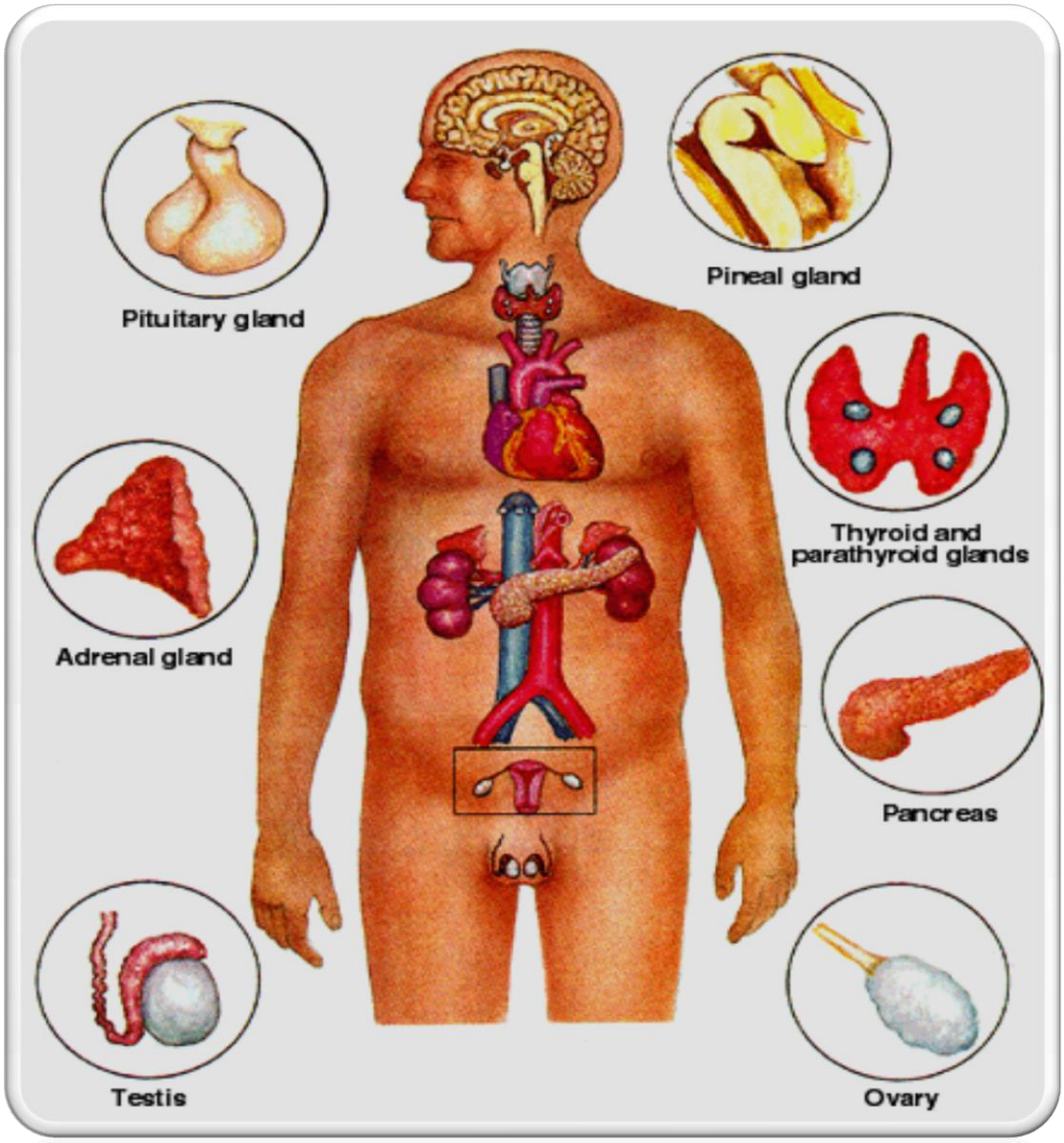
ENDOCRINE BLOCK

PHYSIOLOGY TEAM 431



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Diabetes insipidus

Objectives:

- Types and causes of DI
  - Central
  - Nephrogenic DI
- Symptoms and signs of DI

What is Diabetes insipidus (DI)?

Diabetes insipidus is a disorder resulting from deficiency of anti-diuretic hormone (ADH) or its action and is characterized by (1) the passage of copious amounts of dilute urine, **(2) Feels thirsty most of the time, (3) drinks excessive amounts of water (polydipsia)**

It must be differentiated from other polyuric states such as primary polydipsia & osmotic dieresis (DM).

Deficiency in action here includes: deficiency in receptors, second messenger, Proteins involved and aquaporin.

Polydipsia: Excessive or abnormal thirst.

Diabetes insipidus (DI)	Diabetes Miletus
NO excess sugar, cause for this disease is different	There is sugar in urine
Urine is dilute **Reduction of fluid intake does not change urine concentration**	
Excessive urination	

Types of DI

- **Central DI** (Defect in the production process) is due to failure of the pituitary gland to secrete adequate ADH:
  - Defect in hypothalamus.
  - Defect in pituitary stalk.
  - Defect in posterior pituitary.
- **Nephrogenic DI** (Defect in the kidney) results when the renal tubules of the kidneys fail to respond to circulating ADH.
- **Psychogenic (primary) polydipsia**
  - Physiological ADH inhibition.

With excessive thirst there is increase in water intake → the osmolarity will decrease → cause ADH inhibition.

CAUSES OF CENTRAL(cranial) DI "the most common type of DI"

- Idiopathic – 30-50%.
  - Pituitary atrophy, possible autoimmune.
- Brain tumors primary or secondary.
  - Secondary (Lung cancer, leukemia, lymphoma most common).
- Head trauma.
- Post-neurosurgery.
- Congenital.
  - Mutations of ADH gene, usually autosomal dominant.
- Infiltrative diseases, such as Histiocytosis X or sarcoidosis.
- Infection (meningitis).

Histiocytosis: Any of several abnormal conditions characterized by the appearance of histiocytes in the blood or tissues.

Sarcoidosis: A disease of unknown origin characterized by the formation of granulomatous lesions that appear especially in the liver, lungs, skin, and lymph nodes. Also called *sarcoid*.

CAUSES OF NEPHROGENIC DI

- Acquired
  - Drugs: lithium, amphotericin, gentamicin, loop diuretics.
  - Electrolyte disorders: hypercalcemia, hypokalemia ← Damage the kidney.
  - Renal diseases: obstructive uropathy, chronic renal failure , polysystic kidney ← causes back flow to the kidney then damage it, post-transplant, pyelonephritis .
  - Systemic processes: sarcoid, amyloid, multiple myeloma, sickle cell disease.
  - **Gestational diabetes insipidus** occurs only during pregnancy when an enzyme (*vasopressinase*) made by the placenta destroys ADH in the mother. ←The cause of DI here is not deficiency; it is over destruction of ADH.
- Congenital – rare.
  - Present in 1st week of life (mother notices that the baby urinate a lot).
  - V2 ADH receptor defect –> X-linked recessive.
  - AQP2 water channel defect.

Symptoms and signs of DI Important

- Polyuria > 3 liters in 24 hrs.
  - Sudden onset more typical of central DI.
- Nocturia cause disturbance of sleep.
- Polydipsia.
- Dilute urine (has very low specific gravity), urine osm < 200 (Patient will notice color change. Pale transparent urine instead of yellowish).
- Anorexia, constipation → due to loss of water with urine.
- Serum Na >150 (cause of loss of water) rare with free access to H2o (like in desert or water deprived people)
- Dehydration with limited access to water.
- Hyperthermia → due to dehydration & lack of sweating → patient does not have enough water to produce sweat.
- Diabetes insipidus can cause dehydration, which can cause: (symptoms of DI secondary to dehydration and hypovolemia).
  - Dry mouth, Skin & mucous membranes
  - Muscle weakness.
  - Hypotension (low blood pressure).
  - Sunken appearance of the eyes.
  - Poor skin turgor(Loss of skin elasticity)
  - Small (weak), Rapid pulse (tachycardia)
- Haemoconcentration & increased plasma osmolarity
- Rapid heart rate.
- Weight loss.
- Diabetes insipidus can also cause an electrolyte imbalance.
  - Hypernatremia.
  - Hyperchloremia.
- Electrolyte imbalance can cause.
  - Headache.
  - Fatigue.
  - Irritability and muscle pains.

Dehydration is present in DI patient due to water loss in urine but not extreme due to access to water.

The signs of dehydration are strongly noted in patient with limited access to water.

- Seizure secondary to Hypernatremia can happen.

Management:

- Strict measurement & recording of fluid intake & urine output + Urine specific gravity & 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

We measure fluid intake, because of incase that you give fluid more than needed (overhydration), Heart failure might of overload.

Treatment (the treatment mentioned here is for DI caused by ADH deficiency not by defect in its action like defect in receptors)

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

Psychogenic polydipsia

- In this condition the person has psychologic urge 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 & 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

Questions

1. Symptoms for DI include:
    a. Dehydration.
    b. Polyuria.
    c. A and B.
    d. Skin pigmentation.

2. Electrolyte imbalance can cause:
    a. Abdominal rigidity.
    b. Headache.
    c. Muscle hypertonia
    d. Non of above

Answers: 1→C , 2→ B