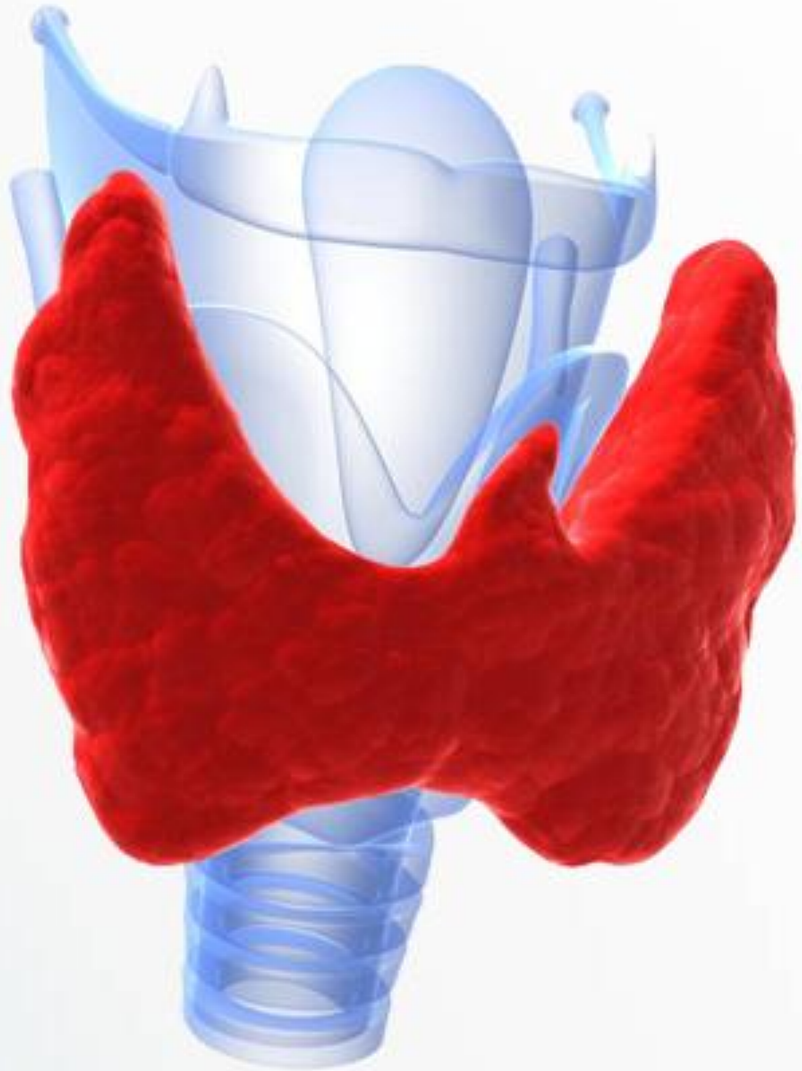
Physiology team



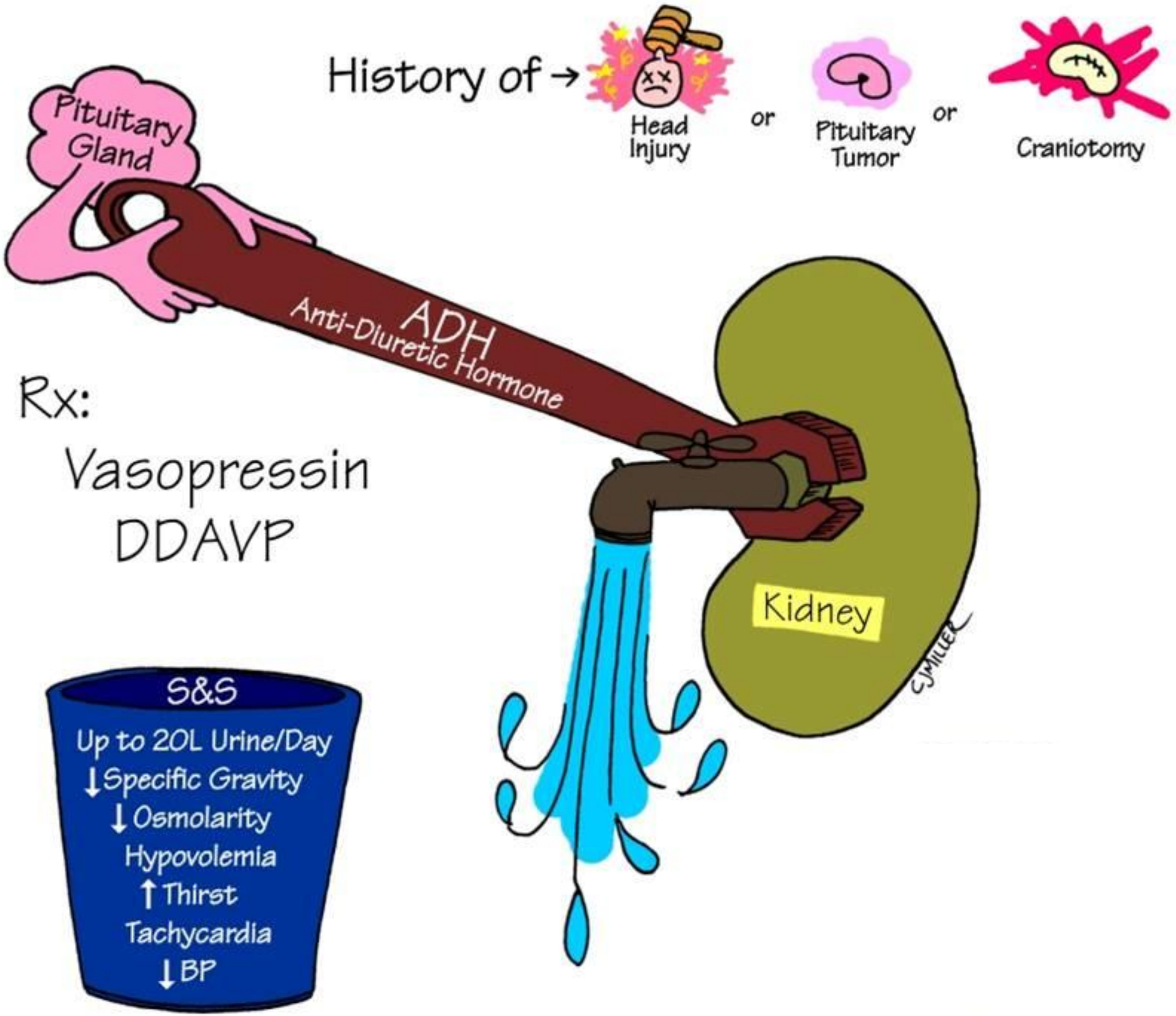
5 Diabetes insipidus

Sources:
Female's slides
GUYTON P354

Objectives

1. **Types and causes of DI**
    i. **Central**
    ii. **Nephrogenic DI**
2. **Symptoms and signs of DI**
3. **Syndrome of inappropriate ADH secretion**

DIABETES INSIPIDUS



Diabetes insipidus:

- It Is a disorder resulting from deficiency of anti-diuretic hormone (ADH) or its action.
- It’s characterized by passage of copious amount of diluted urine
- It must be differentiated from other polyuric states such as primary polydipsia & osmotic duiresis, diabetes mellitus.

Types of Diabetes insipidus

1. Central DI

is due to failure of the pituitary gland to secrete adequate ADH. The defect either in hypothalamus or in pituitary stalk or in posterior pituitary

2. Nephrogenic DI

the renal tubules do not response to the ADH (or due failure from tubules to form hyperosmotic renal interstitium)

3. Psychogenic polydipsia

excessive thirst due to psychogenic problem results in ADH inhibition.

Causes of Diabetes insipidus

Centeral	Nephrogenic
Tumors (Brain tumors, metastasized Lung cancer, leukemia, lymphoma which is the most common)	**Drugs:** lithium, amphotericin, gentamycin, loop diuretics & tetracycline
Head trauma	**Electrolyte disorders:** hypercalcemia, hypokalemia
Post-neurosurgery	**Renal:** obstructive uropathy, chronic renal failure, polycystic kidney, post-transplant, pyelonephritis.
Idiopathic 30-50% (Pituitary atrophy or auto-immune)	**Systemic processes:** sarcoidm amyloid, multiple myeloma, sickle cell, pregnancy
Congenital (mutations of ADH gene which is usually autosomal dominant)	**Congenital:** * Present in 1st week of life. * V2 ADH receptor defect (X-linked recessive) * AQP2 water channel defect – will respond to ADH
Infiltrative disease e.g. sarcoidosis	

Treatment:

Desmopressin (Desamino-desarginino-vasopressin), which is V2-selective analogue and it has little vasoconstrictor activity. It is the drug of chioce in case of central Diabetes insipidus (no effect in nephrogenic DI).

Diabetes insipidus sign and symptoms:

- Polyuria > 3 liters in 24 hrs
  - Sudden onset more typical of central DI
  - Nocturia
- Polydipsia (excessive thirst)
- Dilute urine (urine osmolality < 200, low specific gravity urine).
- Anorexia.

Diabetes insipidus complications:

1. **dehydration** which can lead to:
   - Dry mouth
   - Muscle weakness
   - Hypotension (low blood pressure)
   - Rapid heart rate
   - Weight loss

2. **Electrolyte imbalance**. Which leads to
   - Hypernatremia
   - Hyperchloremia
   - Electrolyte imbalance can cause:
     - **Headache**
     - **Fatigue**
   - Irritability and muscle pains
   - Seizure secondary to Hypernatremia can happen

The syndrome of inappropriate secretion of ADH (SIADH)

Non-physiologic release of ADH

Impaired water excretion with normal sodium excretion

SIADH is associated with disease that affect osmoreceptor in the hypothalamus

Symptoms:

- Headache, nausea & vomiting
- Impaired consciousness & neurological signs (due to severe hyponatraemia) like drowsiness, disorientation, delirium & seizures
- Coma & death (severe cases)

Causes:

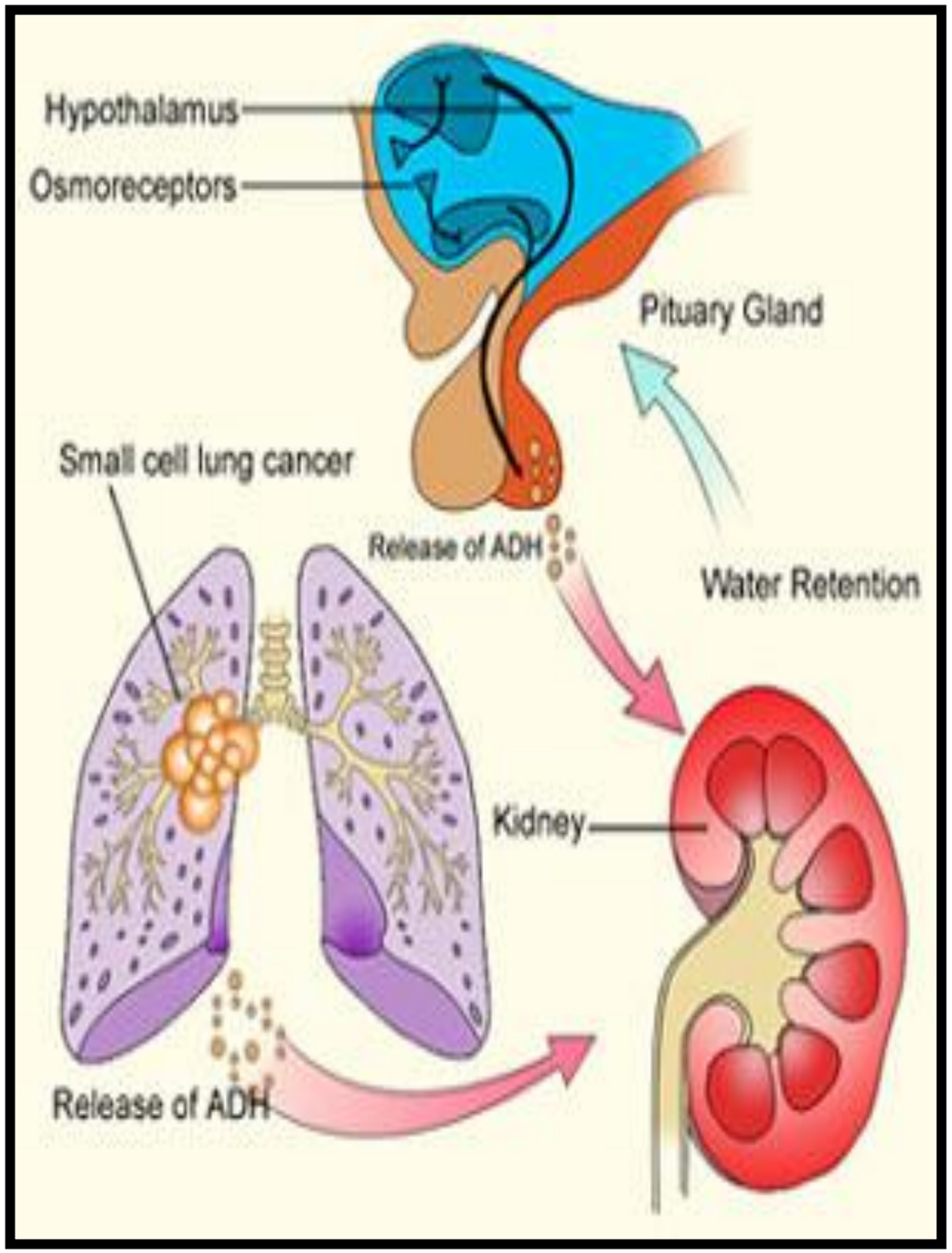
- Tumors (Most common is small cell cancer of the lung)
- Brain (Meningitis, cerebral abscess & head injury)
- Lung (pneumonia, tuberculosis & lung abscess)
- Metabolic disorder
- Drugs

Pathophysiology:

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

(SIADH)



Summery

Diabetes insipidus	Characterized by intense thirst and polyuria with inability to concentrate urine due to lack of ADH. Has a central or nephrogenic cause.	
	Central DI	**Nephrogenic DI**
ETIOLOGY	Pituitary tumor, autoimmune, trauma, surgery, ischemic encephalopathy, idiopathic	Hereditary (ADH receptor mutation), 2° to hypercalcemia, lithium, demeclocycline (ADH antagonist)
FINDINGS	↓ ADH Urine specific gravity < 1.006 Serum osmolarity > 290 mOsm/L Hyperosmotic volume contraction	Normal ADH levels Urine specific gravity < 1.006 Serum osmolarity > 290 mOsm/L Hyperosmotic volume contraction
DIAGNOSIS	Water restriction test[a]: > 50% ↑ in urine osmolarity	Water restriction test: no change in urine osmolarity
TREATMENT	Intranasal DDAVP Hydration	HCTZ, indomethacin, amiloride Hydration

[a]No water intake for 2–3 hr followed by hourly measurements of urine volume and osmolarity and plasma Na^+ concentration and osmolarity. DDAVP (ADH analog) is administered if normal values are not clearly reached.

Summery

SIADH

Syndrome of inappropriate antidiuretic hormone secretion:
- Excessive water retention
- Hyponatremia with continued urinary Na^+ excretion
- Urine osmolarity > serum osmolarity

Body responds to water retention with ↓ aldosterone (hyponatremia) to maintain near-normal volume status. Very low serum sodium levels can lead to cerebral edema, seizures. Correct slowly to prevent central pontine myelinolysis.

Causes include:
- Ectopic ADH (small cell lung cancer)
- CNS disorders/head trauma
- Pulmonary disease
- Drugs (e.g., cyclophosphamide)

Treatment: fluid restriction, IV hypertonic saline, conivaptan, tolvaptan, demeclocycline.

table 5-6 Summary of ADH Pathophysiology

	Serum ADH	Serum Osmolarity/ Serum [Na^+]	Urine Osmolarity	Urine Flow Rate	C_{H_2O}
Primary polydipsia	↓	Decreased	Hyposmotic	High	Positive
Central diabetes insipidus	↓	Increased (because of excretion of too much H_2O)	Hyposmotic	High	Positive
Nephrogenic diabetes insipidus	↑ (because of increased plasma osmolarity)	Increased (because of excretion of too much H_2O)	Hyposmotic	High	Positive
Water deprivation	↑	High–normal	Hyperosmotic	Low	Negative
SIADH	↑↑	Decreased (because of reabsorption of too much H_2O)	Hyperosmotic	Low	Negative

ADH = antidiuretic hormone; C_{H_2O} = free-water clearance; SIADH = syndrome of inappropriate antidiuretic hormone.

MCQs

1. A patient present with polyuria (> 15L/day). From history he car accident and he underwent a major operation in his head. The GP noticed his urine backs to normal after a dose of desmopressin. What is the most likely diagnosis?

A. The syndrome of inappropriate secretion of ADH
B. Central diabetes insipidus
C. Nephrogenic diabetes insipidus
D. B & c are both true.

2. From previous question, which of the following complication could be seen in his condition (as a result of dehydration)?

A. Hypertension
B. Tachypnea
C. Weight gain
D. Muscle ache

3. Nurse develop a teaching plan for a male client diagnosed with diabetes insipidus. The nurse should include information about which hormone lacking in clients with diabetes insipidus?

A. antidiuretic hormone (ADH).
B. thyroid-stimulating hormone (TSH).
C. follicle-stimulating hormone (FSH).
D. luteinizing hormone (LH)

1-B 2-D 3-A

MCQs

4- Adequate fluid replacement and vasopressin replacement are objectives of therapy for which of the following disease processes?

A. Diabetes mellitus.
B. Diabetes insipidus.
C. Diabetic ketoacidosis.
D. Syndrome of inappropriate antidiuretic hormone secretion (SIADH)

5-Damage to what organ would cause central diabetes insipidus?

A. Kidneys
B. Thyroid
C. Hypothalamus
D. Parathyroid

6- 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.

7- Electrolyte imbalance can cause?

A.. Fatigue .
B. Abdominal rigidity.
C. Muscle hypertonia.
D. Non of above.

4-B 5-C 6-B 7-A

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