



Round : Internal medicine.....

Group no : A4.....

Done By : Batool ALzubaidi.....



DIABETES INSIPIDUS & SIADH

I. PATHOPHYSIOLOGY

A. DIABETES INSIPIDUS (DI)

B. SYNDROME OF INAPPROPRIATE ADH (SIADH)

II. COMPLICATIONS OF DI AND SIADH

A. DIABETES INSIPIDUS (DI)

B. SYNDROME OF INAPPROPRIATE ADH (SIADH)

III. DIAGNOSTIC APPROACH TO DI & SIADH

A. DIABETES INSIPIDUS (DI)

B. SYNDROME OF INAPPROPRIATE ADH (SIADH)

IV. TREATMENT OF DI AND SIADH

A. DIABETES INSIPIDUS (DI)

B. SYNDROME OF INAPPROPRIATE ADH (SIADH)

00:44

I. PATHOPHYSIOLOGY

A. DIABETES INSIPIDUS (DI)

00:44

1. Pathophysiology:

Central DI

- Hypothalamic-posterior pituitary dysfunction →

↓ ADH production →

↓ H₂O reabsorption at the collecting duct**Nephrogenic DI**

- Normal ADH production but ADH receptor dysfunction →

Inadequate ADH response →

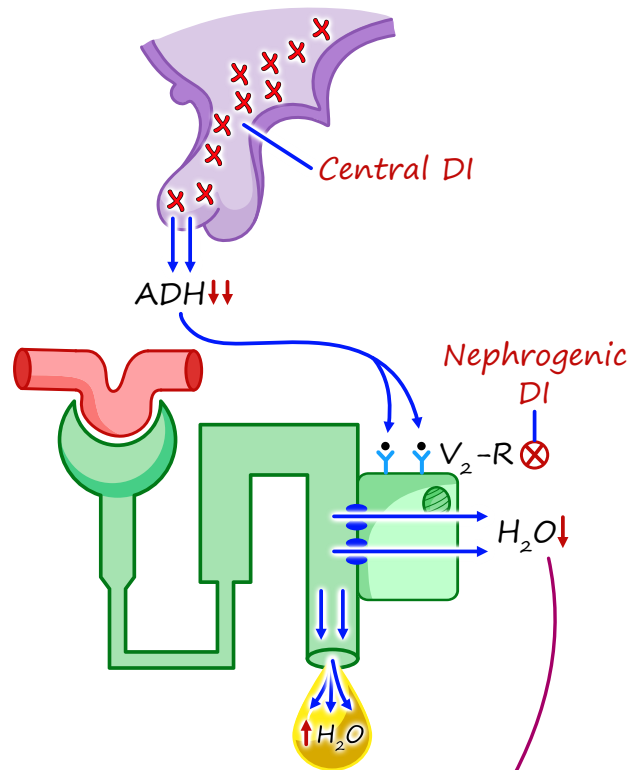
↓ H₂O reabsorption at the collecting duct

Normally ADH goes to the kidneys and works on V₂ receptors and bind to them » to express a protein on the luminal surface called aquaporins » to help move the water from the collecting duct tubules into the bloodstream

ADH is responsible for the activation of this process

Even if ADH is present in normal amounts, the V₂ receptors won't respond » water reabsorption will be reduced » polyuria

Diabetes Insipidus (DI)



When ADH level is reduced » water reabsorption is reduced » tons of water will be lost in the urine » profound polyuria



2. Causes of Diabetes Insipidus:

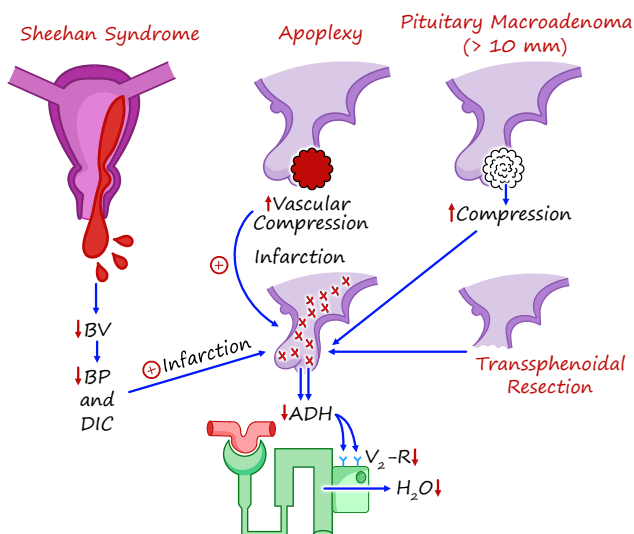
a) Central DI

04:29

Hypothalamic-Pituitary Dysfunction

- **Pituitary Apoplexy**
 - **Pituitary adenoma hemorrhages** → Vascular compression of the pituitary vessels → ↓ Pituitary perfusion → Pituitary infarction → ↓ Release of pituitary hormones such as ADH
 - Assess for a history of mass effect features:
 - **Bitemporal hemianopia**
 - Due to compression of the optic chiasma → Loss of lateral temporal visual fields
 - **Secondary Headache**
- **Sheehan Syndrome**
 - **Postpartum hemorrhage** → Massive blood loss → hypotension and DIC → ↓ Pituitary perfusion → Pituitary infarction → ↓ Release of hormones such as ADH
 - Assess for a patient with recent postpartum hemorrhage with > 1 L blood loss or hypotension within 24 hours
- **Craniopharyngioma**
 - **A tumor that arises from the nasopharynx in children (e.g. Rathke's Pouch)** → Migrates to the vicinity of the pituitary gland → Compression of the pituitary and pituitary stalk → ↓ Release of hormones such as ADH
 - Assess for a history of mass effect features:
 - **Bitemporal Hemianopia**
 - Due to compression of the optic chiasma → Loss of lateral temporal visual fields
 - **Secondary Headache**
- **Pituitary removal**
 - **Transsphenoidal pituitary resection** → Loss of pituitary tissue → ↓ Release of pituitary hormones such as ADH
 - Assess for a prior history of surgery on or near the pituitary gland

Central DI



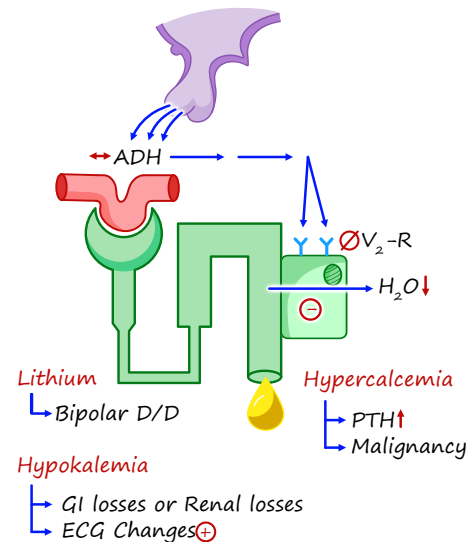
b) Nephrogenic DI

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ADH Receptor Dysfunction

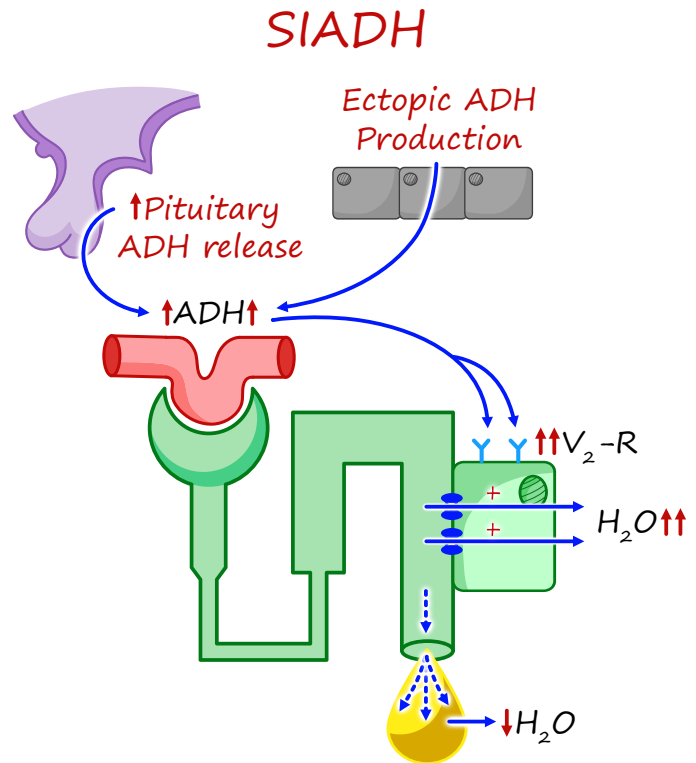
- **Lithium use**
 - Assess for a history of bipolar disorder
- **Hypercalcemia**
 - Assess for the history of hyperparathyroidism or malignancy along with findings of nephrolithiasis, Osteoporosis with pathological fractures, pancreatitis, and ↓ QT-I
- **Hypokalemia**
 - Assess for the history of vomiting or diarrhea or diuretic use alongside ECG changes like T-wave inversion, U-waves, and ↑ QT-I

Nephrogenic DI



1. Pathophysiology:

- **↑Pituitary ADH Release**
 - Hypothalamic-posterior pituitary dysfunction →
 - ↑ADH production →
 - ↑H₂O reabsorption at the collecting duct
- **Ectopic ADH Production**
 - Neoplasm with ADH-producing capabilities →
 - ↑ADH production →
 - ↑H₂O reabsorption at the collecting duct



2. Causes of SIADH:

a) ↑Pituitary ADH release

i) Intracranial disease

- **Stroke, Traumatic brain injury (TBI), or Brain tumors** →
- Stimulate the pituitary → ↑ADH production
- Assess for any neurological deficits or recent head injury

ii) Pulmonary disease

- **COPD, PNA, Intubated patients**
- Stimulate the pituitary → ↑ADH production
- Assess for any underlying lung disease or hypoxia

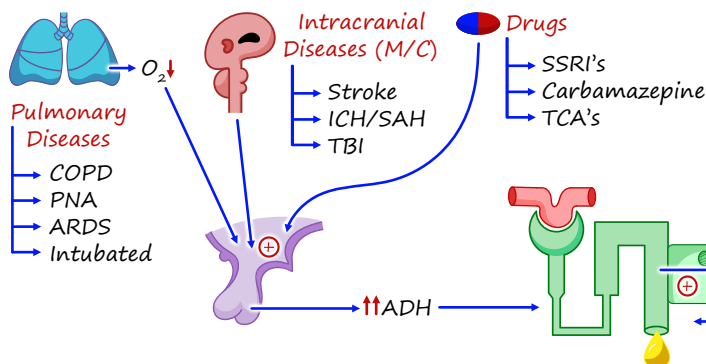
iii) Drugs

- **SSRIs or carbamazepine** →
- Stimulate the pituitary → ↑ADH production
- Assess medication history

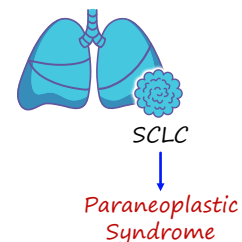
b) Ectopic ADH production

- **Small cell lung cancer (SCLC)** →
- Develop paraneoplastic syndrome →
- Tumors produce ADH → ↑ADH production
- Assess for cough, weight loss, or hemoptysis

↑Pituitary ADH Release



Ectopic ADH Production



A. DIABETES INSIPIDUS (DI)

20:41

Hypernatremia

• Pathophysiology:

- ↓ADH production (e.g. central DI) or
↓ADH response (e.g. nephrogenic DI) →
↓H₂O reabsorption at the collecting duct →
↓Water in the bloodstream → ↑Na⁺ in the
bloodstream

• Presentation:

◦ Polyuria

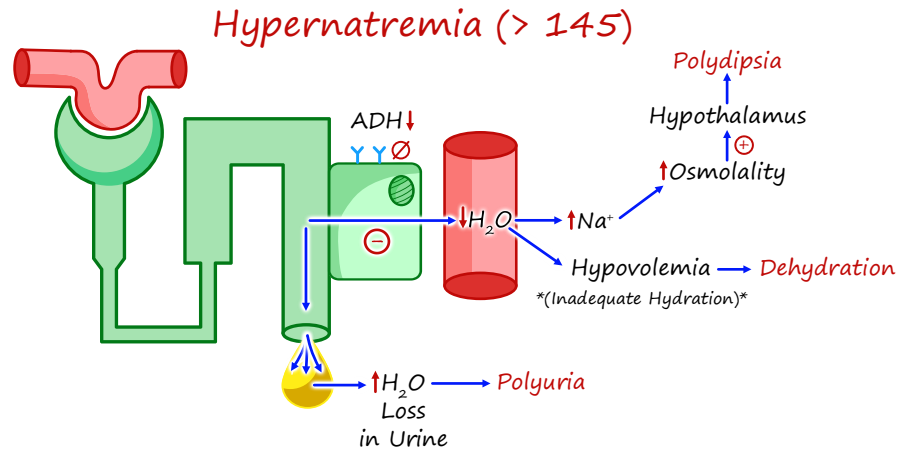
- ↓ADH production (e.g. central DI) or
↓ADH response (e.g. nephrogenic DI) →
↓H₂O reabsorption at the collecting duct →
↑H₂O loss in the urine

◦ Polydipsia

- ↓ADH production (e.g. central DI) or
↓ADH response (e.g. nephrogenic DI) →
↓H₂O reabsorption at the collecting duct →
↓Water in the bloodstream → ↑Serum osmolality →
Stimulation of the hypothalamic thirst center → ↑Thirst

◦ Dehydration

- Polyuria without adequate hydration →
↓Intravascular volume → Hypovolemia



B. SYNDROME OF INAPPROPRIATE ADH (SIADH)

26:16

Hyponatremia

• Pathophysiology:

- ↑ADH production →
↑H₂O reabsorption at the collecting duct →
↑Water in the bloodstream →
↓Na in the bloodstream

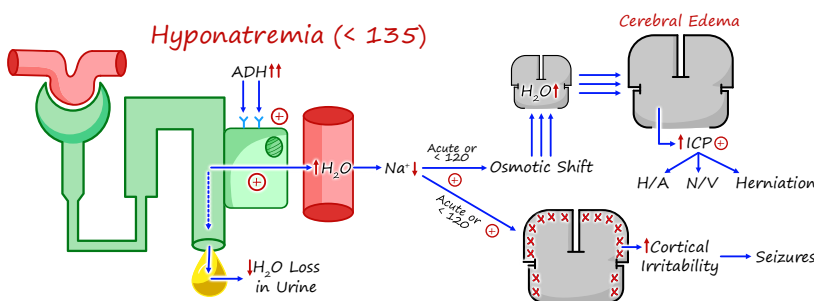
• Presentation:

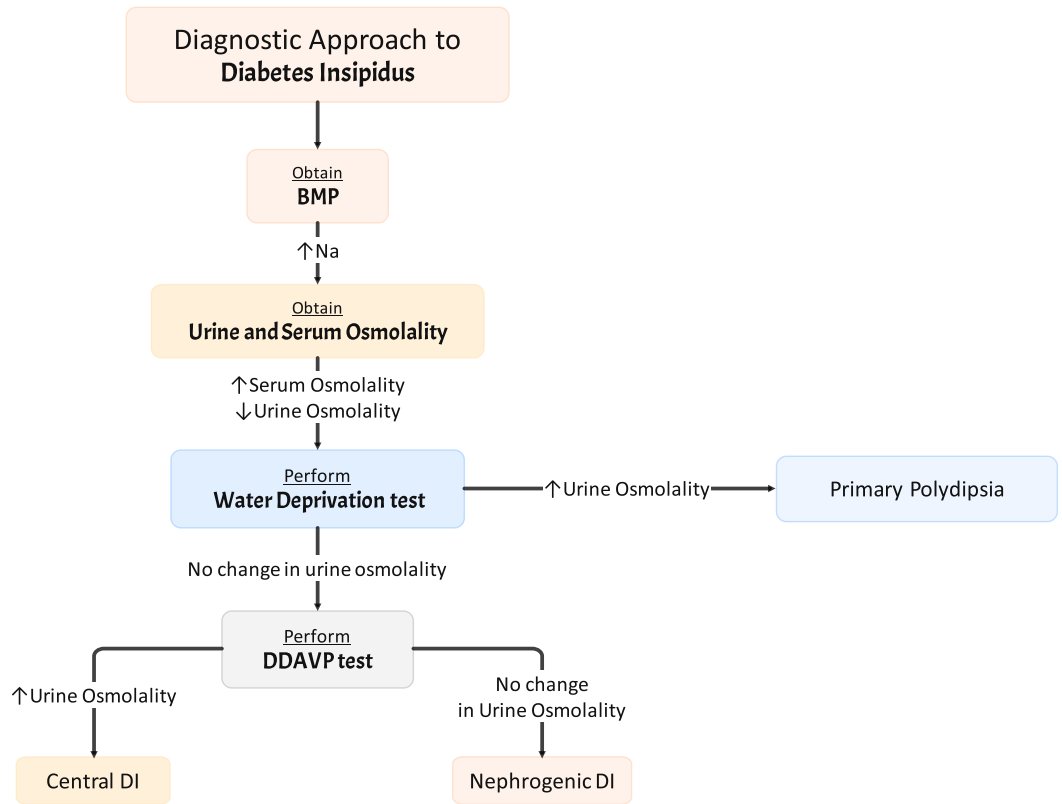
◦ Cerebral Edema

- Hyponatremia → Water pulled from blood into neurons →
Brain swelling → Cerebral Edema →
↑ICP when Na⁺ < 120 acutely
- Encephalopathy
 - Lethargy → Obtunded → Comatose
- Headache
- Nausea and vomiting
- Pupillary changes (e.g. 3rd nerve palsy)

◦ Seizures

- Hyponatremia → Water pulled from blood into neurons →
Brain swelling → Cerebral Edema → Lowers seizure threshold
- Usually, will present with generalized seizures
when Na⁺ < 120 acutely





Assess for the Presence of Central vs Nephrogenic DI

a) Obtain BMP

- **Indications:**
 - Suspicion of Hypernatremia in the setting of polyuria and polydipsia
- **Abnormal Findings:**
 - $\text{Na}^+ > 145 \text{ meq/L}$ → Identifies Hypernatremia

b) Obtain Urine and Serum Osmolality

- **Indications:**
 - Identifying the cause of Hypernatremia
- **Abnormal Findings:**
 - **DI**
 - **↓ Urine Osmolality**
 - ↓ ADH production (e.g. central DI) or
 - ↓ ADH response (e.g. nephrogenic DI) →
 - ↓ H_2O reabsorption at the collecting duct →
 - ↑ H_2O loss in the urine
 - **↑ Serum Osmolality**
 - ↓ ADH production (e.g. central DI) or
 - ↓ ADH response (e.g. nephrogenic DI) →
 - ↓ H_2O reabsorption at the collecting duct →
 - ↓ Water in the bloodstream

c) Obtain a Water Deprivation Test

- **Indications:**
 - Differentiate DI from Primary Polydipsia in patients with polyuria
- **Abnormal Findings:**
 - **DI after water deprivation**
 - **No change in Urine osmolality**
 - This indicates no presence or function of ADH at the collecting duct
 - **Primary polydipsia after water deprivation**
 - **↑ Urine osmolality**
 - This indicates the presence or function of ADH at the collecting duct



d) Obtain **DDAVP Test**

- **Indications:**

- Hypernatremia, ↓Urine osmolality, and ↑Serum osmolality →
- determine if it's nephrogenic vs central DI

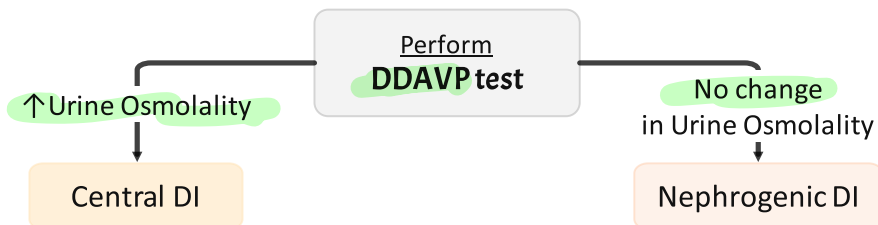
- **Abnormal Findings:**

- **Central DI**

- ↑Urine osmolality
- DDAVP administration of ADH (Missing in Central DI) →
- ↑ADH levels →
- ↑H₂O reabsorption at the collecting duct →
- ↓H₂O loss in the urine

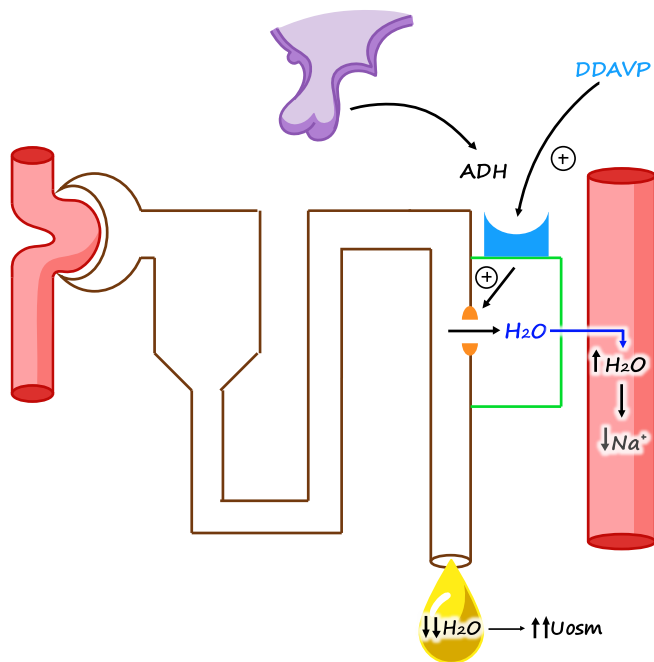
- **Nephrogenic DI**

- No change in Urine osmolality
- DDAVP administration of ADH (Nephrogenic DI → ADH is not functional) →
- ↑ADH levels, but no ADH response →
- ↓H₂O reabsorption at the collecting duct →
- ↑H₂O loss in the urine

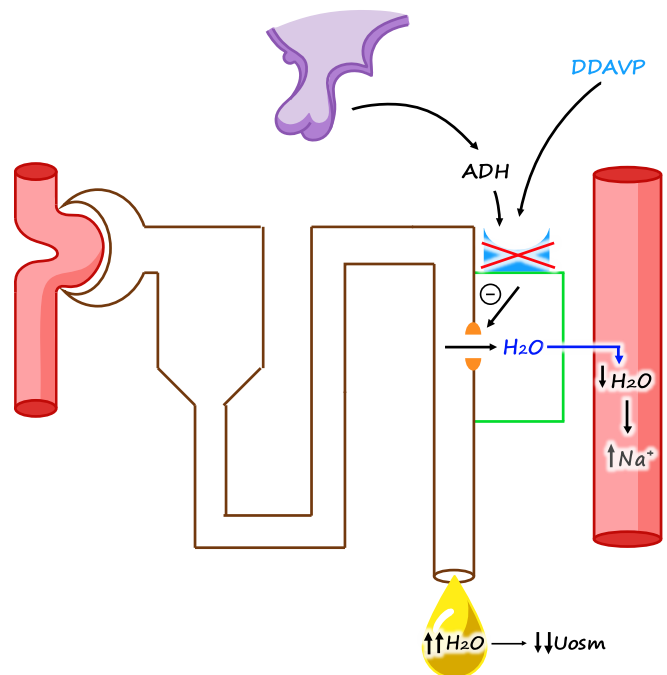


DDAVP test

Central DI



Nephrogenic DI



Assess for the Presence of SIADH

a) Obtain BMP

- **Indications:**
 - Suspicion of hyponatremia in the setting of **Cerebral Edema** and **Seizures**
- **Abnormal findings:**
 - $\text{Na}^+ < 135 \text{ meq/L}$ → Identifies **Hyponatremia**

b) Obtain Urine and Serum Osmolality

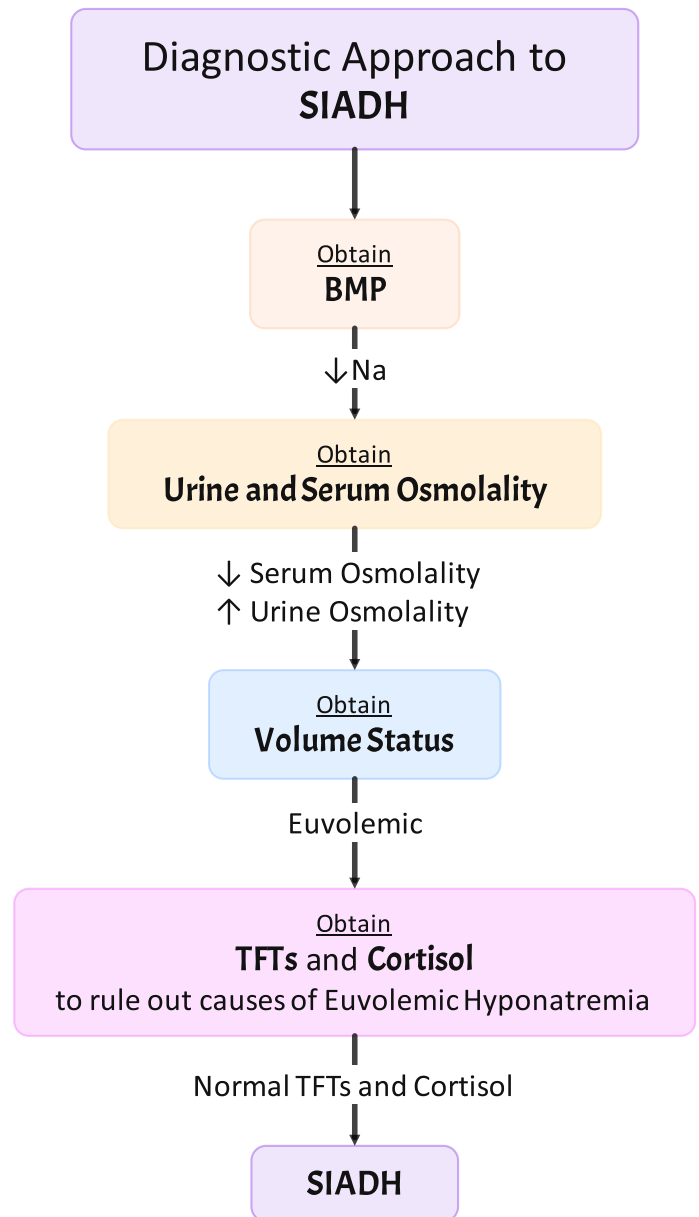
- **Indications:**
 - Identifying the cause of **Hyponatremia**
- **Abnormal Findings:**
 - **SIADH**
 - **↑ Urine Osmolality**
 - ↑ ADH production →
 - ↑ H_2O reabsorption at the collecting duct →
 - ↓ H_2O loss in the urine
 - **↓ Serum Osmolality**
 - ↑ ADH production →
 - ↑ H_2O reabsorption at the collecting duct →
 - ↑ Water in the bloodstream

c) Obtain the Patient's Volume Status

- **Indications:**
 - Hyponatremia
- **Abnormal Findings:**
 - **SIADH**
 - **Euvolemic**
 - Normal BP and HR
 - Normal Mucous membranes and skin turgor
 - Normal JVP
 - Normal Urine output

d) Obtain TSH with Reflex and Cortisol Levels

- **Indications:**
 - Euvolemic Hyponatremia and need to **exclude other etiologies** to rule in SIADH
- **Abnormal Findings:**
 - **SIADH**
 - **Normal TSH with reflex**
 - Hyponatremia can occur in **Hypothyroidism** and would **Exclude SIADH**
 - **Normal cortisol levels**
 - Hyponatremia can occur in **Adrenal Insufficiency** and would **Exclude SIADH**



A. DIABETES INSIPIDUS (DI)

1. Medical Management of DI

- **Therapies:**
 - Desmopressin (DDAVP)
 - Thiazide Diuretics
- **Indications:**
 - **Desmopressin (DDAVP)**
 - Central DI with polyuria and Hypernatremia
 - **Thiazide Diuretics**
 - Nephrogenic DI with polyuria and Hypernatremia
- **Purpose:**
 - **Desmopressin (DDAVP)**
 - Replace loss of ADH from hypothalamic-pituitary injury
 - **Thiazide Diuretics**
 - Promotes mild volume depletion and leads to Na^+ loss from nephron →
 - Volume depletion triggers $\uparrow\text{RAAS}$ and $\uparrow\text{SNS}$ activity →
 - $\downarrow\text{Na}^+$ and water loss from nephron occurs in response →
 - Normalize intravascular water balance
- **Monitoring:**
 - Monitor urine output for improvement with DDAVP
 - Monitor Na^+ levels with DDAVP and Thiazide use

Type	Purpose of Treatment	Treatment
Central DI	Replace ADH	- Desmopressin (DDAVP)
Nephrogenic DI	Induce Mild Hypovolemia	- Sodium restriction and Thiazide diuretics



1. Medical Management of SIADH

• Therapies:

- Water Restriction
 - Limit water intake to < 1500ml/day
- Salt tablets
- Loop diuretics (e.g. furosemide)
- Vaptans (Tolvaptan)
- 3% Hypertonic saline

• Indications:

- **Water Restriction and salt tablets**
 - Chronic and/or Asymptomatic Hyponatremia
- **Loop diuretics**
 - Chronic and/or Asymptomatic Hyponatremia with volume overload
 - Chronic and/or Asymptomatic Hyponatremia refractory to water restriction and salt tablets
- **Vaptans**
 - Chronic and/or Asymptomatic Hyponatremia not able to abide by water restriction
 - Chronic and/or Asymptomatic Hyponatremia refractory to water restriction, salt tablets and loop diuretics
- **3% Hypertonic Saline**
 - Acute, Na < 120 and/or symptomatic hyponatremia (e.g. cerebral edema or seizures)

• Purpose:

- **Water Restriction and Salt Tablets**
 - Water restriction
 - ↓ Water ingested → ↓ Water in bloodstream → ↓ Water reabsorbed across collecting duct → ↑ Na⁺ level
 - Salt tablets
 - NaCl ingested → ↑ Na in the bloodstream → ↑ Na⁺ level
- **Loop Diuretics**
 - Block Na/K/2Cl cotransporters in the loop of Henle → ↑ Water loss in the urine → ↓ H₂O in the bloodstream → ↑ Na⁺ level
- **Vaptans**
 - ADH blocked at the receptor site → ADH response → ↑ Water loss in the urine → ↓ H₂O in the bloodstream → ↑ Na⁺ level
- **3% Hypertonic Saline**
 - Concentrated NaCl in the bloodstream → ↑↑ Na⁺ in the bloodstream → ↑↑ Na⁺ level

• Monitoring:

- Monitor K⁺, Mg²⁺, and Na⁺ levels while on **loop diuretics**
- Monitor BP while on **loop diuretics**
 - Can become **Hypotensive** with **Over-Diuresis**
- Monitor Na⁺ levels very closely while on **Vaptans**, as one can develop **Hypernatremia** easily
- Monitor Na⁺ levels extremely closely (**q4hrs**) while administering **3% Hypertonic Saline**, given the risk of **Osmotic Demyelination Syndrome**
 - Prevention of ODS is maintained by preventing Na⁺ rise of > 6-8meq/L in 24 hours
- **Options to prevent overshooting:**
 - If Na⁺ shoots above the threshold, give **DDAVP** to cause water reabsorption to drop in Na⁺ levels to prevent overshooting
 - If Na⁺ shoots above the threshold, give **free water** to cause a drop in Na⁺ levels to prevent overshooting

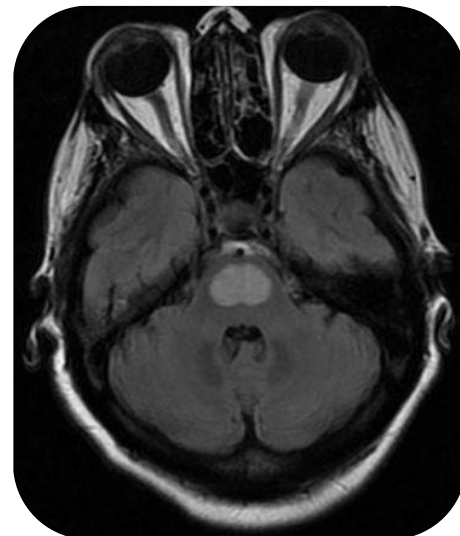
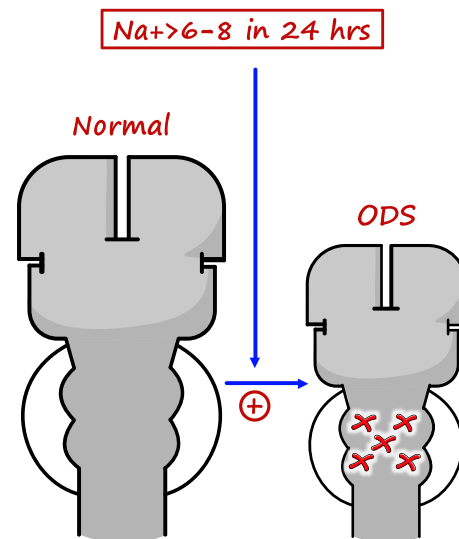


FIGURE 1. OSMOTIC DEMYELINATION SYNDROME

