SIADH, Cerebral Salt Wasting

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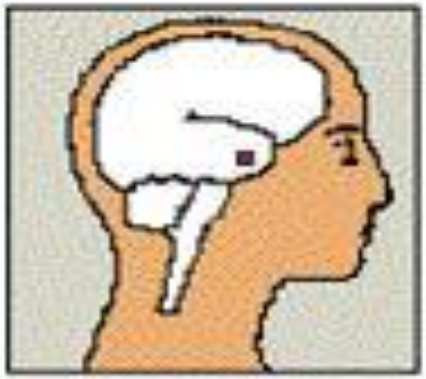
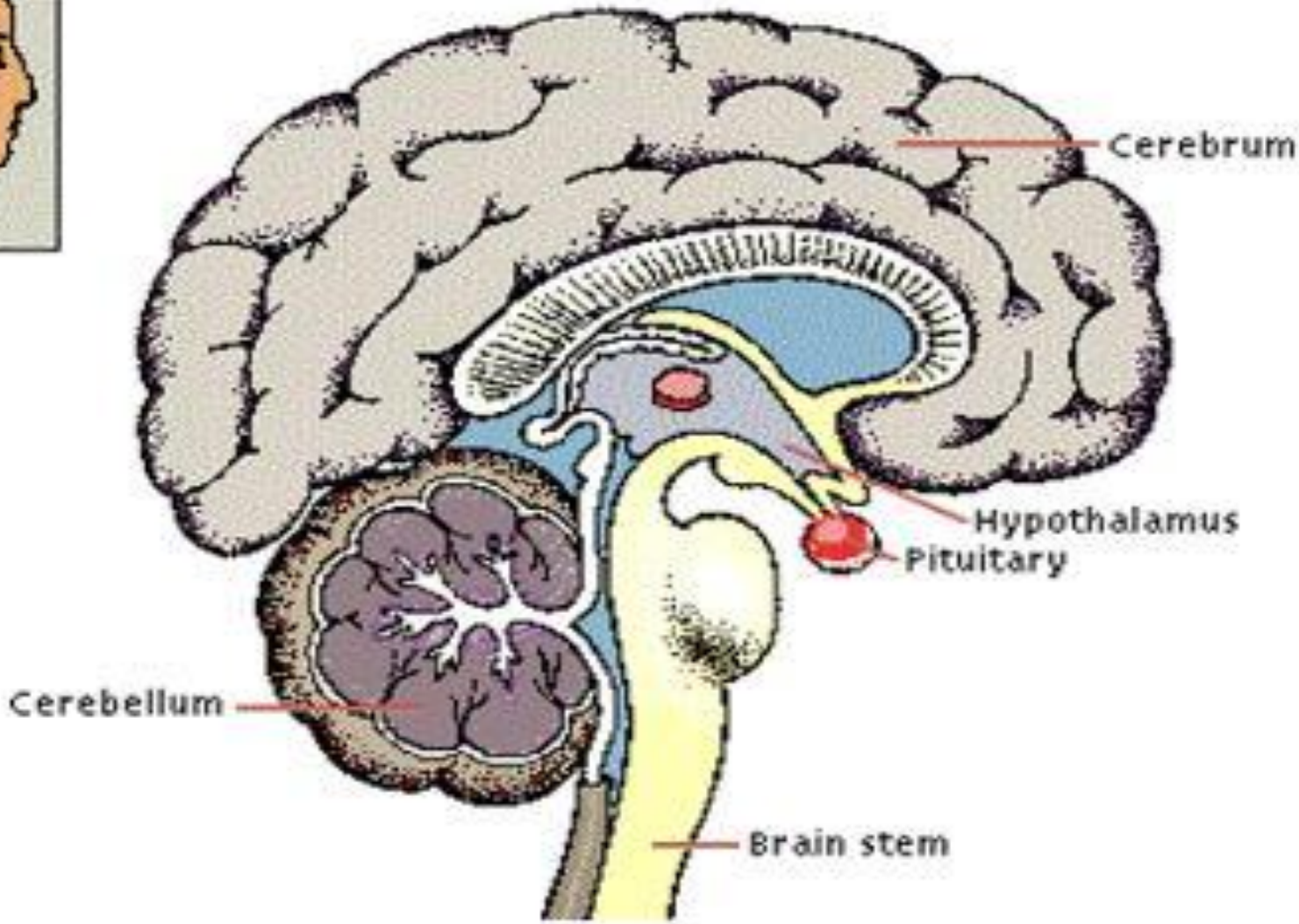
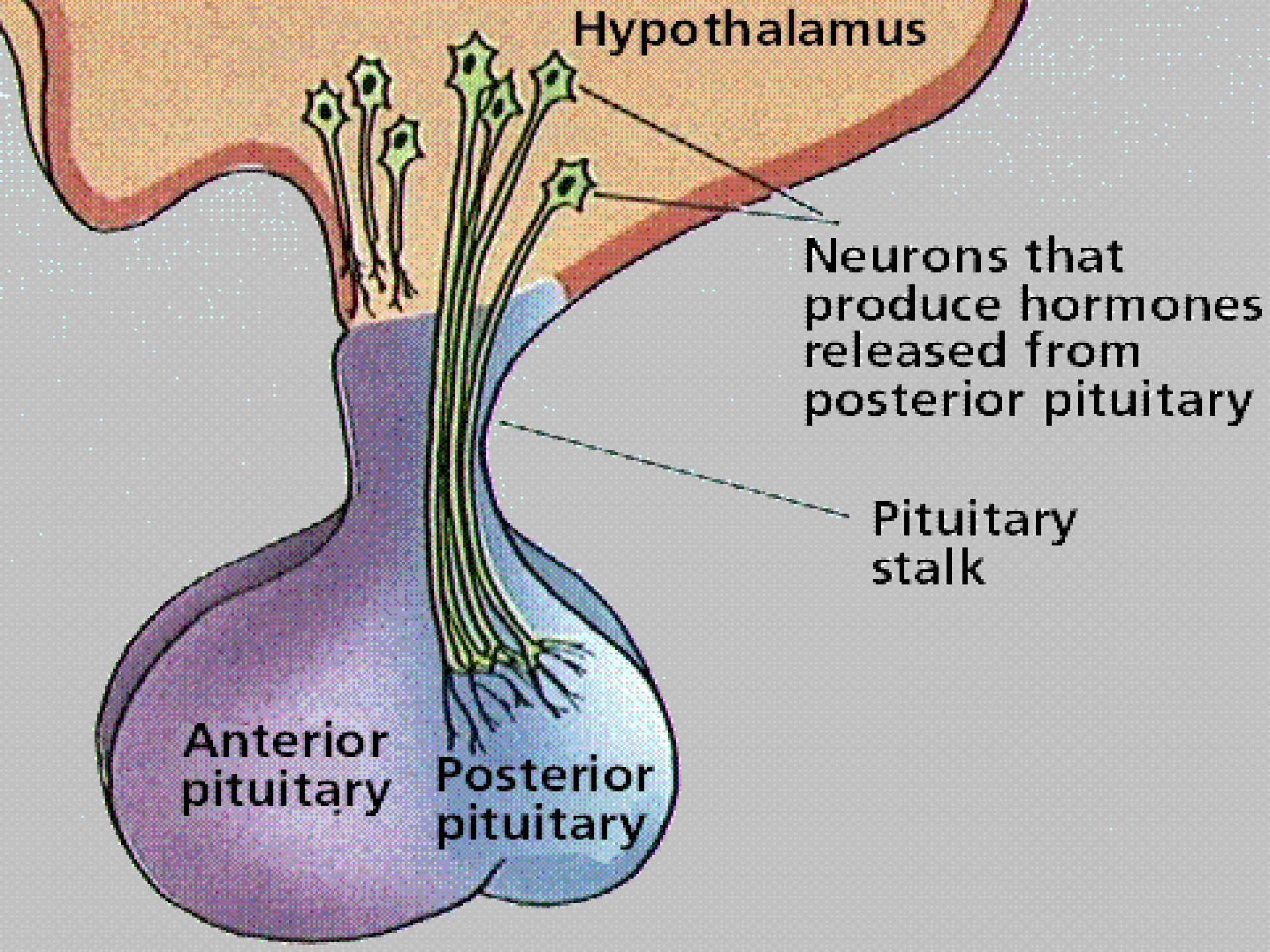
The Pituitary & Hypothalamus






Hypothalamus
Neurons that produce hormones released from posterior pituitary
Pituitary stalk
Anterior pituitary
Posterior pituitary

Functions of ADH

- ADH increases the permeability of the renal distal tubule & collecting ducts to water
- Less free water is excreted in urine
- Urine volume is decreased
- Concentration of urine is increased

Functions of ADH

- Is a potent vasoconstrictor
- is a **neurotransmitter** in CNS regulation of
  - the secretion of ACTH
  - the cardiovascular system
  - temperature and other visceral functions.
- Promotes hemostasis
  - the release of endothelial coagulation factors.
  - increases platelet aggregability

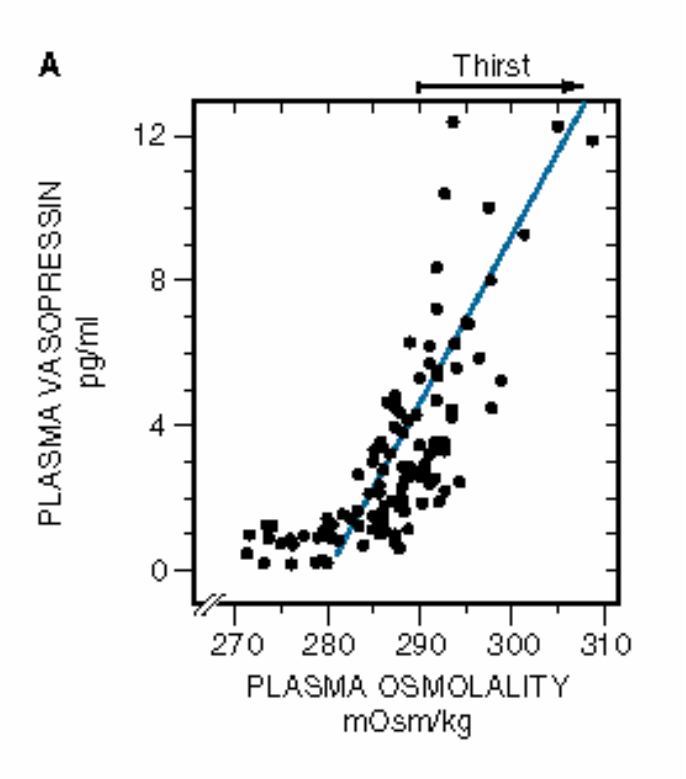
Regulation of Osmolality

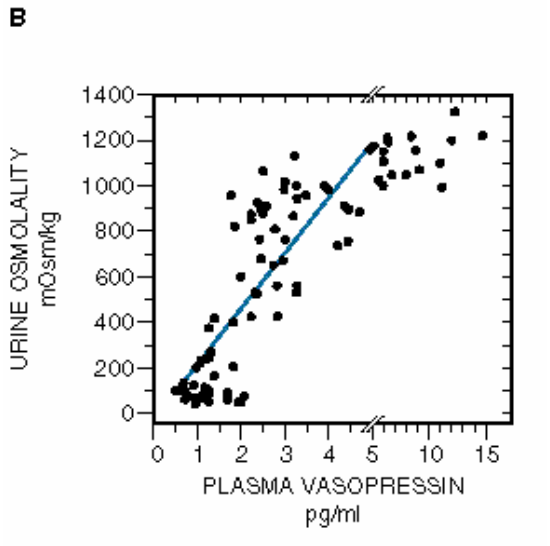
- Plasma Osmolality is monitored by osmoreceptor in the hypothalamus
- Increases in plasma osmolality stimulates secretion of vasopressin
- Small changes above the normal plasma osmotic pressure (290 mosm/kg) stimulate release of vasopressin

Regulation of osmolality

1) Osmoreceptors are neurons in the CNS

2) Baroreceptors in left atrium, left ventricle, and pulmonary veins sense blood volume (filling pressures), and baroreceptors in the carotid sinus and aorta monitor arterial blood pressure


A
Thirst
PLASMA VASOPRESSIN
pg/ml
12
8
4
0
270
280
290
300
310
PLASMA OSMOLALITY
mOsm/kg


B
URINE OSMOLALITY
mOsm/kg
1400
1200
1000
800
600
400
200
0
0
1
2
3
4
5
10
15
PLASMA VASOPRESSIN
pg/ml

Syndrome of Inappropriate antidiuretic Hormone (SIADH)

- SIADH is characterized by the non-physiological release of ADH, resulting in impaired water excretion with normal sodium excretion
- SIADH is characterized by:
  - fluid retention
  - serum hypo-osmolarity
  - dilutional hyponatraemia
  - hypchloremia
  - concentrated urine in the presence of normal or increased intravascular volume
  - normal renal function

Pathophysiology

- Inappropriate ADH secretion occurs when there is dysregulation of cells secreting vasopressin
- The posterior pituitary is not always the source of ADH secretion
- A variety of ADH-secreting tumors has been associated with SIADH, as well as various CNS disorders, pulmonary disorders & drugs

Causes:

- Increased hypothalamic production
  - Infections
    - Meningitis, encephalitis, abscess, HIV
  - Vascular
    - subarachnoid or subdural hemorrhage
  - Neoplasm
  - Guillain-Barré syndrome, acute intermittent porphyria, autonomic neuropathy, post–pituitary surgery, multiple sclerosis, psychosis, BMT or Stem Cell Transplants
  - Drugs
    - Chemotherapeutic - Cyclophosphamide, vincristine, vinblastine
    - Antipsychotic - Thiothixene, thioridazine, haloperidol
    - Antidepressants - Monoamine oxidase inhibitors, tricyclic antidepressants, serotonin reuptake inhibitors
    - Miscellaneous – Bromocriptine
  - Pulmonary diseases
    - Pneumonia , Tuberculosis, Acute respiratory failure ,Positive pressure ventilation, Asthma & Atelectasis
  - Idiopathic

Signs & symptoms

- Decreased / Low urine output
- Symptoms of hyponatraemia
  - Lethargy, apathy, disorientation, muscle cramps, anorexia, agitation
- Symptoms of water toxicity
  - nausea, vomiting, personality changes, confusion
- If Na < 110 mEq/L
  - seizures, bulbar palsies, hypothermia, stupor, coma

Triphasic response post neurosurgery

- Transient DI 12-48 hours postop
- SIADH after transient DI phase lasting up to 10 days post-operative
- Permanent DI

Investigations

- Serum Na < 135 (Na is diluted by excessive free water re-absorption)
- Serum osmolality low, normal is ~ 270 mosmol/l
- Urine Na is inappropriately high, >20 mmol/L (actually losing Na in urine instead of retaining it)
- Urine osmolality is inappropriately high, can range between 300-1400 mosm/l
- CVP is high from free water retention

Investigations

Imaging Studies

- Chest radiographs may reveal an underlying cause (e.g., pulmonary disease)
- CT scan of the head
  - evidence of cerebral edema
  - identify a CNS disorder responsible for SIADH (e.g., brain tumor)
  - rule out other causes of acute changes in neurological status

Clinical Management

- Treatment of underlying medical condition if exists
- Normalize serum sodium (130 meq/l and above) over 24 -48 hours (Max correction of 15meq/day)
  - Warning, if increase Na is too fast, there is a risk for pontine myelinolysis
- Normalize serum osmolality
- Correct excess extravascular fluid volume
  - Restrict fluids
  - 3% NaCl
  - Loop diuretics

Drugs therapy in SIADH

- Demeclocycline & lithium act on the collecting tubules to diminish its responsiveness to ADH, thereby increasing water excretion
- Demeclocycline is more effective and more often used than lithium for the treatment of hyponatraemia in SIADH
- Both drugs are nephrotoxic
- Demeclocycline can cause nausea, vomiting, and photosensitivity
- Lithium has a variety of neuropsychiatric side effects
- In severe cases, haemodialysis could be used

Prognosis

- Ultimately, the prognosis of SIADH best correlates to the underlying cause
- Rapid and complete recovery tends to be the rule for recovery from drug-induced SIADH when the offending agent is withdrawn
- Similarly, successful treatment of pulmonary or CNS infection can lead to correction of SIADH

Cerebral salt-wasting

Is cerebral salt-wasting real?

Some authors have suggested that CSW may not exist

Cerebral salt-wasting (CSW)

- Is another cause of hyponatremia in those with CNS disease, particularly in patients with subarachnoid hemorrhage
- Is characterized by hyponatremia & extracellular fluid depletion due to inappropriate sodium wasting in the urine
- However, some authorities contend that CSW does not really exist and is only a misnomer for what is actually SIADH, with the putative salt wasting being due to unappreciated volume expansion

CSW

- CSW is a much less common cause of hyponatremia in patients with cerebral injury than SIADH
- The pathophysiology of CSW is related to impaired sodium reabsorption, possibly due to the release of brain natriuretic peptide and/or diminished central sympathetic activity
- Regardless of the mechanism (not much understood !!), sodium-wasting can lead sequentially to volume depletion, increased ADH release, hyponatremia due to the associated water retention, and possibly increased neurologic injury
- Since CSW is associated with extracellular fluid depletion, hypotension & decreased skin turgor may also be observed

Cerebral Salt Wasting

Causes

- CNS damage
  - Subarachnoid hemorrhage
  - Closed head injury
  - CNS surgery
  - CNS tumors
  - CNS infections
    - Meningitis, abscess

Cerebral Salt Wasting

- Signs/symptoms
  - Symptoms of underlying CNS insult
  - Symptoms of hyponatraemia
  - Polyurea
  - Weight loss
  - Dehydration / hypovolemia
  - Hypotension
  - Low CVP

Investigations

- Specific laboratory findings include:
  - Hyponatraemia with low plasma osmolality
  - Inappropriately elevated urine osmolality (usually above 300 mosmol/kg)
  - Urine sodium concentration above 40 meq /l
  - Low serum uric acid concentration due to urate wasting in the urine

Differential diagnosis

- In the setting of CNS injury, CSW must be distinguished from other causes of hyponatremia, principally SIADH
- The distinction between CSW & SIADH is critically important since the two disorders are managed differently, with possible adverse consequences if the incorrect therapeutic strategy is administered

		SIADH	CSW
Urine Output		decreased	polyurea
Serum Na		low	low
Urine Na		high	high
Serum osm		low	low
Urine osm		high	high
CVP		high	low

Treatment

- In the setting of CNS disease, the distinction between CSW & SIADH is critically important since the two disorders are managed differently, with possible adverse consequences if the incorrect therapy is administered
  - As example, fluid restriction, the usual first-line therapy for SIADH, may increase the risk of cerebral infarction among patients who actually have CSW

- Volume repletion with isotonic saline is the recommended therapy in CSW, since it will suppress the release of ADH, thereby permitting excretion of the excess water and correction of the hyponatremia
- If CSW is the sole cause of the hyponatremia, volume repletion would result in the urine osmolality falling below 100 mosmol/kg
- For patients with documented CSW, salt tablets can be administered once they are able to take oral medications
- Administration of a mineralocorticoid, such as fludrocortisone can also be used

Prognosis

- Long-term therapy of CSW is not necessary since CSW tends to be transient
- Resolution usually occurs within three to four weeks

Conclusion

- In the setting of CNS disease, accurate distinction between CSW and SIADH is essential since the two disorders are managed differently, with possible adverse consequences if the incorrect therapeutic strategy is administered
- CSW mimics all of the laboratory findings in the SIADH
- The only clue to the presence of CSW rather than SIADH is clinical evidence of extracellular volume depletion, such as hypotension and decreased skin turgor
- Unlike SIADH, volume repletion in CSW leads to a dilute urine, correction of the hypovolemia stimulate ADH release, and subsequent correction of the hyponatraemia

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