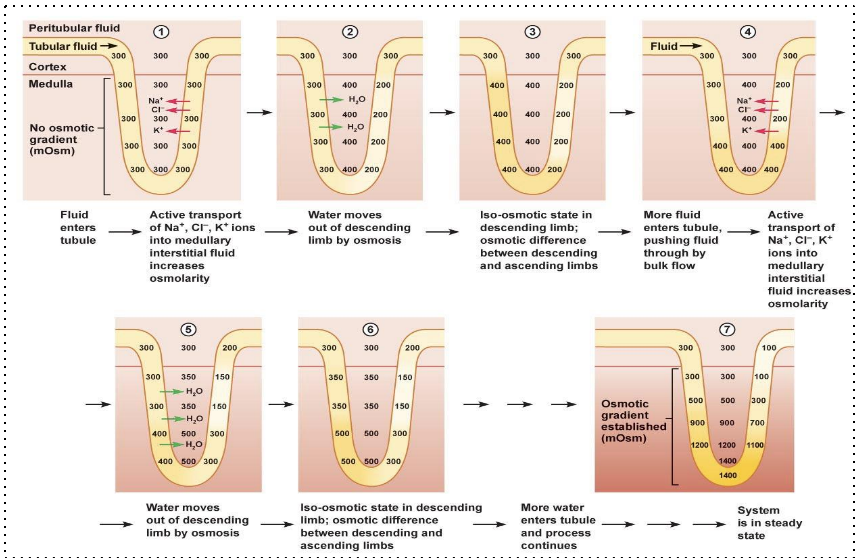
$$\downarrow Osmolarity = \frac{Amount\ of\ solute \downarrow}{Volume\ of\ ECF\ (water)}$$

To summarise:

- the mechanism for forming dilute urine is to continue reabsorbing solutes from the distal segments of the tubular system while failing to reabsorb water.
- The basic requirements for forming a concentrated urine are (1) a *high level of ADH,* which increases the permeability of the distal tubules and collecting ducts to water, thereby allowing these tubular segments to reabsorb water, and (2) *a high osmolarity of the renal medullary interstitial fluid,* which provides the osmotic gradient necessary for water reabsorption to occur in the presence of high levels of ADH.
- **The actions of ADH play a key role in controlling the degree of dilution or concentration of the urine.**

Explanation ..

1.Countercurrent Multiplier Mechanism



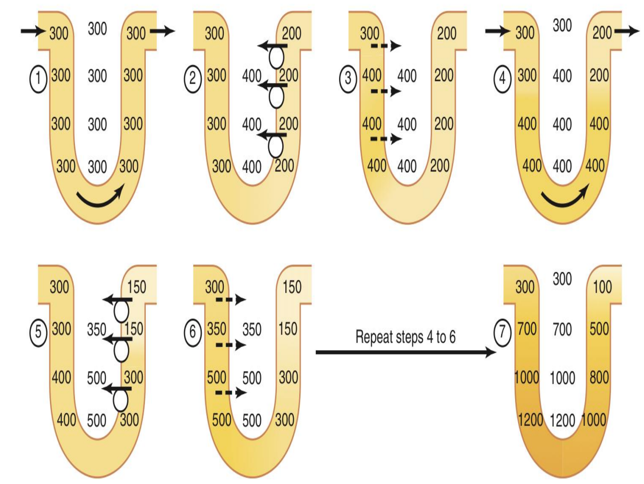


Figure 29-4. Countercurrent multiplier system in the loop of Henle for producing a hyperosmotic renal medulla. (Numerical values are in milliosmoles per liter.)

First you should know the common difference between the Ascending and Descending loop of henle:

Descending	Ascending
1. High permeable to water. **2.** Impermeable to solutes.	**1.** Impermeable to water. **2.** High permeable to solutes. **3.** Has the active pump which is sodium potassium chloride triple transporter (NKCC2)

1. Let's assume that All fluid are present in the lumen and interstitial fluid is equal to 300

2. The Ascending loop
Has triple transporter that pump solutes (Na,Cl,K) out means into the IF **Until the difference of Conc.** between in and out becomes **200:**
-The ascending loop becomes 200 **(dilute)**
-The interstitial fluid and DLoH becomes 400 **(concentrated)**
The active reabsorption of Na+ is the initiator of this mechanism. And remember that water will not follow Na+ in this part of the nephron. So, tubular fluid will become dilute.

3. The Descending loop
The filtrate (300) is coming from PCT into the descending and it will find that the **IF is higher in osmolarity** (400) so the **water will move out** (from the lumen into the IF) until the osmolarity becomes equal in both sides (400)

4. The Filtrate
There is always filtrate (300) are coming into the tubule and this new filtrate will push the old one down until it reaches the ascending loop.

5. The Ascending loop
Again once it reaches ascending loop the Triple transporter will open and the solutes (Na,Cl,K) will move out until the difference between in and out becomes 200:
-The ascending loop becomes 200
-The interstitial fluid becomes 400
Active reabsorption of Na+ will continue without reabsorption of water, making the tubular fluid more dilute in this segment.

6. The Descending loop
Again the osmolarity in IF becomes higher than in descending therefore the water will diffuse out (from descending into the IF) because descending high permeable to water.
until the osmolarity becomes equal in both sides.

7. This is how Na and Cl has been accumulated in the Interstitial fluid of the Kidney playing a role in hyperosmotic medullary.

Obligatory urine volume

- The **minimal volume** of urine that must be excreted to rid the body of waste products of metabolism.
- **87% of filtered water is reabsorbed by osmosis. Independent of ADH.**
- It is determined by the **maximal concentrating ability** of the kidney. In human it is **1200-1400 mOsm/L**
- A 70-Kg human needs to excrete 600 mOsm of solutes per day.
- the obligatory urine volume = **0.5 L/day.** How we determined it?

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

Facultative water reabsorption
- **13%**
- **Under control of ADH.**
- **Occurs In Late DCT& Cortical CD**

Forming a Concentrated Urine

Requires:

1. High levels of ADH.
2. Hyperosmotic renal medulla.
a. Countercurrent mechanism
b. Urea recirculation.

- Urine concentrating mechanisms are important for survival and saves H_2O

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

How did the renal medullary interstitium become hyperosmotic?

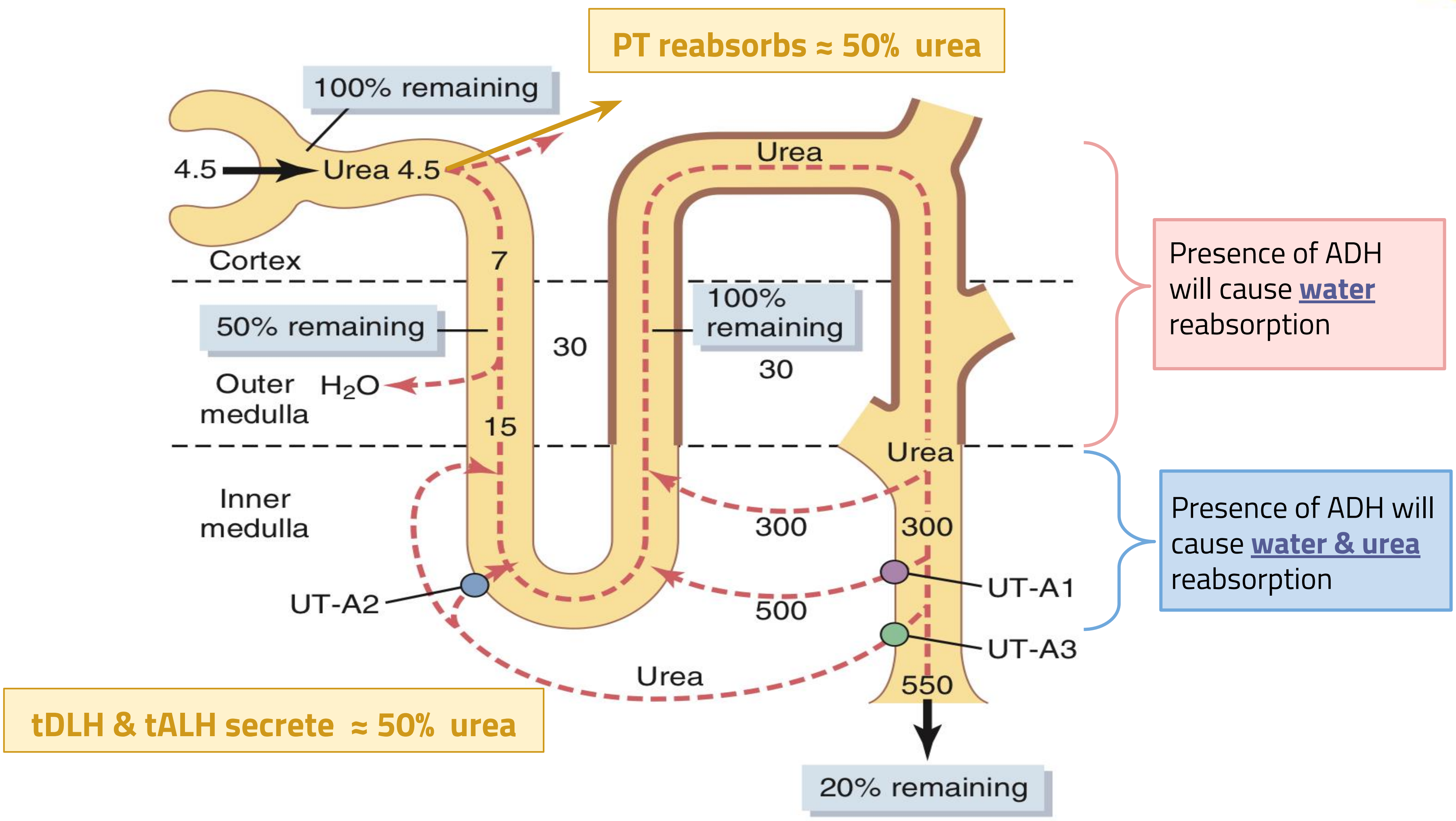
Due to accumulation of NaCl & Urea in the renal interstitium (its accumulating by countercurrent multiplier and urea recirculation mechanisms)

Concentration Mechanisms

Aim:	**Requirements:**	**Mechanisms:**
❖ Excess solute excretion	❖ Anatomical arrangement of Loop of Henle, Collecting Ducts and Vasa Recta. ❖ Parallel, adjacent / close to each other, with opposite flow "countercurrent". ❖ Different permeabilities.	❖ Countercurrent multiplier (Loop of henle) ❖ Countercurrent exchanger (Vasa recta) ❖ Hyperosmotic medullary interstitium (Sodium and urea) ❖ Role of ADH

2.Recirculation of Urea

Urea is byproduct of protein metabolism



Explanation...

1. Urea is Freely filtered (100%)
And as it passing through the proximal tubule 50% get reabsorbed passively with water.

2. The remaining 50%
As it moves down once it reaches **Deep part of loop of henle (thin descending and thin ascending) are Permeable urea.** therefore 50% of urea will be secreted on them.
رجعت كمية اليوريا ١٠٠٪ بـ هذه المنطقة

3. Filtrate passing
As the filtrate passing through the **Thick ascending loop**, urea will **not be either reabsorbed or secreted** in this area.

4. In Early part of Distal tubule (Cortical and outer medullary collecting duct)
Conc. of urea will increase because of Presence of ADH which will increase permeability of water but it will **NOT increase the permeability of urea**.

5. In Late part of Distal tubule (Inner medullary collecting duct)
Once it reaches inner medullary ADH will increase permeability of water **as well as urea.**

6. Permeability of Urea
Because of urea conc. in the tubular has been increased, a large conc. gradient has been created for Urea —> **urea will diffuse down its conc. gradient** into the IF.
Urea will accumulate in IF.

7. Urea that would have otherwise been excreted is recycled into the inner medulla, due to its gradient. And this is how urea playing a role in hyperosmotic medullary.

The Vasa Recta

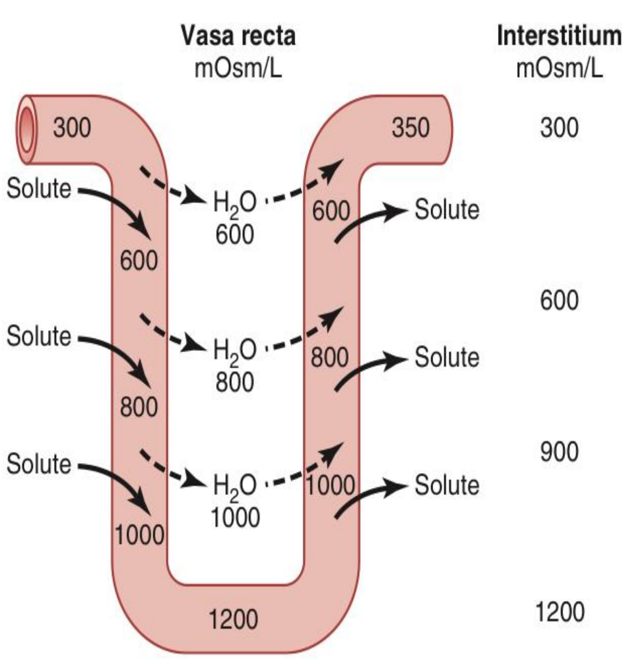
Is Capillary vessels that loop around the loop of henle of juxtamedullary. it's a U shaped.

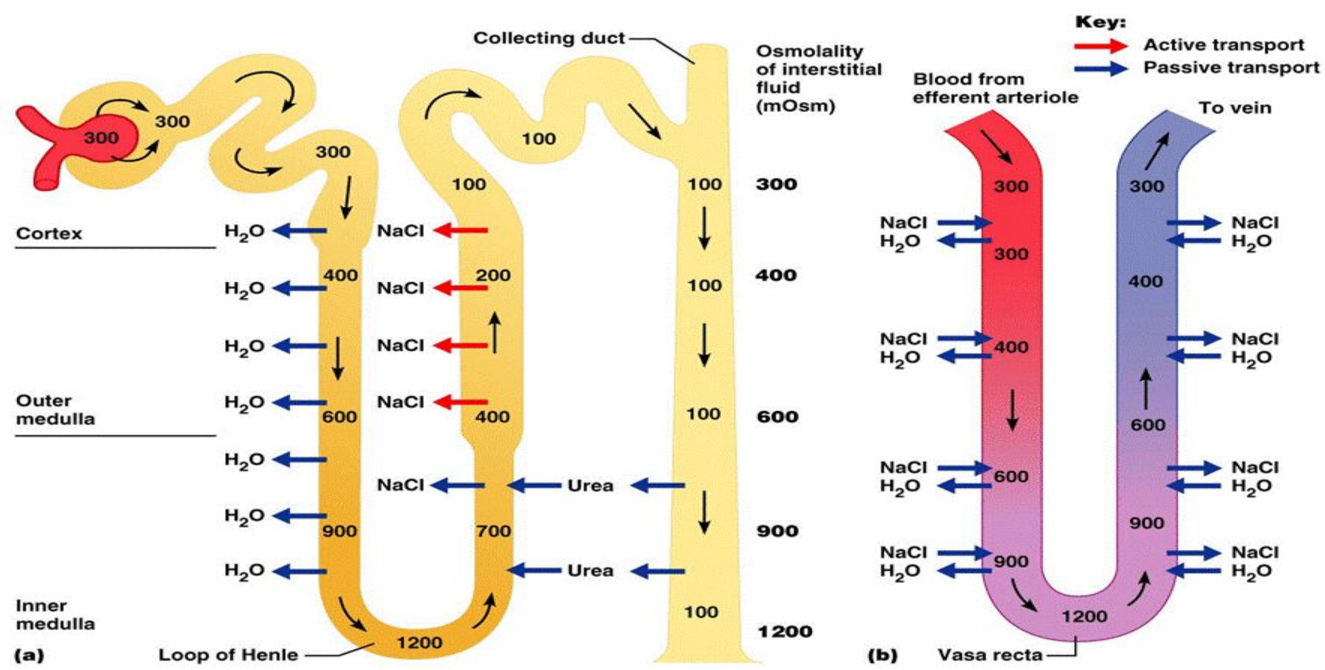
❖ **Why doesn't the blood flowing through the vasa recta into the renal medulla wash out the medullary hyperosmotic gradient?**

1. Medullary blood flow is **low (<5%)** of renal blood flow which makes it very sluggish (1-2%). the rest are going to the cortex.
This less 5% is enough for the cells are present there to take its nutrients and do its function BUT it's not high enough to wash out solutes that have been accumulated. and also because of the anatomy of vasa recta.

2. The vasa recta serve as countercurrent exchangers to maintain Medullary vertical osmotic gradient. And it's Important to give nutrients and oxygen to the medulla.

Explanation...





First you should know that Plasma osmolarity always 300 and interstitial fluid has high osmolarity which is 400.

1. Blood capillary are permeable to both Solutes and Water
So both will diffuse easily.

2. Water diffusion
Water will move out by osmosis and solutes will enter in because of their elevated osmolarity. therefore osmolarity as we going deep and deep it increases until it reaches 1200.

3. Opposite thing happen
Solutes will go out and Water will move in. Osmolarity starts decreasing until it reaches 300 as it was entered.
so the end result; nothing have been changed.

4. What happens in one side the opposite thing of it will happen in the other side and thus how vasa recta protect the hypertonicity of medulla from being washed out the blood.

Regulation of ECF Osmolarity

❖ **ECF osmolarity is regulated by two main mechanisms;**

Changes in urine Osmolality are brought about by changes in ADH , mainly in collecting ducts.

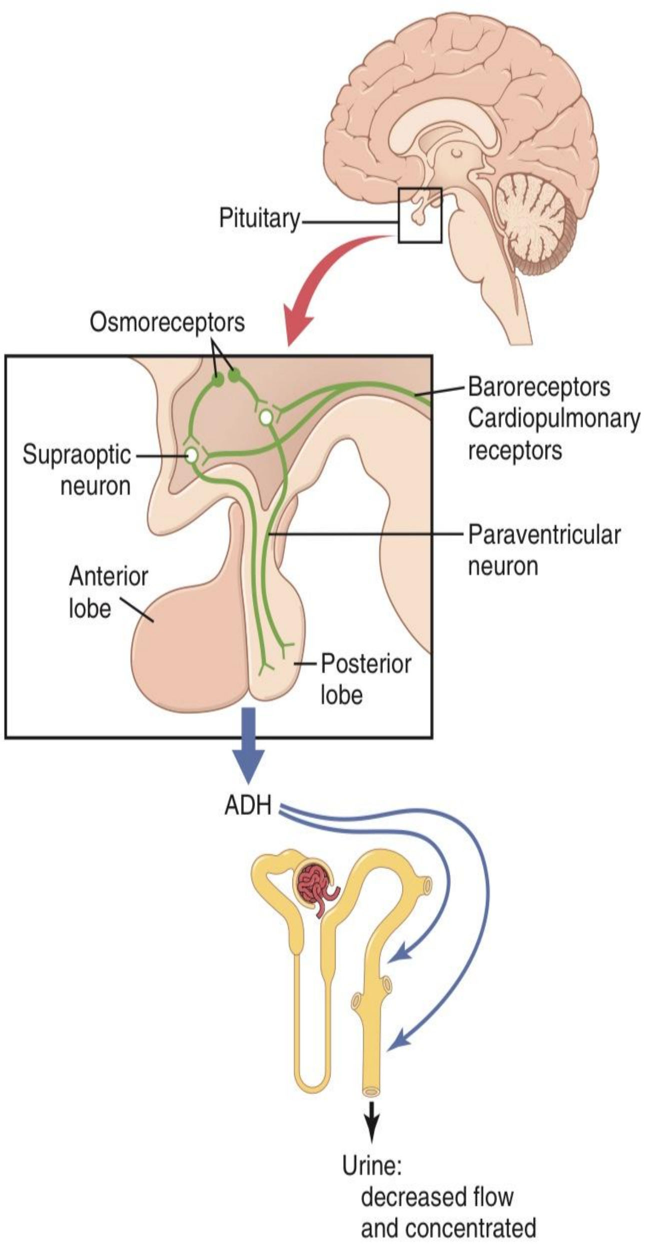
1-Osmoreceptor ADH system. By modifying urine excretion which is the major output route of water

2-Thirst mechanism. By modifying ingestion of water which is the major input route of it.

1-Antidiuretic Hormone (ADH)

What is ADH (or Arginine Vasopressin AVP or VP) ?

It was found in the boys' slides, but the girls' doctor explained it.



01

❖ **ADH** is hormone that's produced (synthesized) in the hypothalamus, stored (and released from) in posterior lobe of the pituitary gland.

02

❖ **The hypothalamus contains two types of magnocellular large neurons that synthesize ADH:**

➢ the supraoptic and paraventricular nuclei of the hypothalamus.

03

❖ **Route of Synthesis:**

➢ Both of these nuclei have axonal extensions to the posterior pituitary.

➢ Then ADH is transported down the axons of the neurons to their tips, terminating in the posterior pituitary gland to be released from there.

04

❖ **How is it released?**

➢ When the supraoptic and the paraventricular ventricular nuclei are stimulated by increased osmolarity or other factors, nerve impulses pass down these nerve endings.

➢ ADH stored in the secretory granules (also called vesicles) of the nerve endings and is released in response to changes that occurred in the nerve endings membrane.

How Osmoreceptors Sense Changes in Osmolarity?

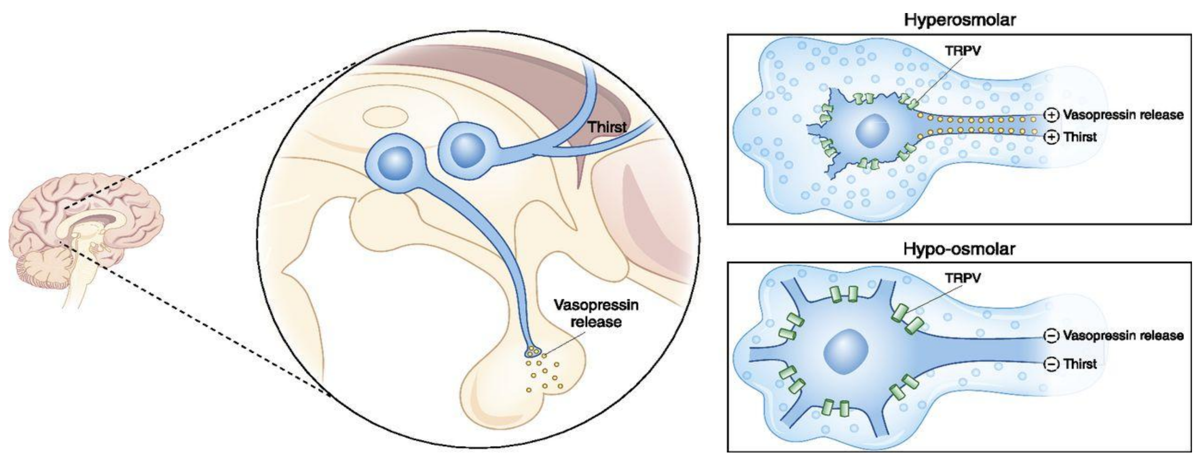
Hypertonic state:
The osmoreceptors will shrink with the cell due to the osmolarity changes that occured in the ECF → increasing the firing rate to the nerve endings → stimulating the release of ADH.

^Based on taken Notes
↑ Osmolality ➨ ↑ ADH release and ↑ H_2O reabsorption in collecting ducts

Hypotonic state:
The osmoreceptors will swell with the cell due to osmolarity changes in the ECF → decreasing the firing rate to the nerve endings → inhibiting the release of ADH.

^Based on taken Notes
↓ Osmolality ➨ ↓ ADH release and ↓ H_2O reabsorption in collecting ducts

ADH is more sensitive to small changes in osmolarity than to similar percentage changes in blood volume.



Stimulants for ADH Secretion | Factors That Can Alter ADH Secretion

Osmotic: (most important)

- Osmolarity of ECF.
- 1% change in osmolarity can alter ADH secretion significantly.
- change in blood or plasma Osmolality affect ADH release

Secretion of ADH in response to an osmotic stimulus is rapid, so plasma ADH levels can increase several folds within minutes, thereby providing a rapid means for altering renal excretion of water.

Factors Increasing ADH

- Nausea
- Hypoxia
- Angiotensin II
- An increase in Osmolarity
- A decrease in blood volume
- A decrease in blood pressure
- Drugs
  - Morphine
  - Nicotine

Hemodynamic:

- BV and ABP the vascular system.

And this make sense because If blood volume or Arterial blood pressure decrease —> ADH secretion will increase —> causing water reabsorption —> Blood volume will increase.

- 5-10% decrease in ABP or BV is required before ADH secretion is stimulated.

Factors Decreasing ADH

- ANP (Atrial natriuretic peptide)
- A decrease in Osmolarity
- A increase in blood volume
- A Increase in blood pressure
- Drugs
  - Alcohol

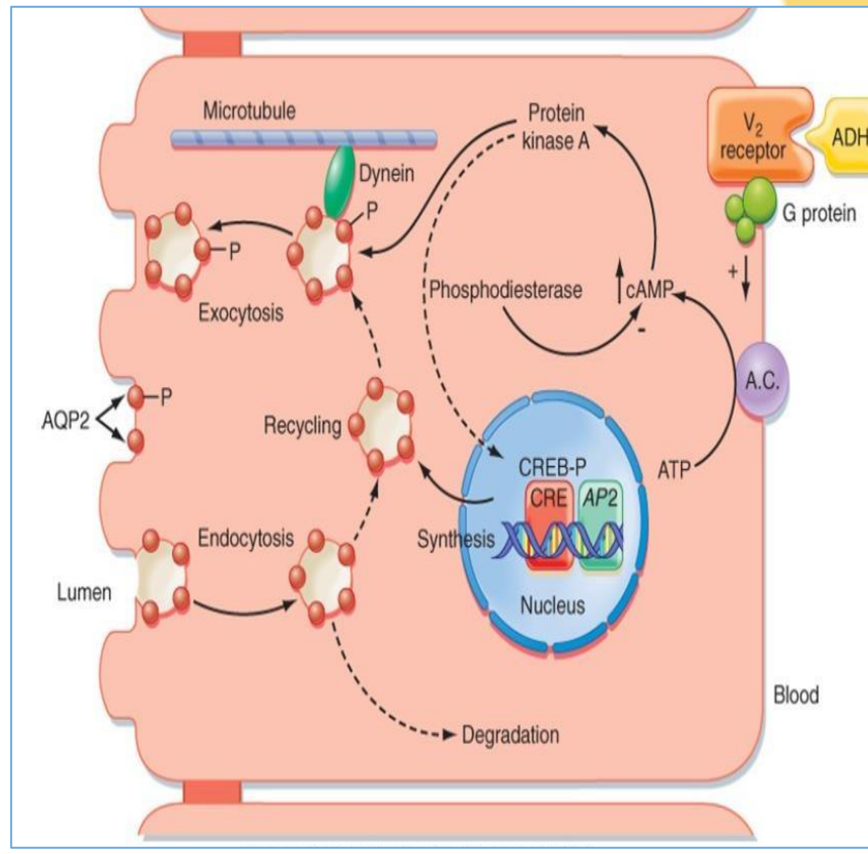
ABP= Arterial Blood Pressure
BV= Blood Volume

ADH Mechanism of Action

Dr Explanation...

As we learned there are some parts in the nephron are **dependent on ADH** they are: (distal tubule and collecting duct).
- There are receptors found in the principal cells of the tubule called **V2 receptors**, Once ADH secretes it will bind to V2 receptor and it will make changes inside the cells.
Also we have aquaporins II (AQP2 = Water channels) in principal cells: this channel is not present on the surface of the cell, it's hidden inside the cell. once ADH bind to V2 Receptor —> the changes that happens inside the cell will cause AQP2 to translocate to the surface of the cell —> once it's translocated it will open and allow to water to flow inside the cell or out of the tubule.

- <u>Note</u> that these AQO2 channels are hidden within the cell, and when ADH binds to V2 receptor, located in the the Basolateral side, the AQP2 channels will move to the Apical side of the cell. **Also** note that the AQP2 are different from AQP1 (which are located on the PCT).



Abnormalities in ADH Secretion

<u>Excessive</u> ADH

E.g. SIADH

Syndrome of Inappropriate Antidiuretic Hormone.

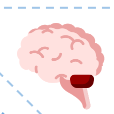
Leads to
- High ADH levels.
- Water retention.
- ECF hypo-osmotic Urine
- hyperosmotic

Means that the urine will have a small volume but it's highly concentrated

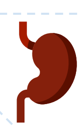
<u>Inadequate</u> ADH effect

E.g. "Diabetes insipidus"[1]

Further explanation in the next slide



<u>Central</u>
due to decreased release of ADH from posterior pituitary.
E.g. Trauma
Leading to
- Polyuria
- Polydipsia



<u>Nephrogenic</u>
Due to Mutations in V2 receptors or AQP2 that Cannot respond to ADH.
Leading to
- Polyuria and
- Polydipsia

[1] Diabetes insipidus and diabetes mellitus—which includes both type 1 and type 2 diabetes—are unrelated, al though both conditions cause frequent urination and constant thirst. Diabetes mellitus causes high blood glucose, or blood sugar, resulting from the body's inability to use blood glucose for energy. People with diabetes insipidus have normal blood glucose levels; however, their kidneys cannot balance fluid in the body.

Diabetes Insipidus

General Definition

A condition where the permeability of the distal tubules and collecting ducts to water is low, causing the kidneys to excrete large amounts of dilute urine. From Guyton

Symptoms:

1-Polyuria:
Passage of large amounts of dilute urine.
(with NO glucose in urine)

2-Polydipsia:
Drinking of large amounts of fluid.
It is the polydipsia that keeps these patients healthy. If the sense of thirst is depressed by loss of consciousness, these patients develop fatal dehydration.

	Central diabetes insipidus	Nephrogenic diabetes insipidus
Definition	Deficiency of ADH secretion from the posterior pituitary. <u>due to</u> lesion of the hypothalamus, hypothalamo-hypophyseal tract or posterior pituitary caused by head injuries or infections or it can be congenital.	Inability of the kidney to respond to ADH <u>e.g.</u> congenital defect in the V2 receptors in the collecting duct. <u>Further causes,</u> failure of the countercurrent mechanism to form a hyperosmotic renal medullary interstitium or failure of the distal and collecting tubule & ducts to respond to ADH. **In other words,** normal or elevated levels of ADH are present but the renal tubular segments cannot respond appropriately.
ADH level	Low	Normal or high
Treatment in males' slides only	ADH (Desmopressin) *Desmopressin* is a synthetic analog of ADH. <u>acts</u> selectively on V2 receptors to increase water permeability in the late distal and collecting tubules. <u>given by</u> injection, as a nasal spray, or orally, and it rapidly restores urine output toward normal.	Drugs to increase ADH sensitivity (Thiazide diuretics) **Why Thiazides?** One of the ways to treat it is by correcting the underlying renal disorders. **E.g.** Hypernatremia which can be attenuated by a low sodium diet and administration of a diuretic that enhances renal sodium excretion, such as a thiazide diuretic.
How to differentiate between the two types? in males' slides only	By administration of Desmopressin. Lack of a prompt decrease in urine volume and an increase in urine osmolarity within 2 hours after injection of desmopressin is strongly suggestive of nephrogenic diabetes insipidus.	

2-Thirst Mechanism

Definition

Thirst is the conscious desire for water.

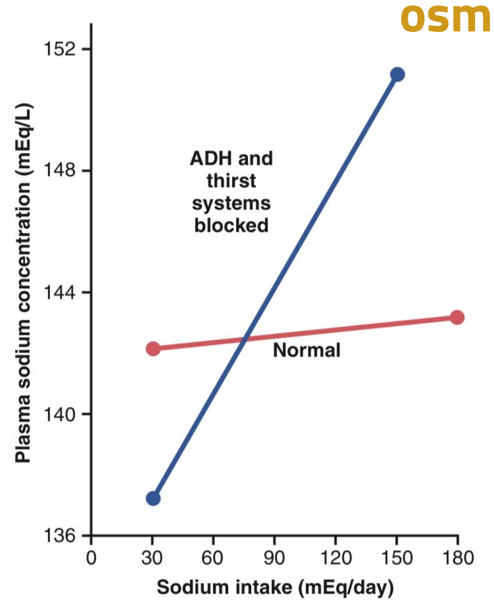
Factors ↑Thirst

- ❖ Increased Osmolarity
- ❖ Increased Angiotensin II
- ❖ Decreased Blood Volume and Pressure
- ❖ Mouth Dryness

Factors ↓Thirst

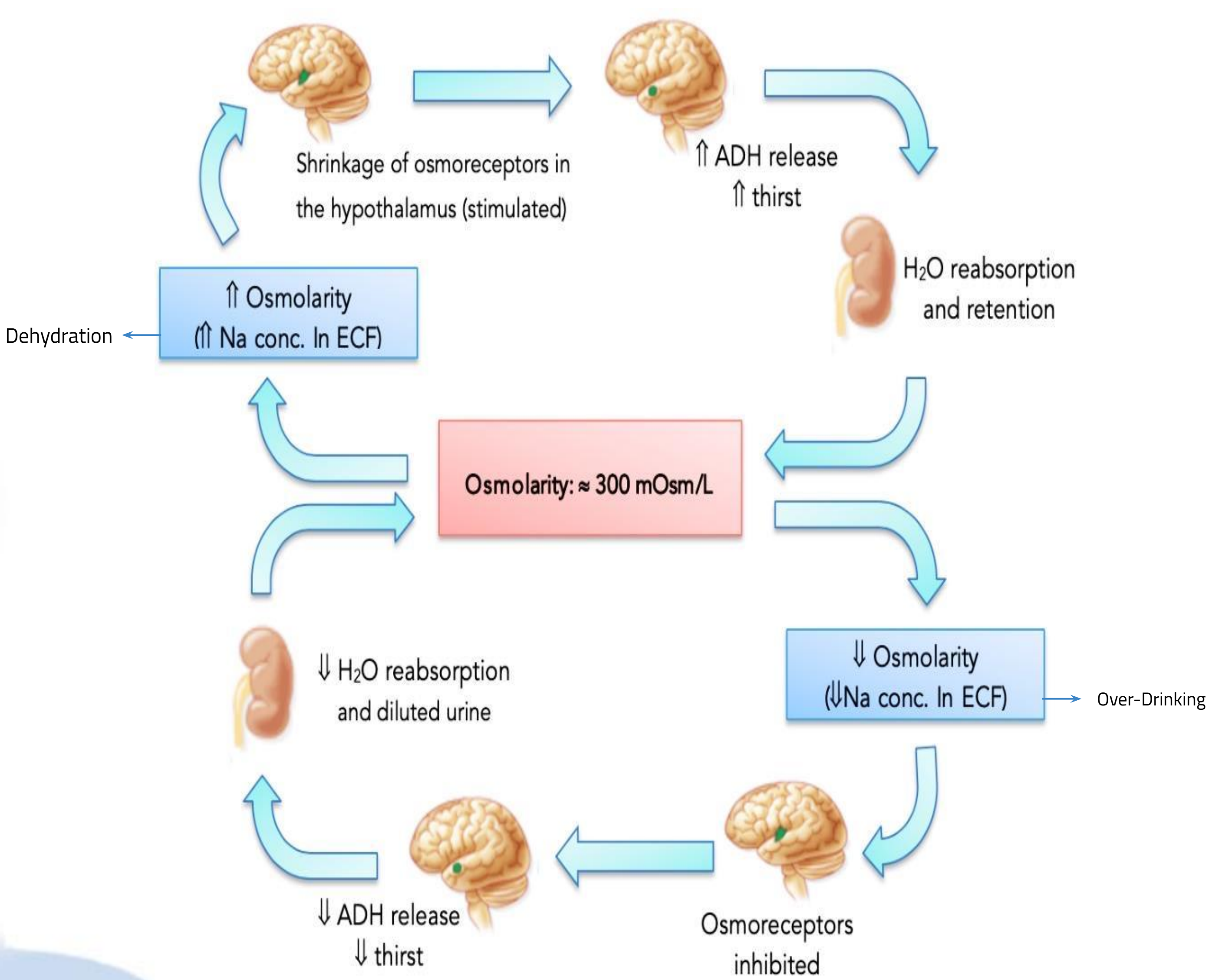
- ❖ Decreased Osmolarity
- ❖ Decreased Angiotensin II
- ❖ Increased Blood Volume and Pressure.
- ❖ Gastric Distention

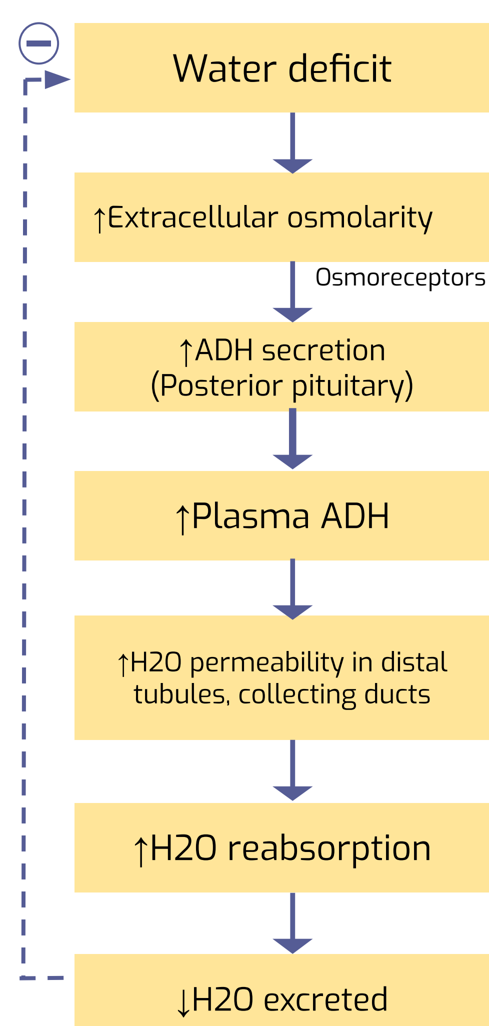
Importance of thirst and ADH mechanisms in regulating ECF osmolarity



Effect of large changes in sodium intake on extracellular fluid sodium concentration in dogs under normal conditions (red line) and after the antidiuretic hormone (ADH) and thirst feedback systems had been blocked (blue line). **Note** that control of extracellular fluid sodium concentration is poor in the absence of these feedback systems.

3-Feedback Mechanisms Involved in Regulation of Water Balance





From Guyton

Diuresis

Definition

An increase in the rate of urine output.

- Osmotic Diuresis
- Water Diuresis
- Medically induced diuresis (Diuretics).

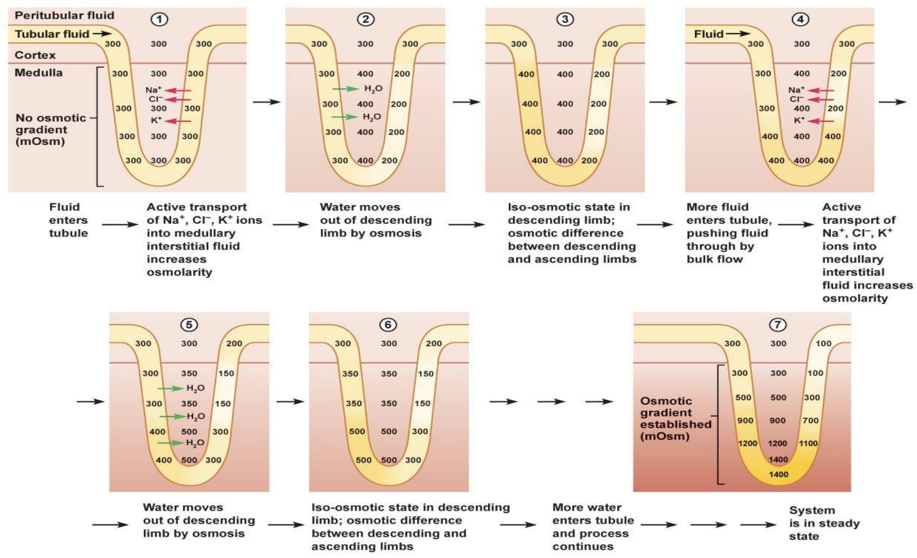
Water Diuresis vs Osmotic Diuresis

Water Diuresis	Osmotic Diuresis
Increased urine flow rate (with No change in urine excretion of solutes) Begins after about 15 min. & reaches max. in about 40 min.	Increased urine flow rate as well as the excretion of solutes
Causes: ❖ Excess ingestion of water (drinking large amounts 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) ❖ Presence of large quantities of unabsorbed solutes . As in diabetes mellitus
Mainly due to: ❖ Decrease in water reabsorption in distal segment of nephron. ❖ No change to the water reabsorbed proximally.	**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.

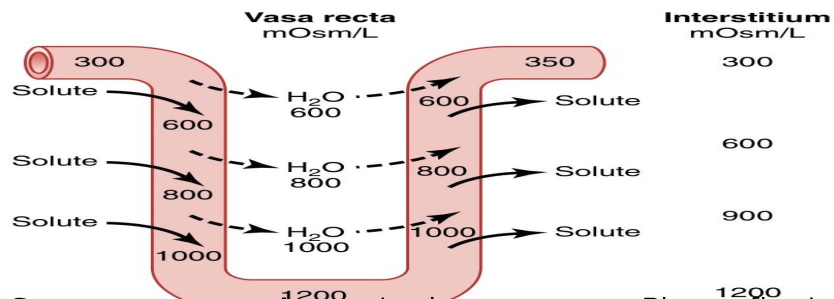
Summary

❖ **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.** **Guyton explanation here**

Countercurrent multiplier:
slide 7 (also it discussed in guyton page NO. 348-349)



Countercurrent exchanger slide 10



Countercurrent exchange in the vasa recta. Plasma flowing down the descending limb of the vasa recta becomes more hyperosmotic because of diffusion of water out of the blood and diffusion of solutes from the renal interstitial fluid into the blood. In the ascending limb of the vasa recta, solutes diffuse back into the interstitial fluid and water diffuses back into the vasa recta. Large amounts of solutes would be lost from the renal medulla without the U shape of the vasa recta capillaries. (Numerical values are in milliosmoles per liter.)

❖ **Explain what happens to osmolarity of tubular fluid in the various segments of the loop of Henle when concentrated urine is being produced.**

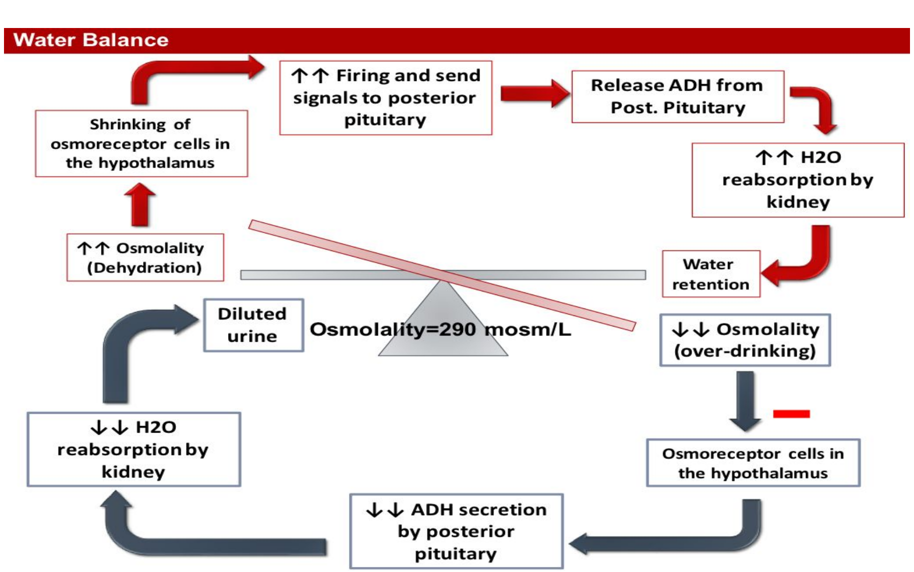
❖ **Slide 4**

❖ **Differentiate between water diuresis and osmotic diuresis.**

- ➢ **Water diuresis Is** Increased urine flow rate (No change in urine excretion of solutes)
- ➢ **Osmotic diuresis Is** Increased urine flow rate as well as the excretion of solutes

❖ **Appreciate clinical correlates of diabetes mellitus and diabetes insipidus.**

- ➢ Diabetes insipidus and diabetes mellitus are unrelated, although both conditions cause frequent urination and constant thirst. **Diabetes mellitus** causes high blood glucose, or blood sugar, resulting from the body's inability to use blood glucose for energy. People with **diabetes insipidus** have normal blood glucose levels; however, their kidneys cannot balance fluid in the body.



Summary here

MCQ & SAQ

Q1: 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

Q2: which one of the following describes water balance?

A. Output = input
B. Output>input
C. Output <input
D. None

Q3: A 70-Kg human needs to excrete:

A. 600 mOsm of solutes per day.
B. 200 mOsm of solutes per day.
C. 300 mOsm of solutes per day.
D. 700 mOsm of solutes per day.

Q4: What happens when the body is under a hypertonic state?
A. osmoreceptors shrink, stimulating the release of ADH.
B. osmoreceptors swell, stimulating the release of ADH.
C. osmoreceptors swell, inhibiting the release of ADH.
D. osmoreceptors shrink, inhibiting the release of ADH.

Q5: Which one of the following Factors Decrease ADH?
A. Nausea
B. ANP
C. Hypoxia
D. Angiotensin II

Q6: Which one of the following options is correct Osmotic diuresis?
A. Urine osmolality falls far below plasma osmolality.
B. increased excretion of pure water
C. Urine osmolality falls but remains above plasma osmolality.
D. Mainly due to Decrease in water reabsorption in distal segment of nephron.

answer key:
1: B
2: A
3: A
4: A
5: B
6: C

1- How Osmoreceptors Sense Changes in Osmolarity?

2- what is the mechanism of Action of ADH?

3-Compare Between Water diuresis And Osmotic diuresis

4- Mention the possible abnormalities in ADH Secretion

A1: Slide 12

A2: Slide 13

A3: Slide 16

A4: Slide 13

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