



ENDOCRINE BLOCK

LECTURE 5

Diabetes Insipidus (ID)



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OBJECTIVES

Not Given :|

■ Slides

■ Important

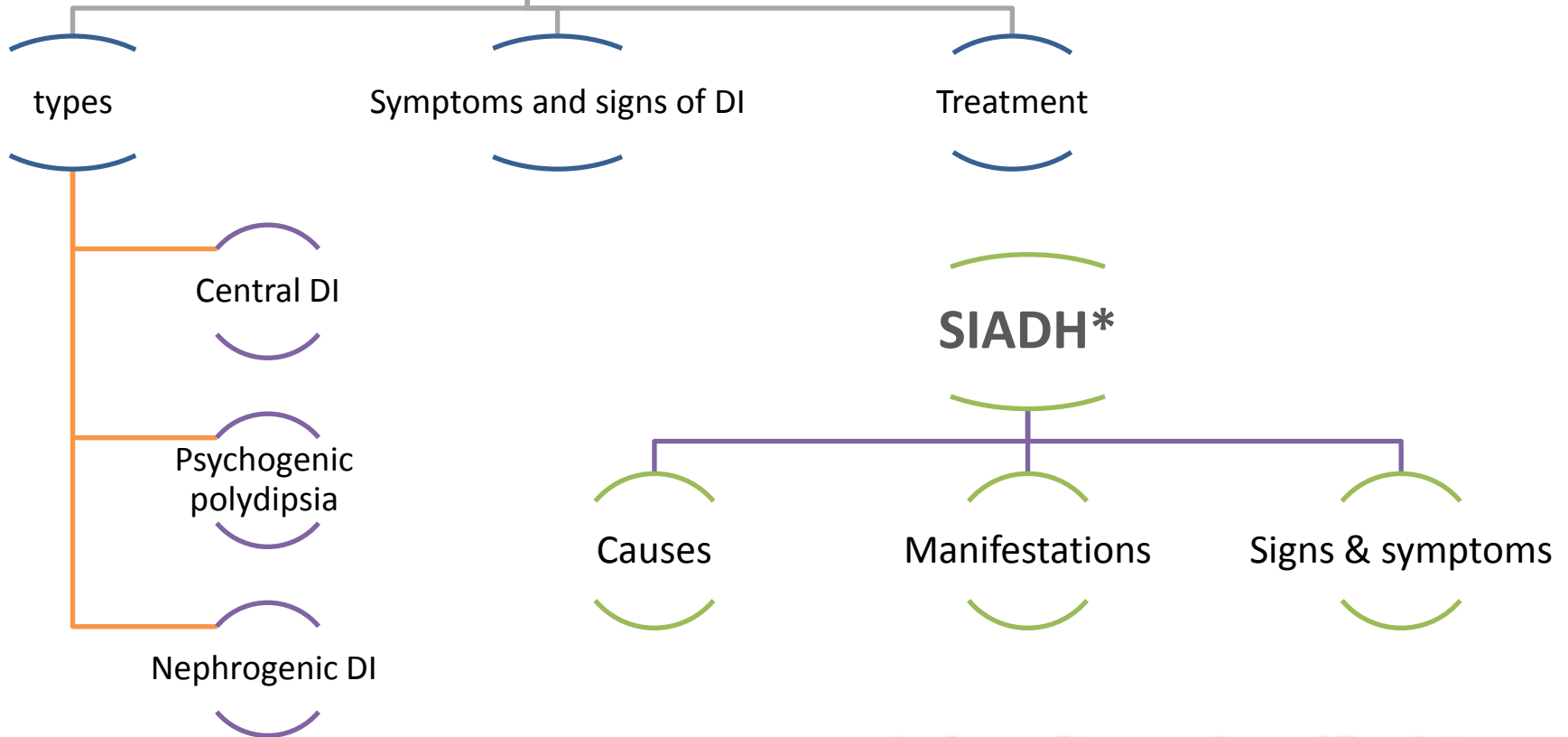
■ Females' Notes

■ Explanation

■ Males' Notes



Diabetes Insipidus



*Syndrome of Inappropriate antidiuretic Hormone



DI is a disorder resulting from deficiency of anti-diuretic hormone (ADH) or its action and is characterized by the passage of **copious amounts of dilute urine**.

It must be differentiated from other polyuric states such as primary polydipsia & osmotic diuresis.

Polydipsia:
Excessive or abnormal thirst

Types of DI:

Central DI	Nephrogenic DI	Psychogenic polydipsia
Failure of the pituitary gland to secrete adequate ADH. -Defect in hypothalamus. -Defect in pituitary stalk. -Defect in posterior pituitary. Related to the synthesis, transmission or the storage.	When the renal tubules of the kidneys fail to respond to circulating ADH. ADH is there (enough) but the problem is with its action or kidney is defective.	Physiological ADH inhibition It doesn't release the amount that it should be. So, the kidney will be unable to retain water, results in Polyuria.



Causes of DI:

1- Central DI (most common)	2- Nephrogenic DI
<ul style="list-style-type: none"> <input type="checkbox"/> Brain tumors or infections: Lung cancer, leukemia, lymphoma most common <input type="checkbox"/> Head trauma e.g. in car accident <input type="checkbox"/> Post-neurosurgery <input type="checkbox"/> Idiopathic – 30-50% Pituitary atrophy, possible autoimmune <input type="checkbox"/> Congenital: Mutations of ADH gene, usually autosomal dominant <p>-Infiltrative diseases, such as histiocytosis X or sarcoidosis.</p> <p>(Sort of error in metabolism then it is infiltrated anywhere and can affect the hypothalamus or hypothalamic secreting cells of ADH)</p>	<ul style="list-style-type: none"> <input type="checkbox"/> Acquired: <ul style="list-style-type: none"> • Drugs: lithium, amphotericin, gentamicin, loop diuretics. • Electrolyte disorders: hypercalcemia, hypokalemia. • Renal dz: obstructive uropathy, chronic renal failure (because the kidney has lost the ability to concentrate urine), polycystic kidney, Post-transplant, pyelonephritis. • Systemic processes: sarcoid, amyloid, multiple myeloma, sickle cell disease, pregnancy. <input type="checkbox"/> Congenital – rare: <ul style="list-style-type: none"> • Present in 1st week of life. • <u>V2 ADH receptor defect</u> – X-linked recessive. • <u>AQP2 (Aquaporin2)</u> water channel defect – will respond to ADH.
3- Psychogenic polydipsia	



Psychogenic Polydipsia :

- In this condition the person has psychological urge (strong desire) to drink much water though he doesn't need it.
- He has normal ADH secretion & normal kidney response to ADH, but the patient has psychiatric disturbance that produces urges to drink large amounts of water.
- Urine has large volume and it is dilute.
- However, if you deprive this person of water → urine volume decreases & urine osmolarity increases (urine becomes more concentrated).
- Subject shows normal response to water restriction.



Symptoms and signs of DI:

1. Polyuria > 3 liters in 24 hrs.
2. Sudden onset more typical of central DI.
3. Nocturia (the complaint that brings the patient to the clinic).
4. Polydipsia (If the thirst center is damaged, they will die because they don't sense the desire that they should drink water).
5. Dilute urine, urine osm < 200 . (Patient will notice color change. Pale transparent urine instead of yellowish).
6. Anorexia, constipation
7. Serum Na > 150 , rare if free access to H₂O.
8. Dehydration when access to water limited (if the problem is in hypothalamus).
9. Hyperthermia & lack of sweating (hypothermia may occur in shock).
10. Diabetes insipidus can cause dehydration which can cause:
 - Dry mouth. Muscle weakness (because of loss of energy).
 - Hypotension (low blood pressure). Sunken appearance of the eyes.
 - Rapid heart rate. Weight loss.



11. Diabetes insipidus can also cause an electrolyte imbalance
 - Hyponatremia
 - Hyperchloremia
12. Electrolyte imbalance can cause
 - Headache
 - Fatigue
 - Irritability and muscle pains
13. Seizure secondary to Hyponatremia can happen

Treatment:

- **Desmopressin**
 - Desamino-desarginino-vasopressin (DDAVP)
 - V₂-selective analogue
 - Little V₁ (vasoconstrictor) activity
 - Drug of choice in Diabetes insipidus
- **Administration:**
 - Oral, sub-cut, nasal spray



- ✓ **Diabetes insipidus (DI) is a condition where the person:**
 - Passes large amounts of urine (polyuria).
 - Urine is dilute (has very low Specific Gravity) & does not contain sugar.
 - Feels thirsty most of the time.
 - Drinks excessive amounts of water (polydipsia).

- ✓ **Signs of hypovolemia (decreased ECF volume) & dehydration such as:**
 - Poor skin turgor & dryness of the skin & mucous membranes.
 - Small (weak), rapid pulse (tachycardia).
 - Hypotension (fall in BP).

- ✓ **Haemoconcentration & increased plasma osmolarity .**
- ✓ **If treatment is delayed,** increased body temperature & hyperthermia.
- ✓ **If we decrease the patient's water intake,** his urine output does not decrease → patient can not produce ADH in response to decreased ECF volume.
- ✓ **If left untreated,** diabetes insipidus can result in severe dehydration, shock and death.



Other conditions:

- ✓ Other conditions that also manifest polydipsia and should not be confused with DI are:
 - Psychogenic Polydipsia.
 - Diabetes mellitus.
- ✓ ID differs from diabetes mellitus in that:
 - Urine is dilute.
 - Urine does not contain sugar (no glycosuria).
 - Blood sugar is normal.
- ✓ Reduction of fluid intake does not change urine concentration.



Management:

- Strict measurement & recording of fluid intake & urine output + urine specific gravity & testing and osmolarity testing hourly in the early stages.
- Recording the pulse and BP hourly in the early stages, to detect early any signs of shock.
- Vasopressin test → If desired, Vasopressin can be injected subcutaneously → if urine output decreases → this is not nephrogenic DI.
- Pitressin (aqueous vasopressin) can be used for treatment.



(SIADH) :

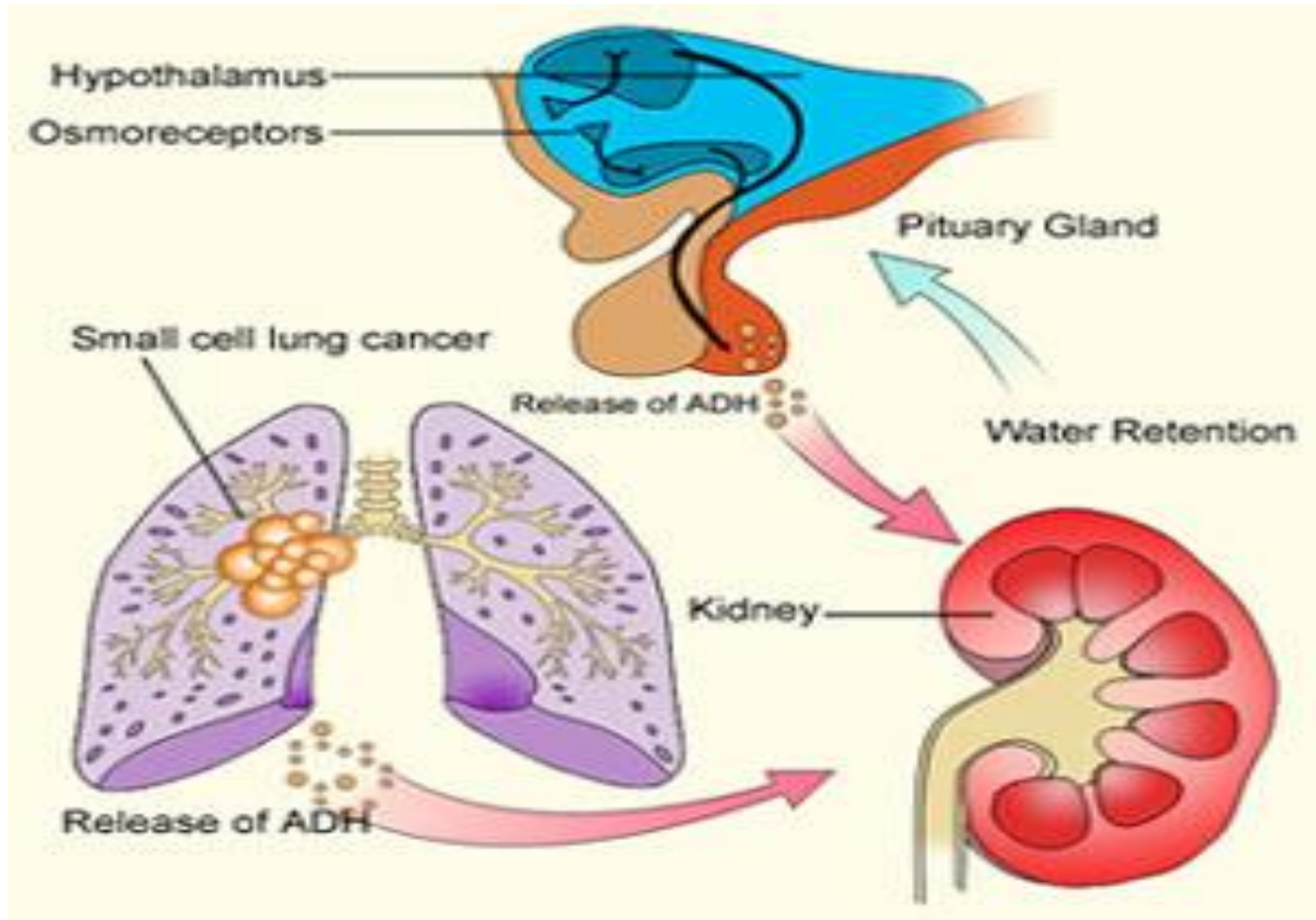
- The syndrome of inappropriate secretion of ADH (SIADH) is characterized by :
 - Non-physiologic release of ADH
 - Impaired water excretion with **normal** sodium excretion (**dilutional hyponatremia**).
- SIADH is associated with disease that affect **osmoreceptors** in the hypothalamus.

Causes:

- **Cancer** :Many tumours. Most common is small cell cancer of the lung (**oat cell carcinoma of the lung**)
- **Brain** : Meningitis ,Cerebral abscess ,Head injury,Tumors
- **Lung** :pneumonia (**severe stress**) ,Tuberculosis, lung abscess
- **Metabolic**
- **Drugs**



Syndrome of Inappropriate antidiuretic Hormone





Manifestations:

- Fluid retention
- Serum hypo-osmolarity
- Dilutional hyponatraemia
- Hypochloremia
- Concentrated urine in the presence of normal or increased intravascular volume
- **Normal renal function**

❖ Hyponatraemia and hypo-osmolarity lead to acute edema of the brain cells.

(If there is a tumor (oat cell) secretes ADH, it will increase water absorption by the kidney.

Normally ADH which is secreted by posterior pituitary is under negative feed back by the drop of serum osmolarity. But the tumor secretes excessive ADH (inappropriately) without negative feed back, so excessive water distributes throughout total body water. As water flowed into the cells (intracellular fluid ICF), their volume is increased → brain cells swelling occur .. It might end up by coma and death.

❖ An increase in brain water content of more than 5-10% is incompatible with life.



Symptoms and signs:

- Headache.
- Nausea.
- Vomiting .
- Impaired consciousness.
- Neurological signs (severe hyponatraemia):
 - Drowsiness.
 - Disorientation.
 - Delirium.
 - Seizures.
- Coma & death (severe cases).

- (SIADH) is treated with an ADH antagonist Or water restriction.
- There is no edema why ? Because it is dilutional hyponatremia lead to increase ICF rather than ECF.



DIABETES INSIPIDUS



SIADH & DI



PROBLEMS WITH ADH



- DI results from deficiency in ADH secretion or in its action :

Central DI	Nephrogenic DI
Posterior pituitary fail to secrete ADH	Renal tubule fail to respond to ADH
Large volume diluted urine	
Increase serum osmolarity	
Low ADH	Elevated ADH (high osmolarity stimulates its secretion)
- Treated with an ADH analogue (desmopressin) - Mostly as nasal spray	- Treated with thiazide diuretic
- It can be caused by: tumors, trauma, post surgery, infiltrative disease, congenital, idiopathic.	- Acquired (electrolyte disorder, drugs, renal diseases). - Congenital (V2 receptor defect).

Signs and symptoms of ID:

Polyuria, nocturia, polydipsia, dehydration, constipation, hyperthermia, electrolyte imbalance, seizures.

❑ (SIADH):

- Inappropriate secretion of ADH
- Impair water excretion with normal Na excretion.

❑ Causes:

- Tumors (oat cell of the lung).
- Brain (meningitis, abscess, tumor, injury).
- Lung (pneumonia, TB).
- Metabolic and Drugs.

❑ Manifestations and symptoms:

- Fluid retention, hyponatremia and concentrated urine.
- Headache, vomiting, neurological signs, coma & death.

1. Treatment of nephrogenic DI ??

- A) ADH antagonist
- B) ADH analogue
- C) Thiazides diuretics

2. Regarding syndrome of inappropriate secretion of ADH (SIADH) ??

- A) low level of ADH
- B) serum hyperosmolarity and diluted urine
- C) could be caused by oat cell carcinoma (small cell cancer of the lung)

3. What electrolyte abnormalities can cause diabetes insipidus ??

- A) Hypercalcemia and hyperkalemia
- B) Hypercalcemia and hypokalemia
- C) Hypocalcemia and hyperkalemia
- D) Hypocalcemia and hypokalemia

4. The drug of choice for central diabetes insipidus is desmopressin. Mechanism of action of it is to ??

- A) Block vasopressin and increases kidney salt excretion.
- B) Mimic vasopressin and increases kidney salt excretion.
- C) Mimic vasopressin and increases kidney water reabsorption.

5. Dehydrated patient with Diabetes insipidus can present with all of the following except ??

- A) Dry mouth.
- B) Weight gain.
- C) Sunken appearance of the eyes.
- D) Muscle weakness.



THE END

If there are any Problems or Suggestions,
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THANK YOU



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ANY OTHER SUBJECT .. YOU CAN MENTION THIS ACCOUNT **@MED432**

Actions Speak Louder Than Words