Diabetes Insipidus

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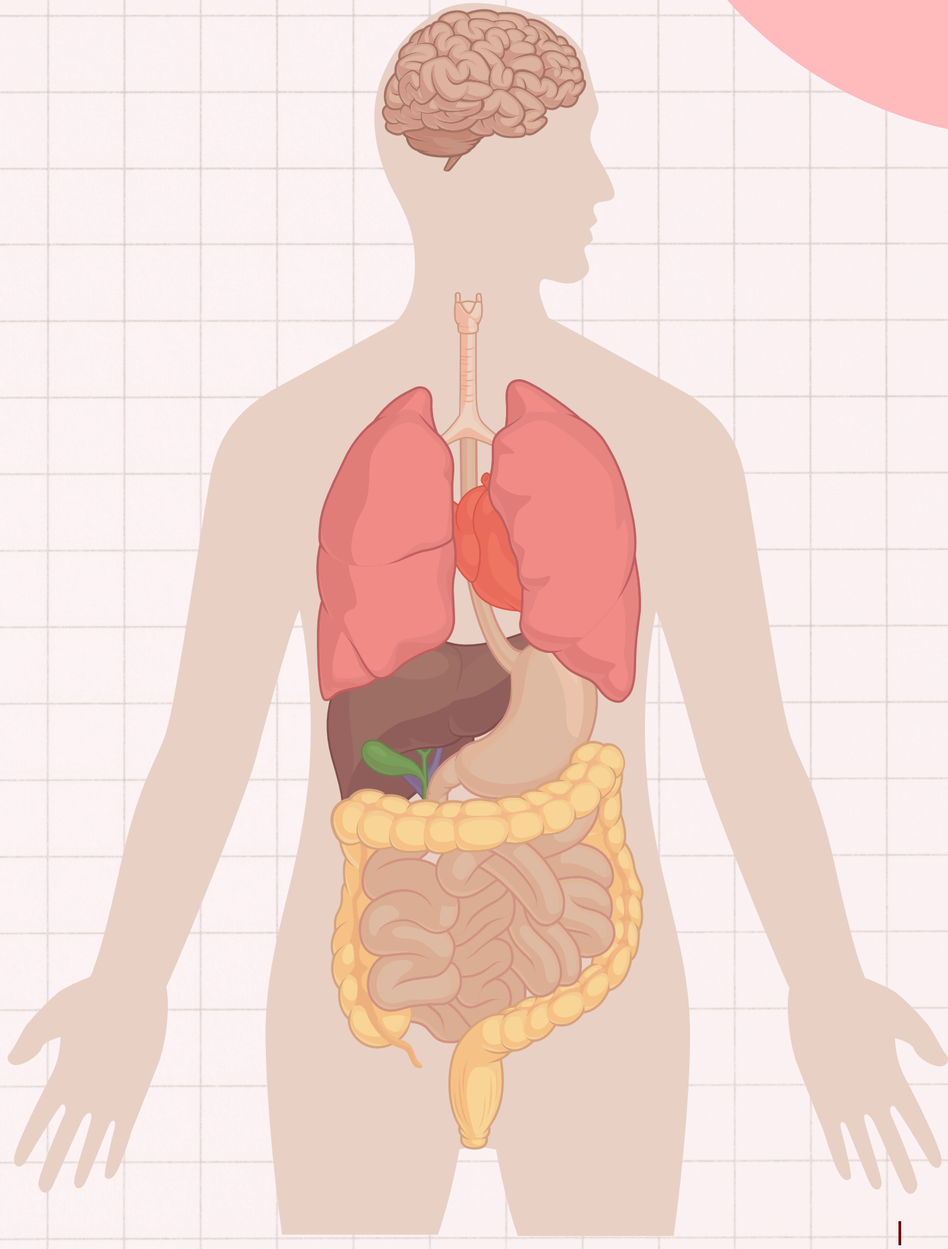


Overveiw

DEFINITION OF DI

Types of DI

DI VS SIADH

MANAGEMENT

ADH PHYSIOLOGY

CLINICAL FEATURES

DIAGNOSES

TREATMENT

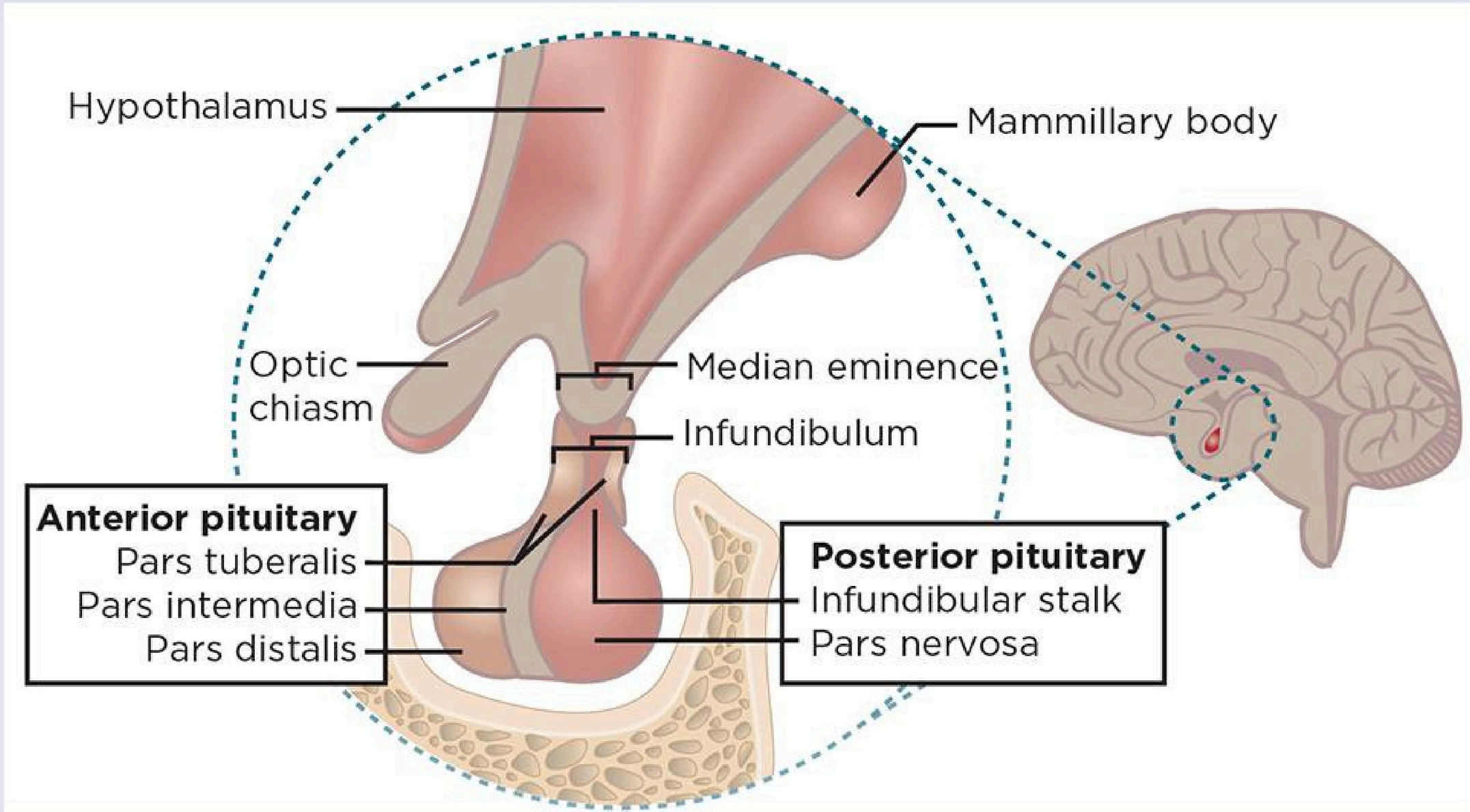
ADH FUNCTION ON THE NEPHRONS

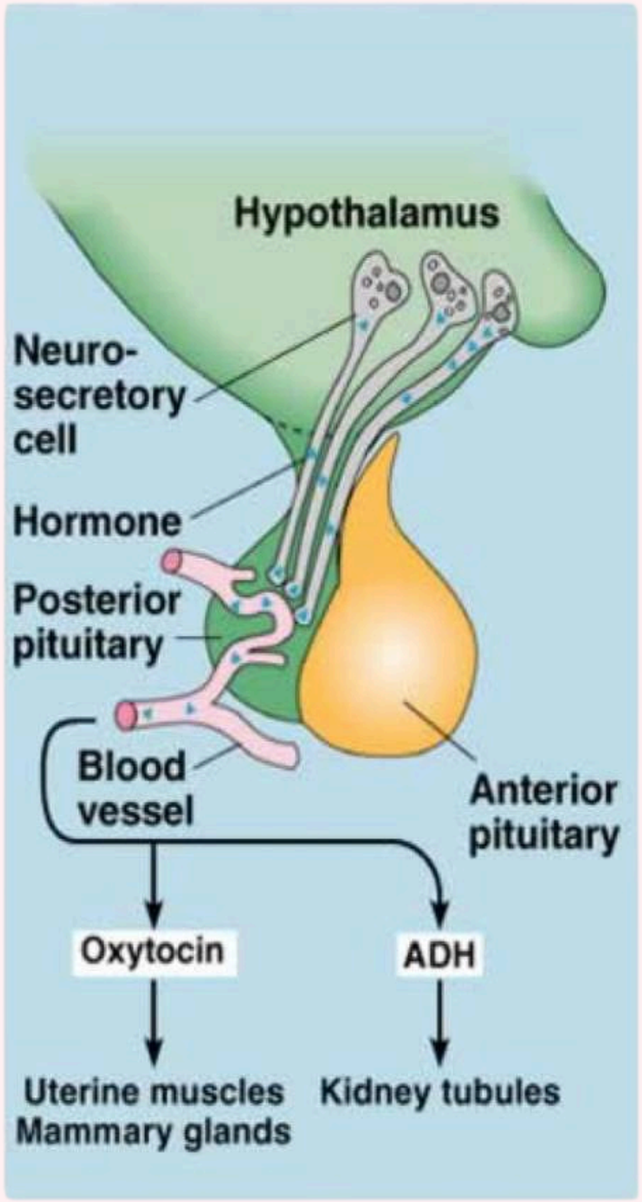
DM VS DI

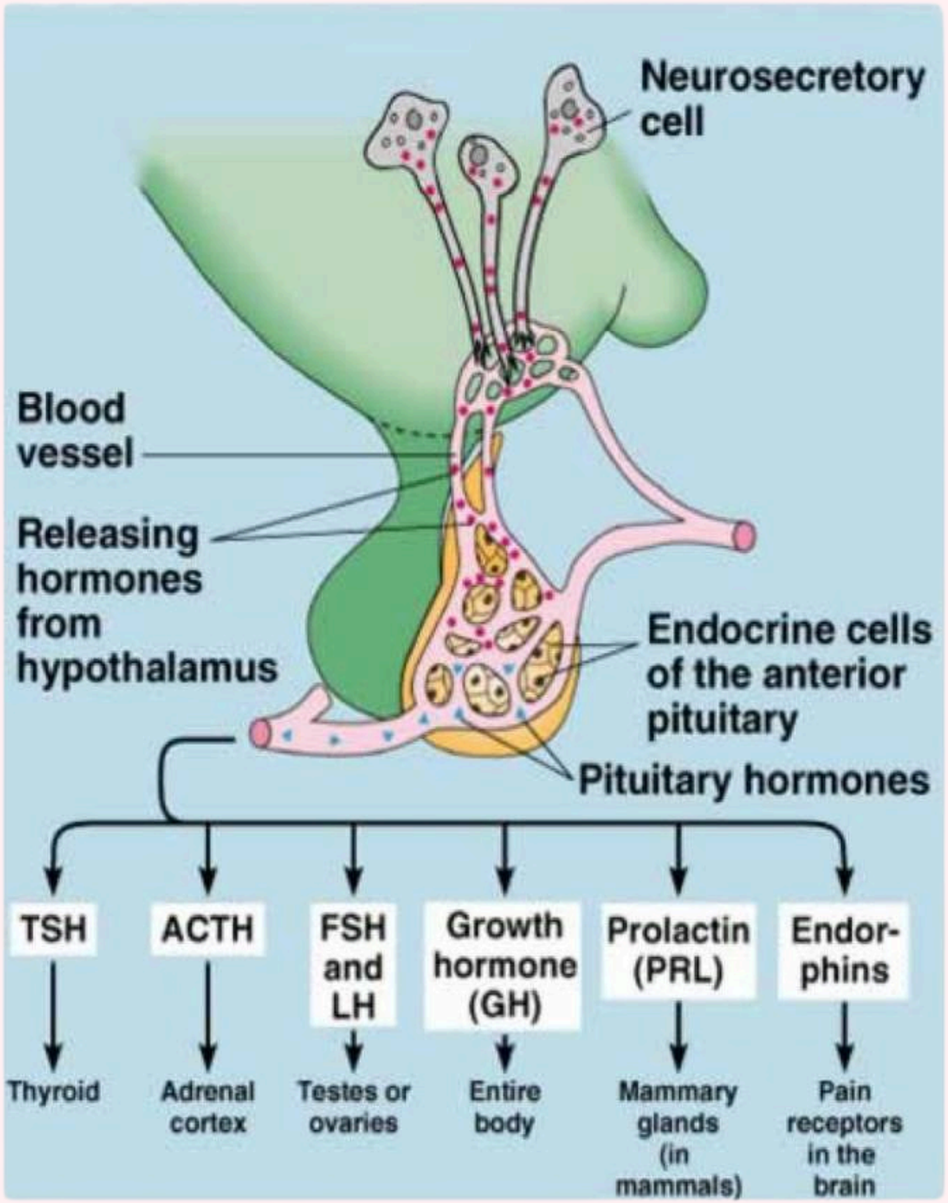
WATER DEPRIVATION TEST

ADH Physiology

Fig 1. **Anatomy of the hypothalamus and pituitary gland**




Hypothalamus
Neuro-
secretory
cell
Hormone
Posterior
pituitary
Blood
vessel
Anterior
pituitary
Oxytocin
ADH
Uterine muscles
Mammary glands
Kidney tubules


Neurosecretory
cell
Blood
vessel
Releasing
hormones
from
hypothalamus
Endocrine cells
of the anterior
pituitary
Pituitary hormones
TSH
ACTH
FSH
and
LH
Growth
hormone
(GH)
Prolactin
(PRL)
Endor-
phins
Thyroid
Adrenal
cortex
Testes or
ovaries
Entire
body
Mammary
glands
(in
mammals)
Pain
receptors
in the
brain

ADH Physiology

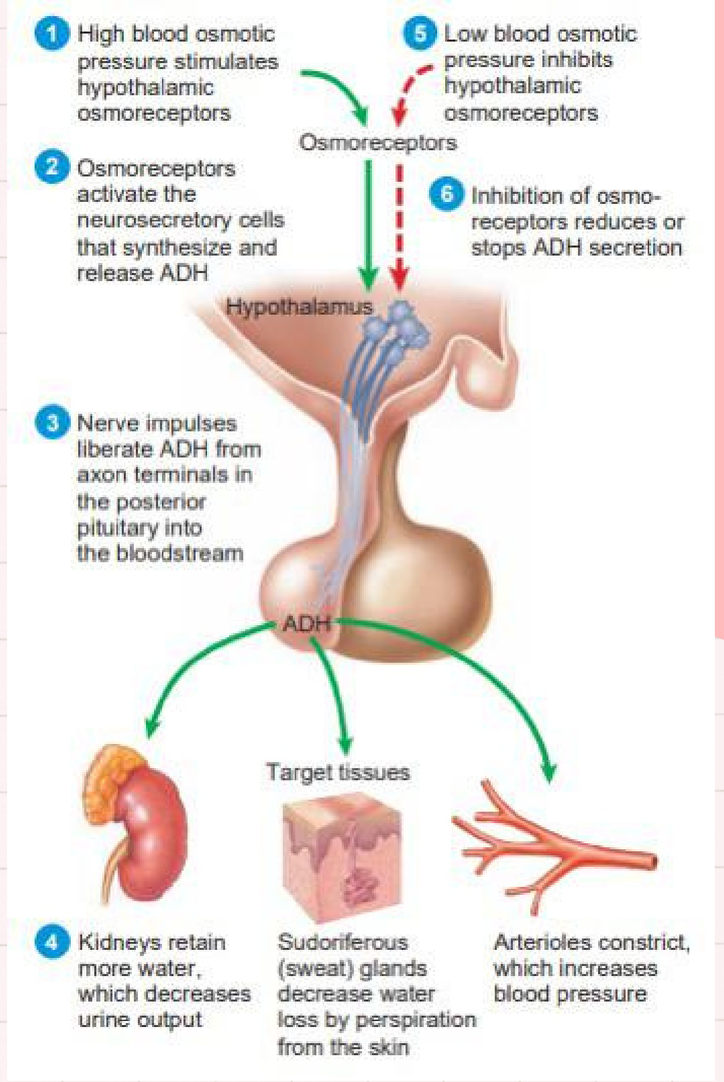
Vasopressin - Antiduiretic hormone (ADH) - Arginine Vasopressin (AVP)

It is synthesized in the Hypothalamus, and stored then secreted in the Posterior pituitary (neurohypophysis).

ADH has an important role in controling body's osmotic balance, blood preassure regulation, sodium homeostatis, kidney function.

- **<u>Secretion of ADH is stimulated by:</u>**

1. **High blood osmalality:** when the concentration of solutes in the blood is high, Osmoreceptors in the Hypothalamus respond by releasing ADH from the Pituiary gland.
2. **Low blood volume:** when blood volume is reduced, as in dehydration, ADH is released to help retain water in the body.
3. **Drugs:** certain drugs, such as Nicotine, Morphine, and Barbiturates.
4. **Others:** pain, stress, and nausea.



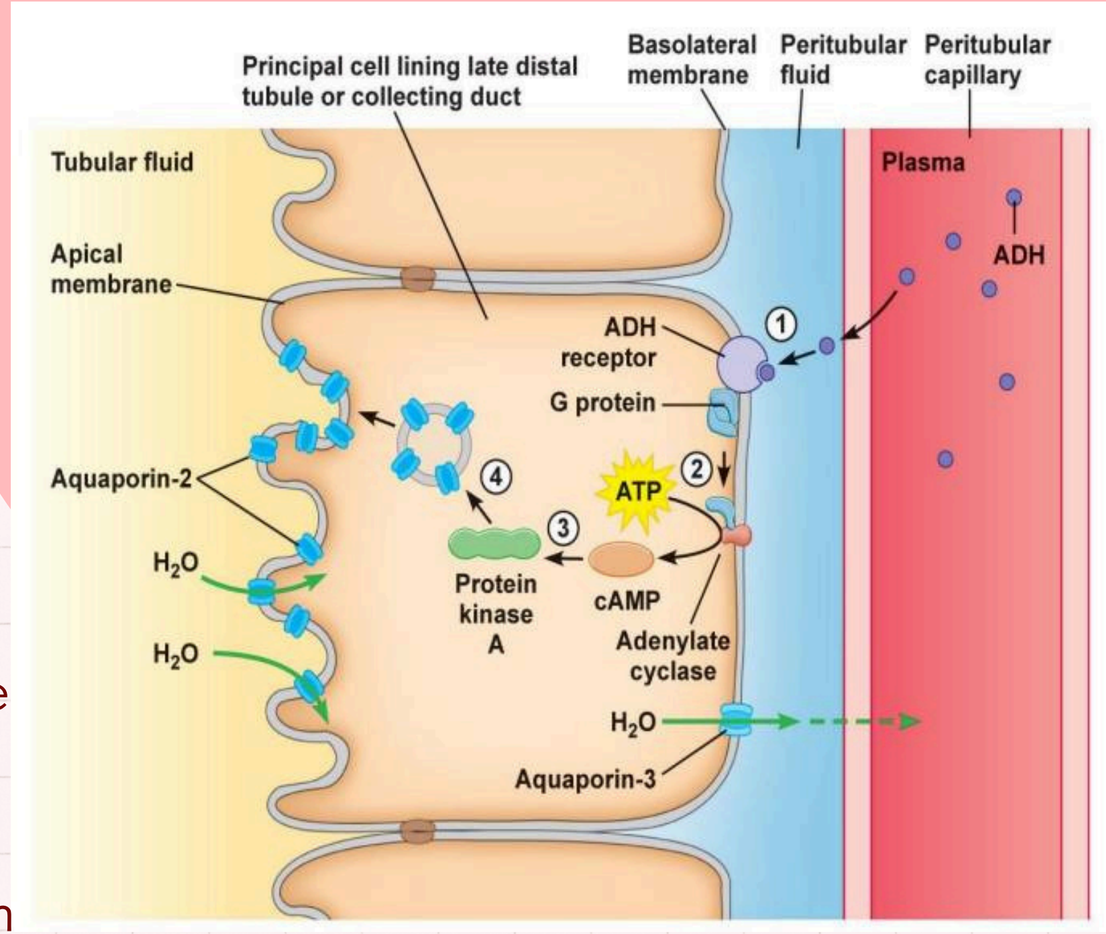
Osmoregulation and baroregulation are the two principal negative feedback mechanisms that control the secretion of ADH.

ADH Physiology

ADH function on the nephrons

ADH affects the ability of the kidney to reabsorb water in Late Distal Tubule and Collecting duct

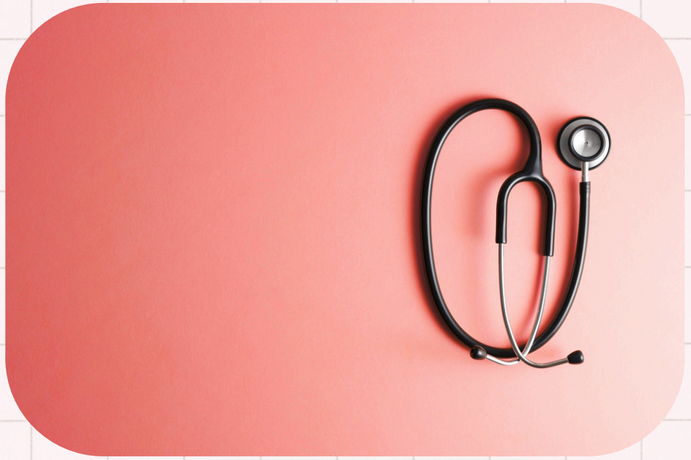
1. When the body is in state of Hypovolemia or Hyperbatremia, ADH is released from the Posterior Pituitary gland
2. ADH binds to type-2 receptors (V2) in the basolateral membrane of the collecting duct (Principal cells).
3. This binding activates the signaling pathway causing the insertion of aquaporin-2 channels into the apical membrane of tubular cells
4. Aquaporin-2 channels allow water to be reabsorbed from the urine back into the bloodstream, increasing water reabsorption by the kidney and reducing the amount of urine produced.



What is Diabetes Insipidus

Lack of production and release of ADH from posterior pituitary or decreased efficacy of ADH action. So kidneys are unable to retain water, causing dilute urine and progressively plasma osmolality.

It is a rare disorder, affecting roughly 1 in 25,000 people or about 0.004% of the global population, it does not show a predilection for males or females and it can develop at any age with hereditary forms developing earlier in life



Osmolality

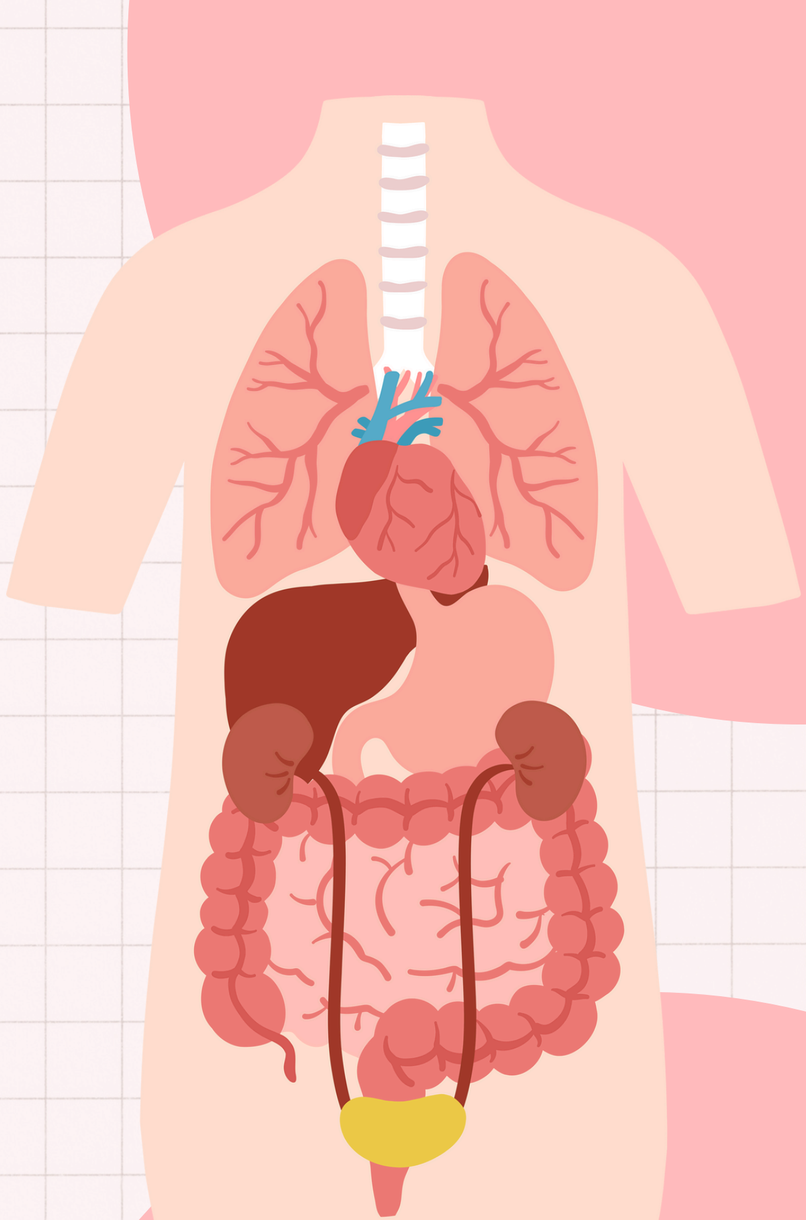
The concentration of disolved particles in the blood plasma.

- Normal blood osmolality is between 275 and 295 (Mosm/Kg).
- Major components are glucose, Na, and blood urea nitrogen.

What is Diabetes Insipidus

It is mainly characterized by:

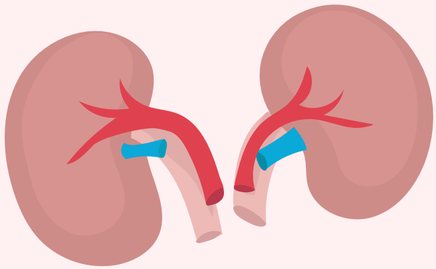
- Polydipsia (thirst)
- Polyuria (Urine output exceeding 3L/day for adults or 2L/day for children) (>40 to 50 mL/kg/day). It is characterized by the passage of large volumes of pale dilute urine.



Types of DI

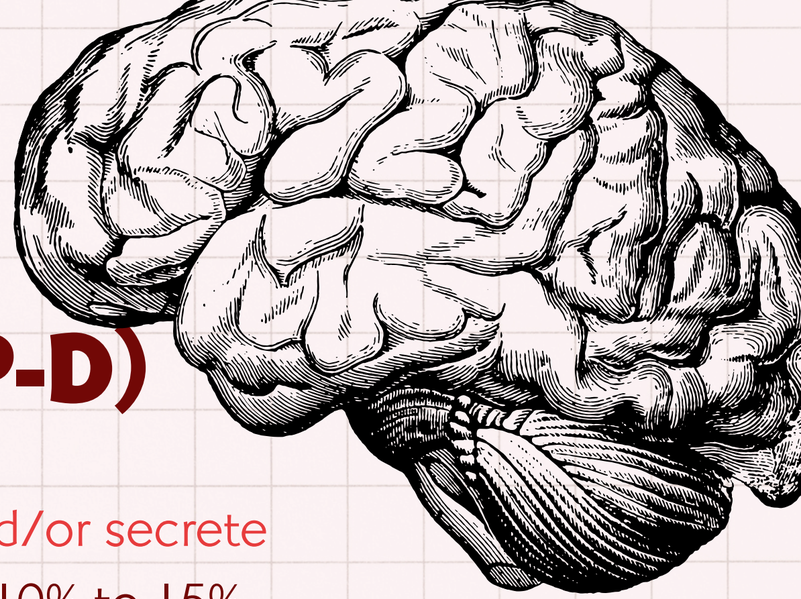
Central Di

Nephrogenic Di



Gestational Di

Dipsogenic Di



1 Central DI (Arginine Vasopressin Deficiency AVP-D)

AVP-D is caused by the inability of the neurohypophysis to synthesize and/or secrete AVP in response to increased plasma osmolality. Normal function of only 10% to 15% of the AVP producing neurons is sufficient to secrete enough AVP to prevent symptoms.

Adipsic AVP-D (Adipsic Diabetes Insipidus):

AVP-D caused by dysfunction of the osmoreceptors in the anterior hypothalamus.
Thus neurohypophysis and AVP production are normal, but the damage to the osmoreceptors leads to reduce stimulation of AVP secretion.
The symptoms resulted are without Polydipsia, because the damaged osmoreceptors are responsible for triggering thirst in response to increased plasma osmolality.

Central DI

Causes:

Acquired

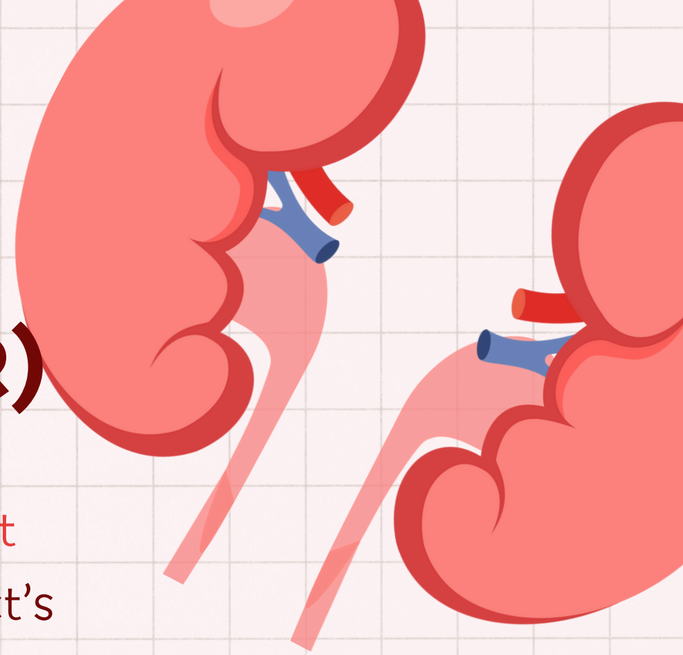
- Neurosurgery or Trauma
- Malignancy
- Drugs
- Infections
- Idiopathic

Genetic

- Familial AVP-D
- Wolfram syndrome (AVP-D, DM, Opticatrophy and deafness, cognitive and psychiatric issues)
- PCSK-1 gene deficiency
- Congenital hypopituitarism

2 Nephrogenic DI

(Arginine Vasopressin Resistance AVP-R)



In AVP-R, the body's Vasopressin production is not altered, but the kidnies don't respond to the hormones. Terminal distal convoluted tubule and collecting duct's become insensitive to circulating ADH

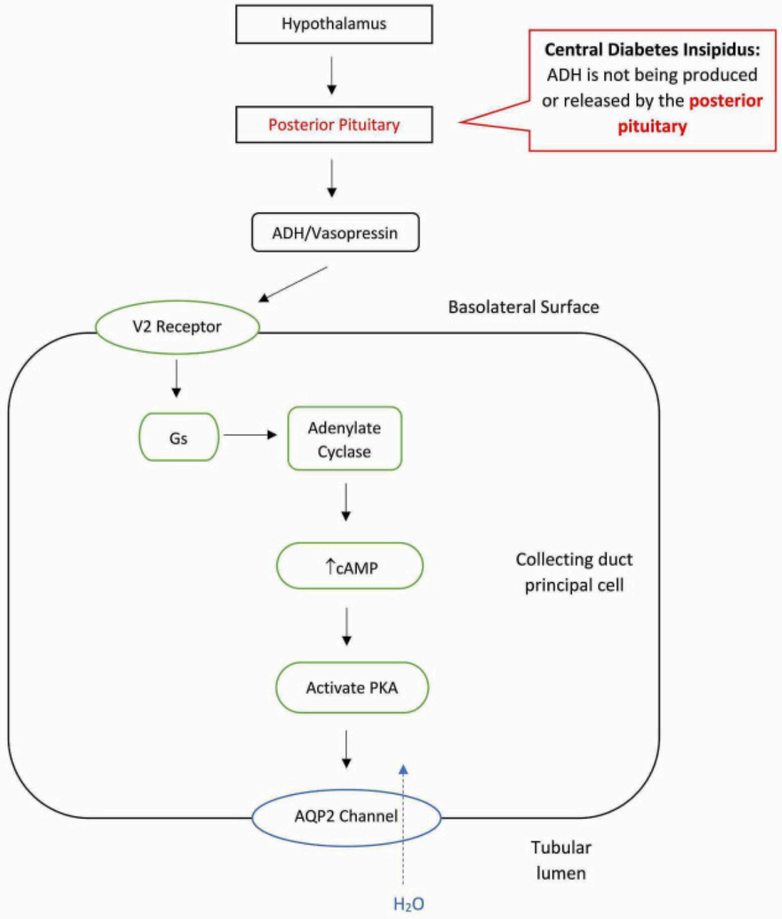
Causes:

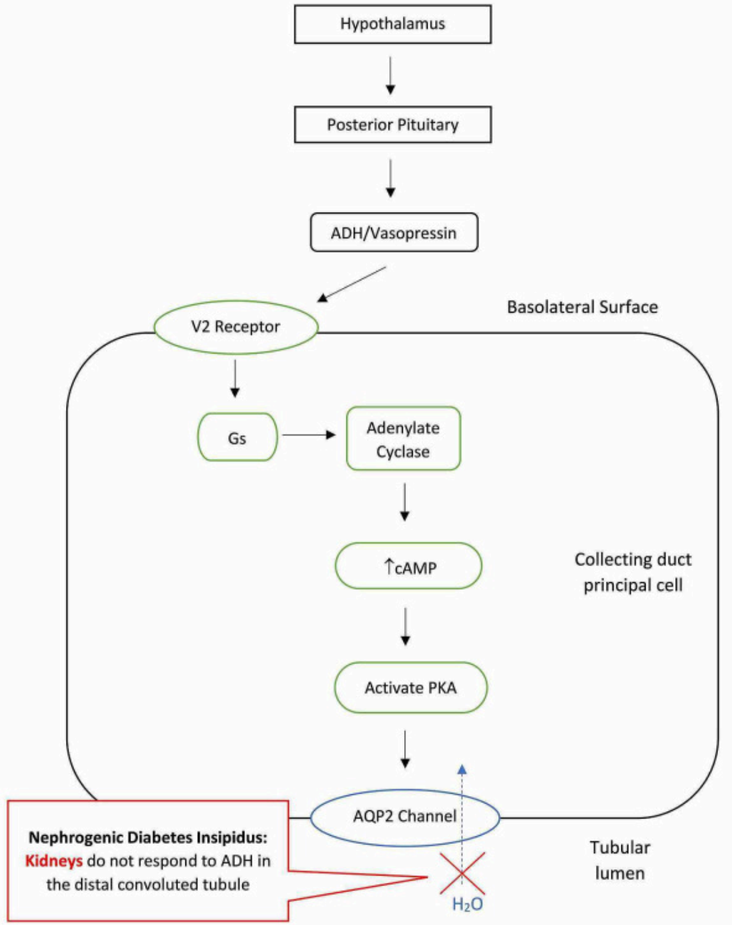
Acquired

- Drugs (Lithuim, Demeclocycline)
- Hypercalcemia, Hypokalemia
- Secondary to other diseases (Sjoren's sundrome, polycystic kidney disease, sickle cell anemia)

Genetic

- Mutation in ADH receptor or Aquaporin


Hypothalamus
Posterior Pituitary
ADH/Vasopressin
V2 Receptor
Basolateral Surface
Gs
Adenylate Cyclase
↑cAMP
Activate PKA
AQP2 Channel
Collecting duct principal cell
Tubular lumen
H2O
Central Diabetes Insipidus: ADH is not being produced or released by the posterior pituitary


Hypothalamus
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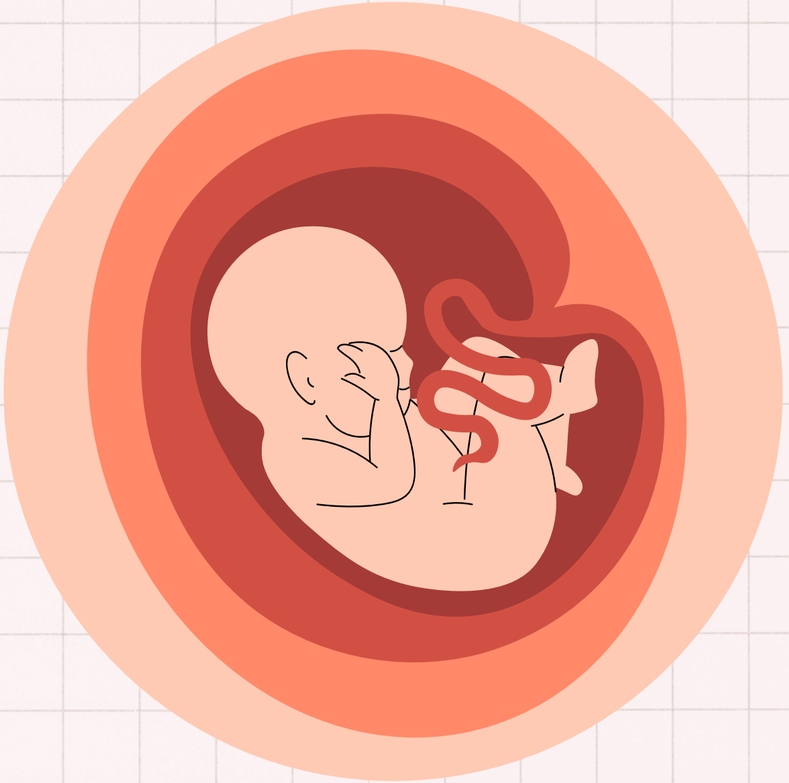
V2 Receptor
Basolateral Surface
Gs
Adenylate Cyclase
↑cAMP
Activate PKA
AQP2 Channel
Collecting duct principal cell
Tubular lumen
H2O
Nephrogenic Diabetes Insipidus: Kidneys do not respond to ADH in the distal convoluted tubule

3 Gestational DI



This is a rare, temporary condition that can develop during the end of the second trimester or during the third trimester of pregnancy.

Gestational diabetes insipidus happens when the placental trophoblasts make too much of an enzyme called Vasoprossinase that breaks down ADH.

Its activity is proportional to the placental weight, explaining the higher vasopressinase activity in the third trimester or in multiple pregnancies.

4

Dipsogenic DI

DDI is considered a subtype of Primary polydipsia, classified as having an abnormally low osmotic thirst threshold.

- People with this disorder feel thirsty constantly and drink lots of fluids, causing physiological suppression of ADH secretion.
- Can be caused due to damage to thirst-regulating mechanism in the Hypothalamus.
- Not related to how body handles the ADH.

Cause

Hypothalamus damage related to surgery, infection, inflammation, brain injury or tumor.

Summary

	Central	Nephrogenic	DIPSOGENIC
AVP	Decreased	Normal or increased	Normal or decreased
Mechanism	AVP deficiency	AVP resistance	Compulsive water intake

DI VS SIADH

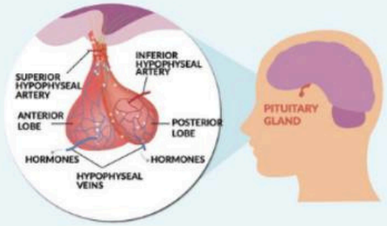
Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a condition in which the body makes too much antidiuretic hormone (ADH). SIADH causes your body to retain too much water, leading to hyponatremia, low serum osmolarity, and high urine ormolarity

Causes:

- Brain trauma, storke
- Lung diseases (Tuberculosis, cancer, chronic infections, such as pneumonia)
- Drugs
- Ectopic ADH production (SCLC)

Symptoms:

- Small amount of concentrated urine
- Low plasma osmolarity
- Water retention causing increased ICP, produces headache, nausea and vomiting, mental changes, and siezures in severe cases



ADH
Anti-Diuretic Hormone
Adds Da H_2O

NURSING CARE

D DAILY WEIGHTS
(**NOT** weekly)

W WEIGHT GAIN
Water Gain

SIADH "Soaked"
"Yes" ADDS DA H_2O
Syndrome of Inappropriate Antidiuretic Hormone

PATHO, S/S, TREATMENTS

- S **STOPs** urination (**LOW** urine output)
- S **STICKY** & THICK "urine" HIGH Sp. Gravity 1.030+
- S **SOAKED Inside** "Low & Liquidy" Labs
  - **HYPO**-osmolality (**LOW**) NCLEX TIP
  - **HYPO**natremia below 135 Na+ (**LOW**)
- S **SODIUM** Low!! (Headache Early Sign) NCLEX TIP
- S **SEIZURES** - **NCLEX** key words: **Headache, Confusion**
- S **SEVERE HIGH** blood pressure
- S **STOP ALL FLUIDS + GIVE Salt** + Diuretics

(**NO IV** or drinking) + (**IV 3% Saline + Eat Salt**)

CAUSES

- S Small cell lung cancer NCLEX TIP
- S Severe Brain Trauma (trauma/surgery)
- S Sepsis infections of brain (meningitis)

LABS

SOAKED Inside "Low & Liquidy" Labs:
- **HYPO**-osmolality (**LOW**).
- **HYPO**natremia below 135 Na+ (**LOW**).

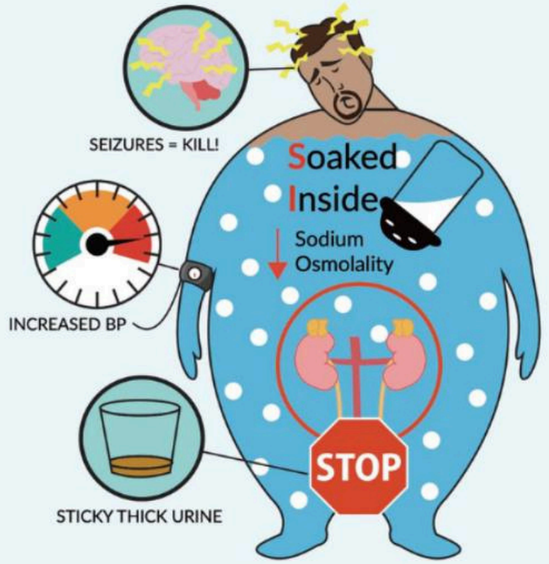
STICKY thick urine" Outside • **LOW** urine output (**STOPS** urine):
- HIGH specific Gravity 1.030+

COMMON NCLEX QUESTION

What does the nurse expect to find in a client with syndrome of inappropriate antidiuretic hormone?
Select all that apply.

- ✓ 1. **Low blood osmolality.**
- 2. Increased serum osmolality.
- 3. Low urine specific gravity.
- ✓ 4. **Hyponatremia.**
- ✓ 5. **Decreased urine output.**

SIADH "Soaked Inside"



COMMON NCLEX QUESTION

When caring for a client with **SIADH**, what does the nurse **expect to implement?**
Select all that apply.

- 1. IV maintenance fluid 0.9% normal saline.
- ✓ 2. **Fluid restriction.**
- 3. Sodium restriction.
- ✓ 4. **Seizure precautions.**
- ✓ 5. **Monitor urine I & O (intake & output).**
- 6. Measure weight weekly.

DI VS SIADH

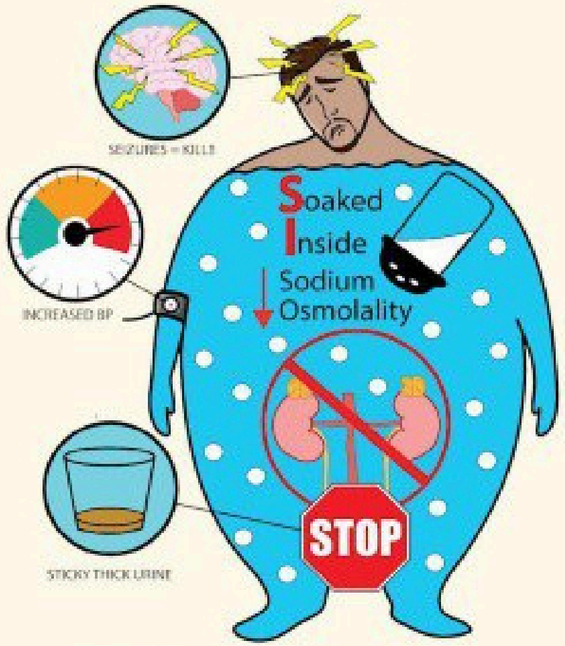
SIADH "Soaked"

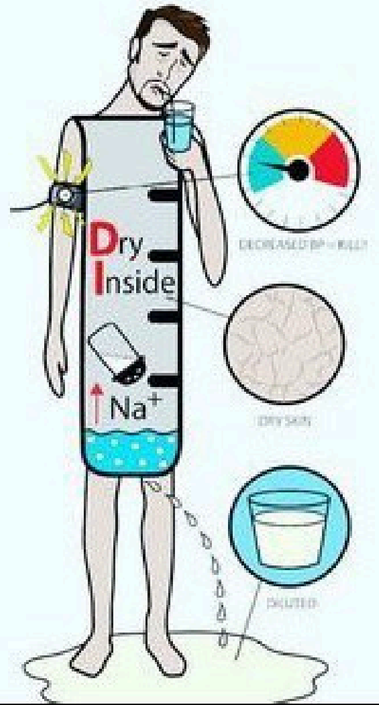
"Yes" ADDS DA H_2O

Syndrome of Inappropriate Antidiuretic Hormone

7 S's

1. S **STOPs** urination (**LOW** urine output)
2. S **STICKY** & THICK "urine" HIGH Sp. Gravity 1.030+
3. S S **OAKED** I nside "Low & Liquidy" Labs
   - **HYPO** osmolality (**LOW**) **NCLEX TIP**
   - **HYPO**natremia below 135 Na+ (**LOW**) **NCLEX TIP**
4. S **SODIUM** Low!! (**Headache** Early Sign)
5. S **SEIZURES**- **NCLEX** key words: **Headache, Confusion**
6. S **SEVERE HIGH** blood pressure
7. S **STOP ALL FLUIDS** + **GIVE Salt** + Diuretics (**NO IV** or drinking) + (**IV 3% Saline + Eat Salt**)





DI "*Dehydrated*"

"Die" ADH!

Diabetes Insipidus

7 D's

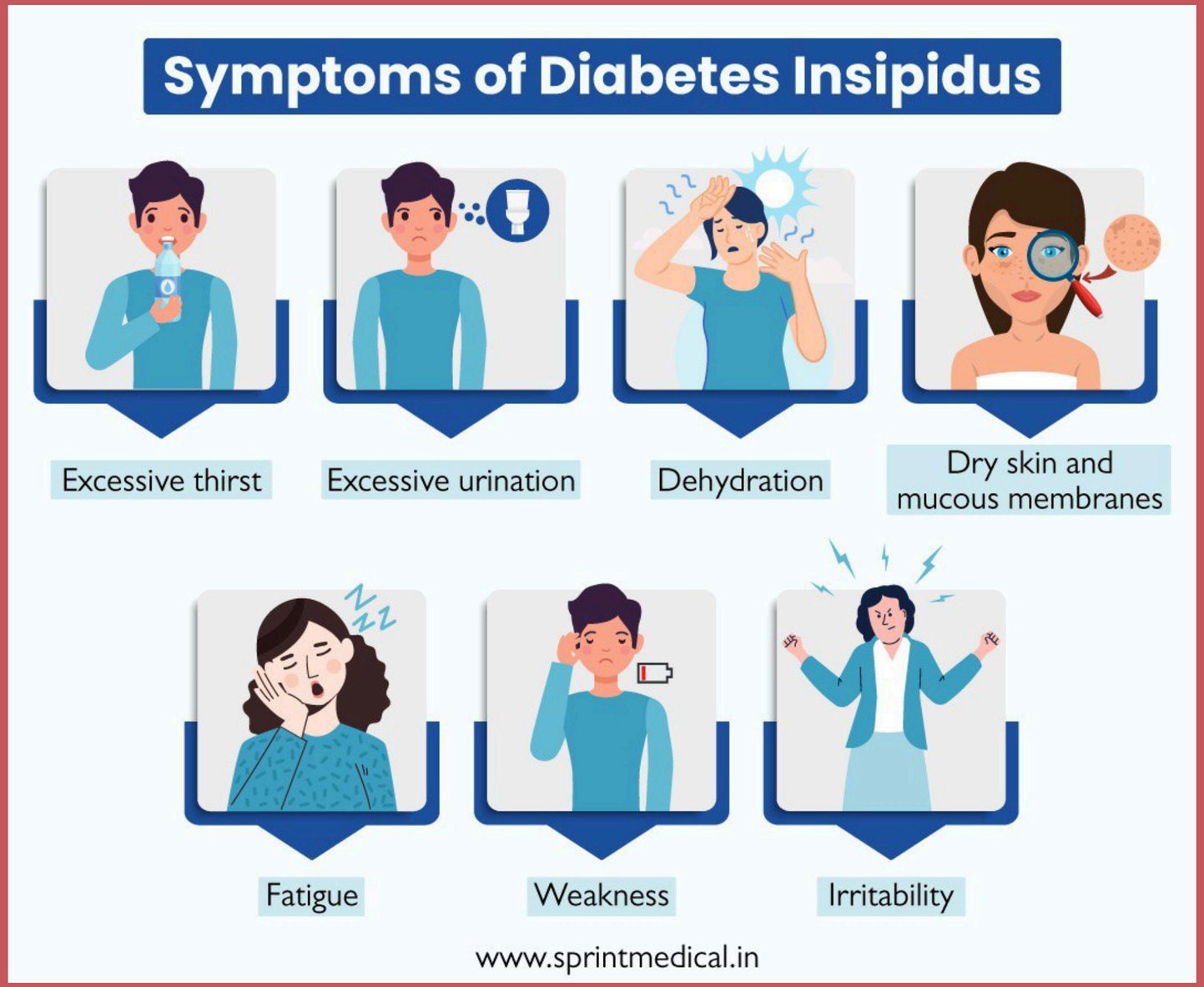
1. D **DIURESE** "Drain" fluid (**HIGH** urine output)
2. D DI **LUTED** urine Low specific Gravity (1.005)
3. D D **RY** I nside "High & Dry" Labs
   - **HYPER** osmolality (**HIGH**) **NCLEX TIP**
   - **HYPER**natremia over 145 Na+ (**HIGH**)
4. D **DRINKING** a lot "thirsty"
5. D **DEHYDRATED** Dry Mucosa & Skin
6. D **DECREASED** blood pressure
7. D **DESMOpressin** "Vaso**pressin**" (ADH)
   - **D**ecrease Urine Output **NCLEX TIP**
   - **D**eath by **Headache!** (Low Na+) 135 or Less

Clinical Manifestation

Clinical Manifestation

- Polyuria (excessive urine output, typically >40-50 mL/kg/day).
- Polydipsia (excessive thirst) due to initial elevation in serum sodium and osmolality, in case of low water intake severe dehydration (Altered Mental Status, Lethargy, Seizures, Coma) and hypotension.
- Nocturia (need to urinate at night).
- Serum sodium often in the high normal range in untreated patients.
- Moderate to severe hypernatremia can develop if thirst is impaired or there's no access to water.
- Neurologic symptoms related to the underlying cause (e.g. diplopia, headache).
- Psychological symptoms such as: Increased anxiety, social isolation ,generally decreased quality of life.

Clinical Manifestation



Diagnosis

Diagnosing and evaluating of (AVP-D/R)

Step 1: Confirm Polyuria

- Measure urine output to confirm polyuria (typically >40-50 mL/kg/day).
- Conduct a 24-hour urine collection to quantify excessive urine production, as seen in both.

Step 2: Differentiate Water Diuresis from Solute Diuresis

- Determine if polyuria is due to water diuresis (less than 300mOsm/kg, typical in diabetes insipidus) or solute diuresis (more than 600mOsm/kg, typical in DM or medication-induced).

Diagnosing and evaluating of (AVP-D/R)

<u>Step 3</u>: Confirm AVP-D or AVP-R Diagnosis

1) Water deprivation test: A test to assess the kidney's ability to conserve water by restricting fluid intake.

2) Desmopressin challenge: A test to evaluate the body's response to synthetic vasopressin (desmopressin) to differentiate between central and nephrogenic diabetes insipidus.

Water deprivation test

Water Deprivation Test for Diabetes Insipidus

Start at 8am
- Empty bladder, record the volume, send urine osmolality
- Take a serum osmolality
- Record the patient's weight

For next 8 hours check:
- Urine osmolality and weight every hour
- Serum osmolality every 2 hours

Stop test and get help if weight loss >3% or serum osmolality >300mOsm/kg

After 8 hours (4pm), if urine osmolality:

>600 mOsm/kg → **No diabetes insipidus**

Urine osmolality >600mOsm/kg excludes diabetes insipidus and test can be stopped when this is achieved

<600 mOsm/kg

- Give desmopressin 2µg IM
- Measure urine osmolality hourly for next 4 hours
- Patient can eat or drink freely now

No increase in urine osmolality → **Nephrogenic DI**

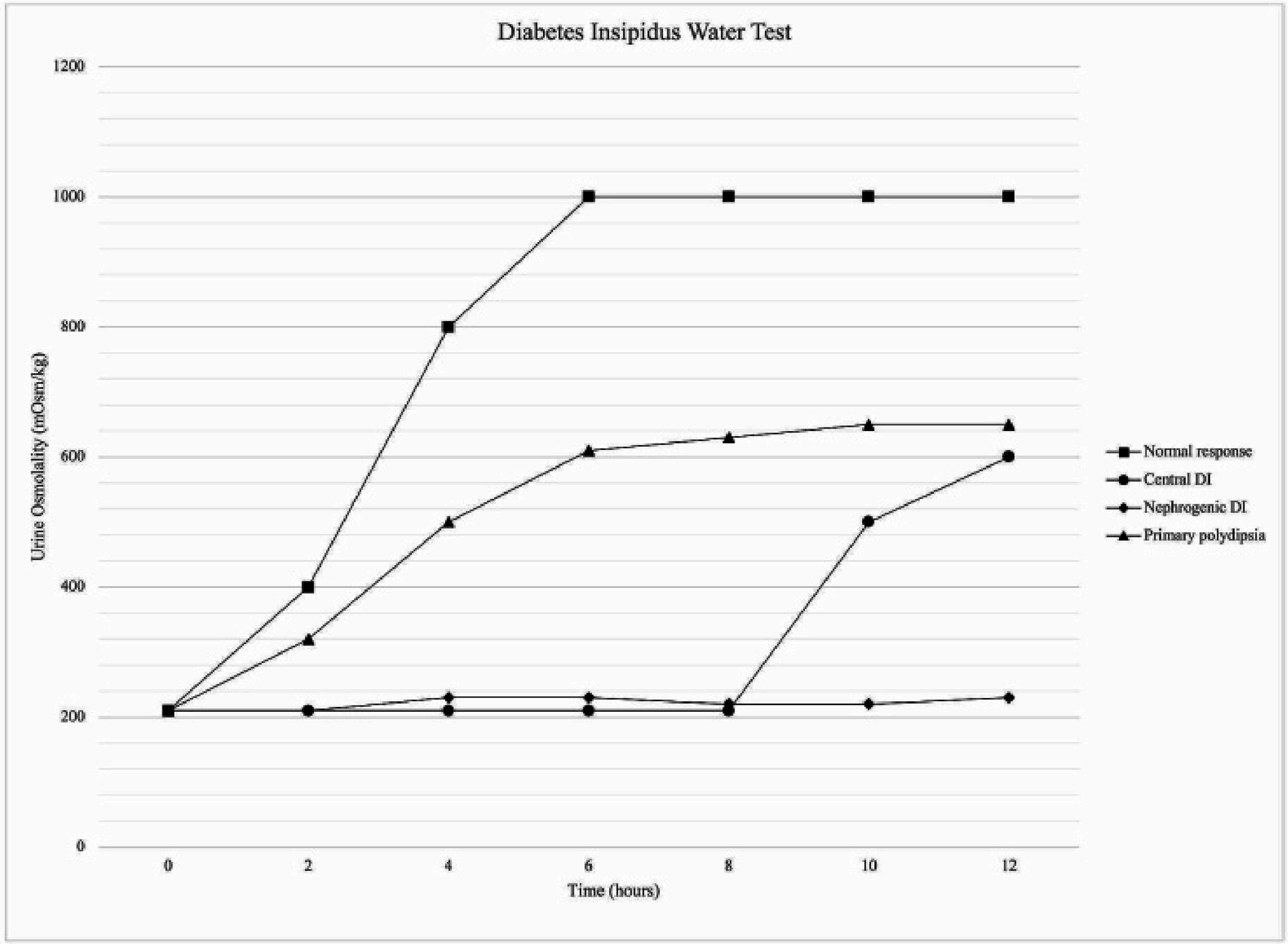
Causes: Hypokalemia, hypercalcemia, chronic renal disease, drugs (lithium, demeclocycline)

Urine osmolality increases to >600mOsm/kg → **Cranial DI**

Causes: Idiopathic, DIDMOAD, pituitary tumour, trauma, sarcoidosis, Sheehan's syndrome, infection, haemorrhage

GRAM PROJECT

Water deprivation test



Diagnosing and evaluating of (AVP-D/R)

<u>Step 4</u>: Determine Etiology

For Post-Surgical or Trauma Patients: In AVP-D, deficiency is often transient following neurosurgery or head trauma.

- MRI Imaging:

-For AVP-D: Perform brain MRI to examine the suprasellar region, pituitary stalk, and pituitary gland, especially for structural abnormalities or tumors.
In some patients, MRI will identify the cause of AVP-D, such as a malignancy or infarction.
-For AVP-R: Kidney ultrasound or MRI may be used if there are concerns about structural renal abnormalities.

- Identify Underlying Causes:

-For AVP-R: Check for factors like lithium(Li) use, hypercalcemia(Ca), or hypokalemia(K)

Diagnosing and evaluating of (AVP-D/R)

<u>Step 5</u>: Evaluate risk of complications and monitor high-risk groups

Both AVP-D and AVP-R patients should be monitored for dehydration and hypernatremia, especially if they have impaired thirst.

High-risk populations include infants, young children, neurologically impaired adults, and postoperative patients.

<u>Step 6</u>: Follow-Up and long-term monitoring

- For AVP-D: If initial tests are negative, repeat MRI in 3-6 months and then yearly for up to 5 years; assess anterior pituitary function yearly.
- For AVP-R: Routine follow-up to monitor urine output, electrolyte balance, and associated conditions (e.g., lithium therapy) is advised.

<u>Step 7</u>: Consider Genetic Testing- For patients with family history suggestive of DI.

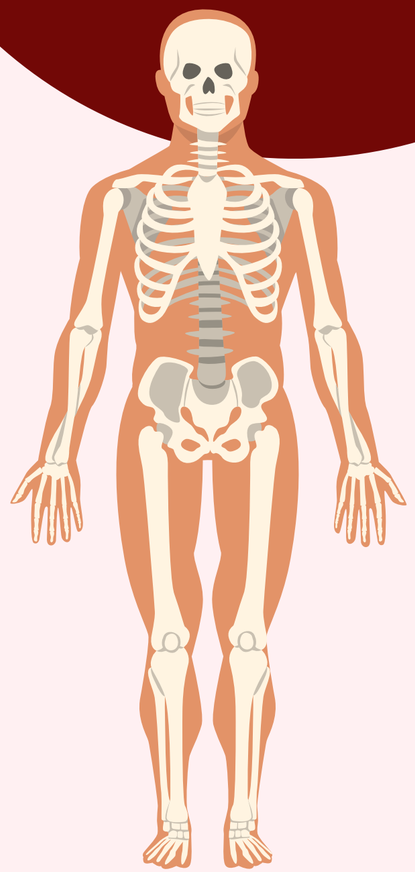
Management

Management

First concern is adequate hydration and replacement of water deficit:

In most individuals who have normal thirst mechanism, it can guide the intake of oral fluids. However, in individuals with adipsic DI who have impaired thirst, a daily fluid intake should be fixed at which euvolemia and eunatremia are maintained. In unconscious patients, water deficit can be corrected with plain water administered through Ryle's tube and with intravenous hypotonic fluids (5% dextrose or 0.45 saline).

- Isotonic fluid (0.9 saline) should be avoided as it can worsen hypernatremia.



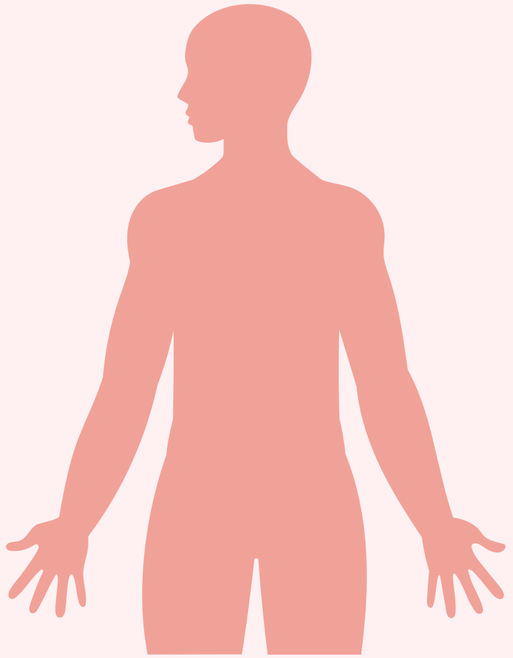
If the serum Na+ is already high (>145mmol/l) :

- Don't restrict the water (to avoid hypernatremia).
- Measure plasma and urine osmolality and skip to demopressin administration.

Management

If the serum NA+ is in the normal level:

- First : restrict the water/fluid intake.
- Then measure plasma osmolality urine osmolality & Serum Na+ every 2 Hours



Central DI:

1. **Desmopressin (synthetic ADH analog):**

- Is the primary therapy for DI.
- It has the anti-diuritic effect of the ADH without the vasoconstrictive effect .
- It can be given intranasally (most potent) , orally, or by injection.
- start with a low dose to avoid overcorrection .

2. **Treat the underlying cause.**

Management

Nephrogenic DI:

1. **Thiazide Diuretics:**

- The induction of mild volume depletion with a low-sodium diet plus the thiazide diuretic (such as hydrochlorothiazide)is a first-line therapy in AVP-R .
- Thiazide diuretics inhibit the sodium-chloride co-transporter in the distal convoluted tubule.
- By blocking sodium reabsorption, they cause increased sodium (and accompanying water) to remain in the urine.
- The decrease in sodium reabsorption results in a reduction of extracellular fluid volume.
- This triggers compensatory water reabsorption in the proximal tubule despite the ineffective action of ADH.

Management

Nephrogenic DI:

2. **NSAIDs like ibuprofen or indomethacin: :**

- They increase urinary concentrating ability by inhibiting the renal synthesis of prostaglandins, which are ADH antagonists and increases the antidiuretic effect of a submaximal dose of ADH.
- In paitents with renal disease , NSAIDs must be used with caution because of the potential nephrotoxic effects.

3. **Amiloride:**

- May be particularly beneficial in patients with reversible lithium nephrotoxicity.

Management

Gestational DI:

- **Desmopressin**.

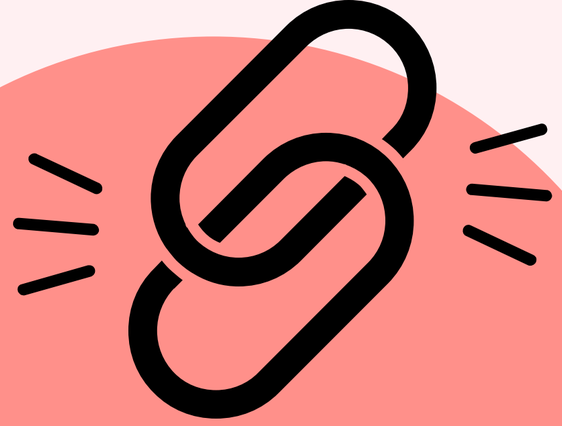
Diposogenic DI:

- **Behavioral therapy**

Question

A 70-year-old Japanese woman developed T2D with hyperglycemia symptoms, including thirst, polydipsia, and polyuria. After starting medical treatment, the hyperglycemia and its symptoms improved. The glycated hemoglobin level decreased from 9% to 6%. However, 5 years later (at 75 years of age), she re-exhibited thirst, polydipsia, and polyuria despite stable glycemic control. Her urine volume was large (6.3 L/day). A urine glucose test was negative. The plasma osmolality was high (321 mOsm/kg), while the urinary osmolality was low (125 mOsm/kg). A significant increase in urinary osmolality following vasopressin administration.

Reference



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Thank
you