

The Management of Hyponatremia in Neurological Disease

Catherine Wentowski, MD MPH
Pulmonary and Critical Care Medicine
Ochsner Medical Center

Disclosures

- Advisory Board: Sanofi/Regeneron
- No actual or potential conflicts of interest in relation to this topic/presentation.



Call Nephrology?

A dreaded problem...



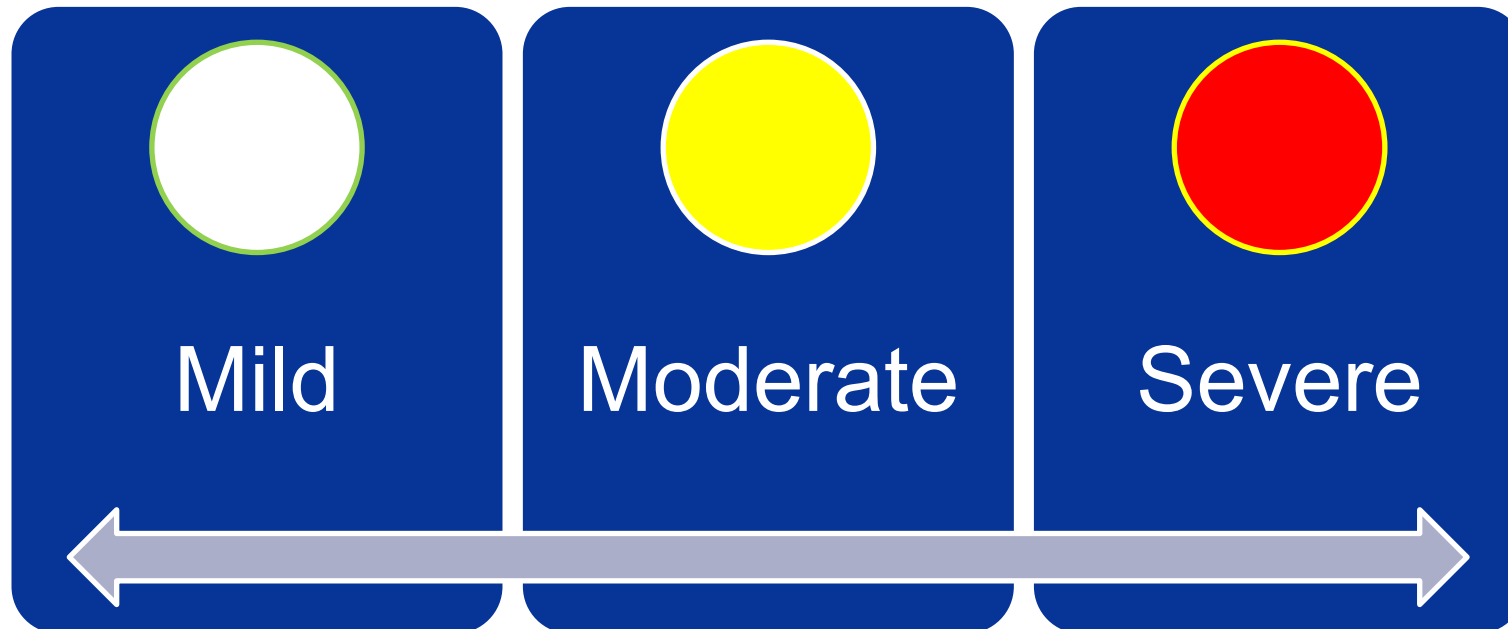
Frequently encountered!

- SAH
- TBI
- CVA
- CNS infections
- Brain Tumors

Hyponatremia
is present in
38-54% of
cases

Acute

Chronic



Definitions

Acuity

- Acute: <48 hours
- Chronic: >48 hours

Severity

- Mild: 130-134 mEq/L
- Moderate: 120-129 mEq/L
- Severe: <120 mEq/L

Symptoms

Acute

- Nausea/Vomiting
- Headache
- Seizure
- Respiratory Arrest
- Coma
- Death

Chronic

- Nausea/Vomiting
- Fatigue
- Gate instability/Falls
- Attention deficit

Sodium Regulation



- Regulated by osmoreceptors in the hypothalamus
- Normal circumstances:
 - Hyponatremia=decreased thirst and suppression of ADH
 - This results in dilute urine and normalization of sodium

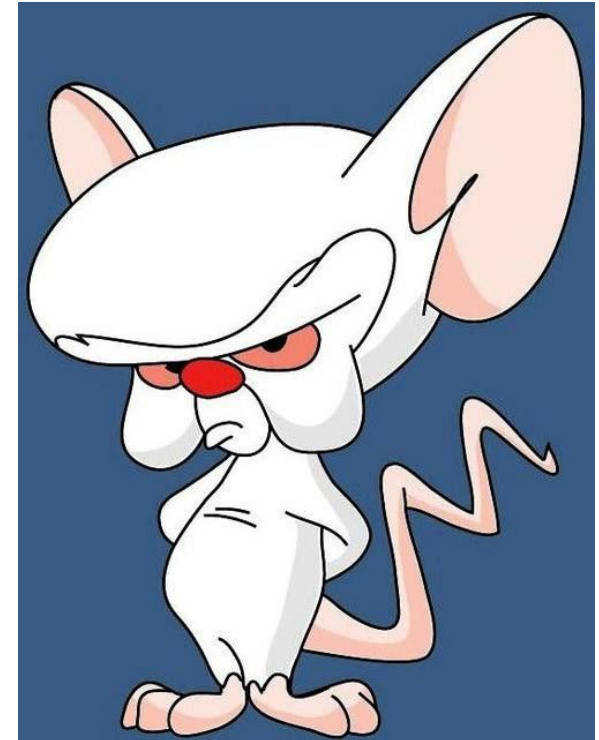
Hyponatremia and the Brain

Decreased
serum
osmolality

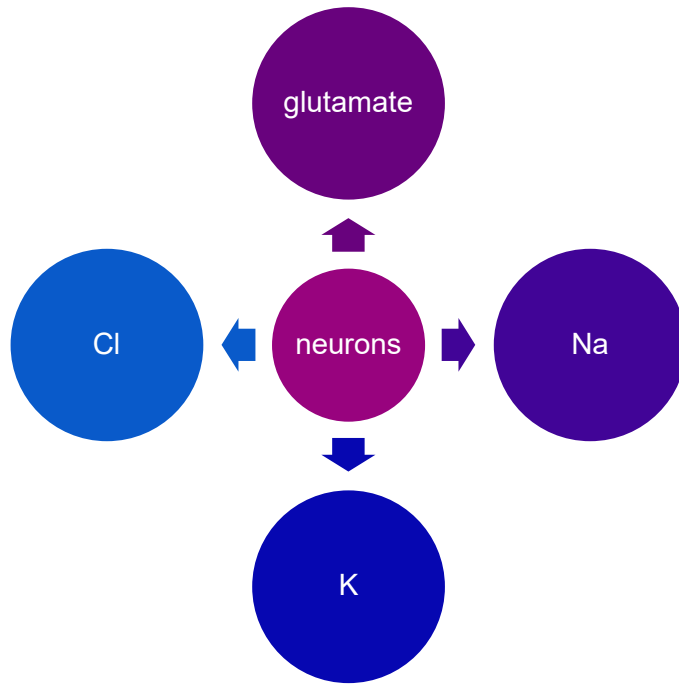
Osmotic
gradient

Water moves
into glial and
neuronal cells

Interstitial
fluids migrate
into the
CSF → thecal
sac → systemic
circulation



Acute Compensation



decreases
the
osmotic
gradient
water loss

A pink arrow curves from the text "decreases the osmotic gradient" down to the text "water loss". To the right of this text is a cartoon illustration of a brown neuron with a grumpy face, surrounded by wavy lines indicating it is vibrating or shaking.

Correction...

- Overly rapid = neurologic injury
- Water moves from the *intracellular* compartment causing rapid $\uparrow$ in electrolyte concentration & $\downarrow$ in *intracellular* volume



Cerebral Dehydration



Osmotic Demyelination Syndrome

Take it SLOW: 4-6 mEq is all it takes!



ODS: Pathophysiology

- Most **feared** complication of sodium correction
 - Previously called *central pontine myelinolysis*
- Risk Factors:
 - Severe hyponatremia (<120 mEq/L) for more than 2-3 days
 - Alcoholism
 - Malnutrition
 - Hypokalemia
 - *Cirrhosis/Liver Transplant

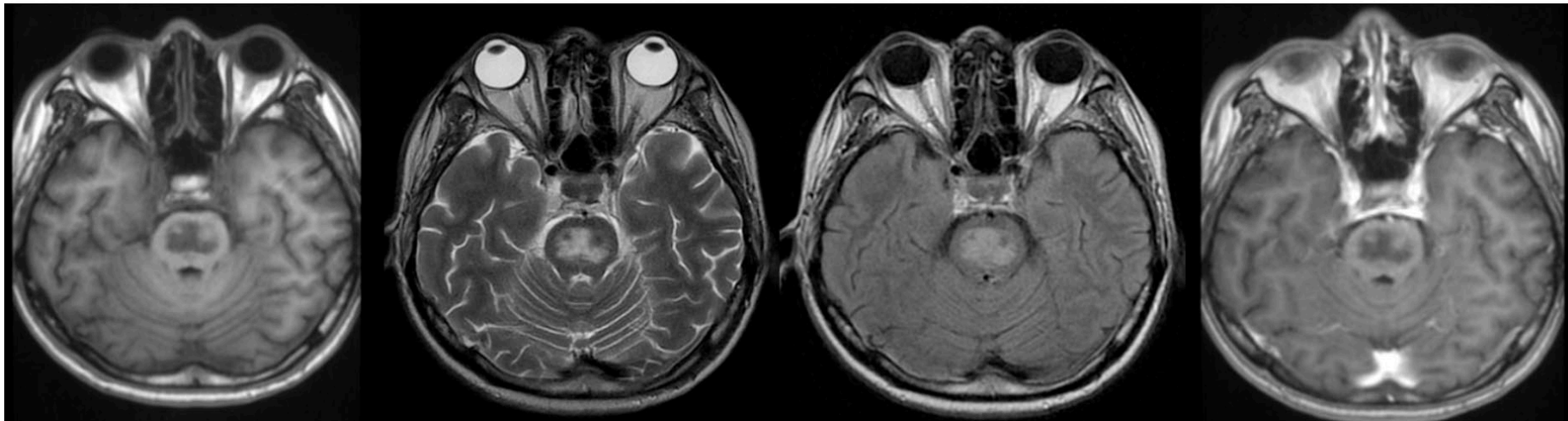
ODS: Diagnosis

- Slow process
 - Delayed presentation for 2 to 6 days after rapid correction
 - More common in correction of chronic hyponatremia

Clinical Signs	
Psychomotor changes	Limb tremor
Psychiatric changes	Myoclonus
Catatonia	Parkinsonism
Paresis/Plegia (in and all limbs including bulbar musculature)	

ODS: Imaging

- Imaging can be normal for 4 weeks after onset
- MRI with diffuse restriction within the central pons with a trident pattern that predates T2 signal changes



ODS: Treatment

DDAVP: 2 μ g IV q6h

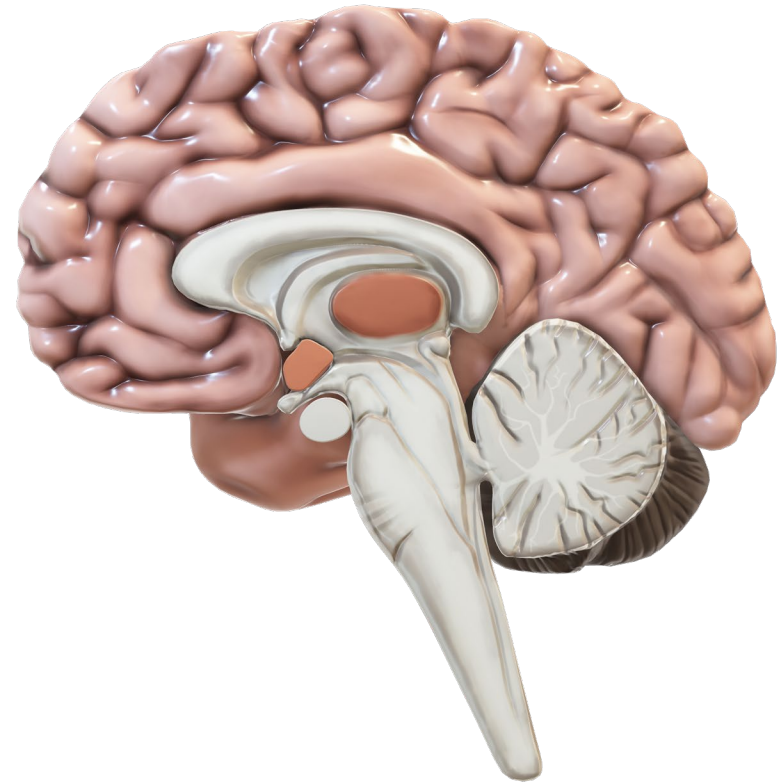
AND/OR

D5W: 6ml/kg bolus over 2 hours



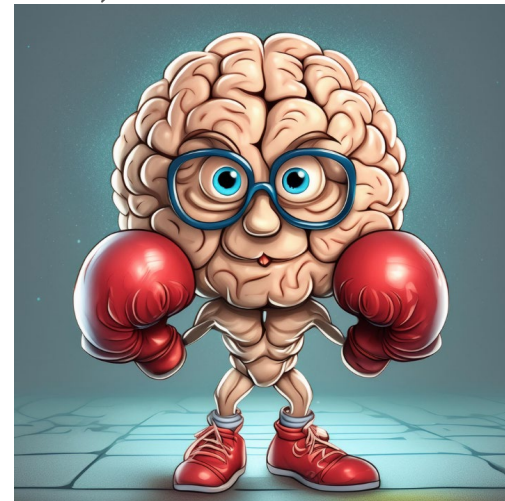
ODS: Prognosis

- Potential for neuro devastation
- Some evidence for possible improvement
 - 1/3 recover fully
 - 1/3 debilitated but independent
 - 1/3 fully dependent
- Presentation $\neq$ Outcome



Causes of Hyponatremia

- Polydipsia
- Low dietary solute (beer potomania)
- Diuretic Induced
- Heart Failure/Cirrhosis
- Low osmostat (pregnancy, reset)
- Exercise Induced
- SIADH
- Cerebral Salt Wasting





Cerebral Salt Wasting

Potential cause of hyponatremia in those with CNS disease- particularly subarachnoid hemorrhage.

CSW-pathophysiology?

- Unclear
 - Dysregulation of the sympathetics?
 - Natriuretic peptides
 - Adrenomedullin
- Is it real?

CSW: Clinical Features

- Moderate to Severe Hyponatremia
- Polyuria
- Occurs *within 10 days of neurosurgery or event*
- Dehydration



CSW: Diagnosis

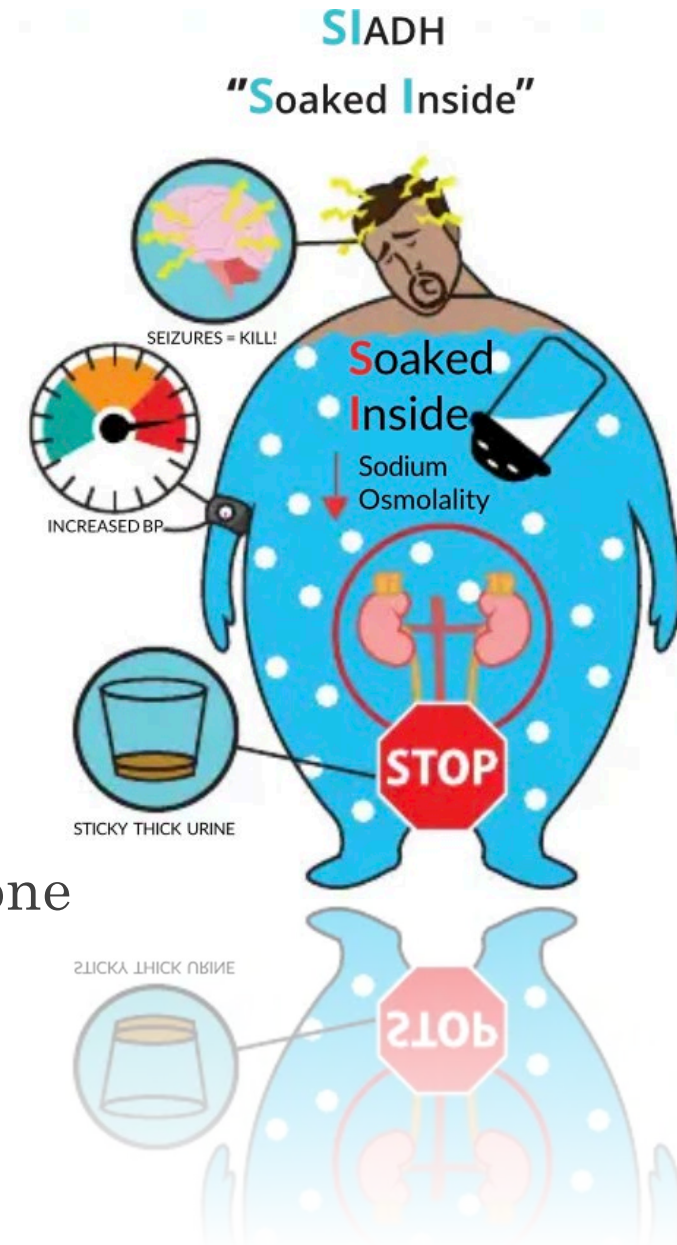
- Hypovolemia
- Hyponatremia ($\text{Na} < 135 \text{ mEq/L}$)
- Low serum osms ($< 280 \text{ mOsm/kg}$)
- Elevated urine osmolality ($> 300 \text{ mOsm/kg}$)
- Elevated urinary sodium ($> 40 \text{ mEq/L}$)
- Low serum uric acid

CSW: Treatment

- Replace the sodium & water deficit
 - Infuse isotonic fluid (e.g. normal saline)
- Achieving euvolemia may not correct hyponatremia
 - Hypertonic saline (3%- 50-100ml)

SIADH

Syndrome of Inappropriate Antidiuretic Hormone



SIADH: Pathophysiology

- **Supraphysiologic** ADH levels $\neq$ osmotic changes
 - **Ectopic secretion** of ADH
 - **‘Osmostat Reset’**: low osmotic threshold for ADH release

urine remains concentrated

Type of Disorder	Examples
Brain or nervous system	An abscess in the brain Bleeding (hemorrhage) within the layers of tissue covering the brain Encephalitis (inflammation of the brain) Guillain-Barré syndrome Head injury Hypothalamus disorders, including tumors (rare) Meningitis Stroke Tumors
Lung	Acute respiratory failure Pneumonia Tuberculosis
Cancers	Brain cancer Lung cancer Lymphoma Pancreatic cancer Cancer of the small intestine
Other	Surgery Undernutrition
SIADH = syndrome of inappropriate secretion of antidiuretic hormone.	

Causes of SIADH

Medications Associated With Syndrome of Inappropriate Antidiuretic Hormone.

Antiepileptic Medications

Carbamazepine

Lamotrigine

Oxcarbazepine Sodium valproate

Oncologic Medications Alkylating agents

(cyclophosphamide) Ifosfamide

Imatinib

Methotrexate

Platinum (cisplatin)

Vinca alkaloids (vincristine)

Pain Medications

Non-steroidal anti-inflammatory

Opiates

Psychiatric Medications

Butyrophenones (haloperidol)

Monoamine oxidase inhibitors

Phenothiazine (fluphenazine, chlorpromazine)

Risperidone

Selective Serotonin Reuptake Inhibitors

Tricyclic antidepressants Venlafaxine

Miscellaneous

Amiodarone

Bromocriptine

Ciprofloxacin

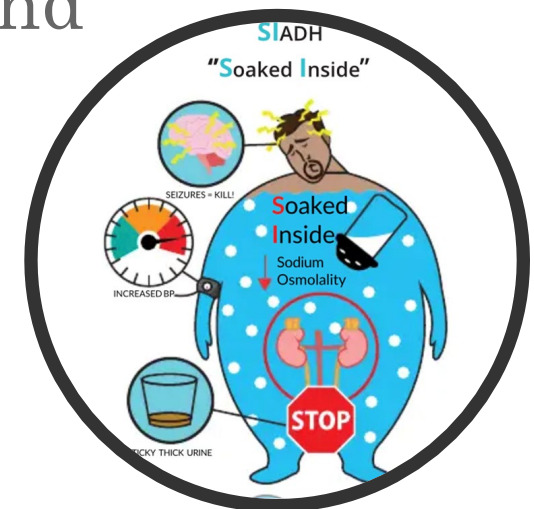
Desmopressin or Vasopressin

Ecstasy (methylenedioxy methamphetamine)

Interferon-alpha

SIADH: Diagnosis

- Decreased serum osmolality (<275 mOsm/kg)
- Urinary osmolality >100 mOsm/kg
- Clinical euvolemia
- Urinary sodium >40 mmol/L
- No recent diuretic use, normal thyroid, and adrenal function





Feeling Confused?

Me too...

Differentiating Cerebral Salt Wasting and Syndrome of Inappropriate Antidiuretic Hormone.

	Cerebral Salt Wasting	Syndrome of Inappropriate Antidiuretic Hormone
Extracellular volume status	Decreased	Unchanged
Heart rate	Unchanged to increased	Unchanged
Body weight	Decreased	Unchanged
Urine output	Unchanged to increased	Unchanged to decreased
Hematocrit	Increased (relative to baseline)	Unchanged
Blood urea nitrogen	Increased	Unchanged
Serum bicarbonate	Increased	Unchanged
Serum urate	Unchanged to decreased	Unchanged
Urine osmolality	>100 mOsm/kg	>100 mOsm/kg
Urine Na excretion	>40 mmol/L	>40 mmol/L

SIADH: Treatment

- Identify underlying cause
- **Stop unnecessary medications**
- Treatment of underlying infection
- Control pain
- Fluid restriction!!!
 - $< 800 \text{ mL/d}$ $\longrightarrow$ increase of 2 mEq/L in 24 hours
- Demeclocycline & Lithium

SIADH: Hypertonic Saline



Sodium & water excretion are regulated by independent systems → aldosterone & ADH



IV saline will not change the rate of excretion of sodium



Hypertonic saline will cause excretion of free water

Salt tablets and more...

- Increasing solute intake with:
 - Salt tablets
 - Urea
 - High-protein diet

And urine output should increase (water excretion)...



Vaptans

Activate V2 receptors in the collecting ducts to increase water excretion

Useful for both euvolemic and hypervolemic hyponatremia

Vaptans

Oral *Tolvaptan*

- Studied in cirrhosis, heart failure, and SIADH
- SALT trial: Tolvaptan vs placebo
 - Mild HN: achieved sodium >135 within 5 days
 - Marked HN: achieved goal at 10-15 days
 - Low doses (7.5mg) are likely all that's required to normalize sodium

IV *Conivaptan*

- Vasopressin receptor antagonist (V1,V2)
- Loading dose: 20mg over 30 minutes
- Continuous 20-40mg continued from 24-96 hours
- Good for patients in heart failure
- For TBI and neurologic injury: ↓ intracranial pressure and ↑ sodium in 4 hours

SLOW....

Take it SLOW



3%

The need for speed....



Hyponatremia Associated Seizure

Moderate-severe hyponatremia is also associated with seizures and even SE

Mostly generalized, but could be focal

EEG c/w metabolic encephalopathy

Rapid correction of Na will control seizure

5mmol/L should control seizure

- 100ml bolus of 3% over 10 minutes; repeat twice more if symptoms persist

Hyponatremic Encephalopathy

- Neurologic dysfunction 2/2 hyponatremia
- Symptoms:
 - Impaired Gait
 - Inattention
 - Headache
 - Nausea
 - Lethargy
 - Confusion/Agitation
- Risk Factors for permanent sequelae:
 - Younger age: <16, larger brain: intercranial volume
 - Premenopausal women



Hyponatremia & Cerebral Edema

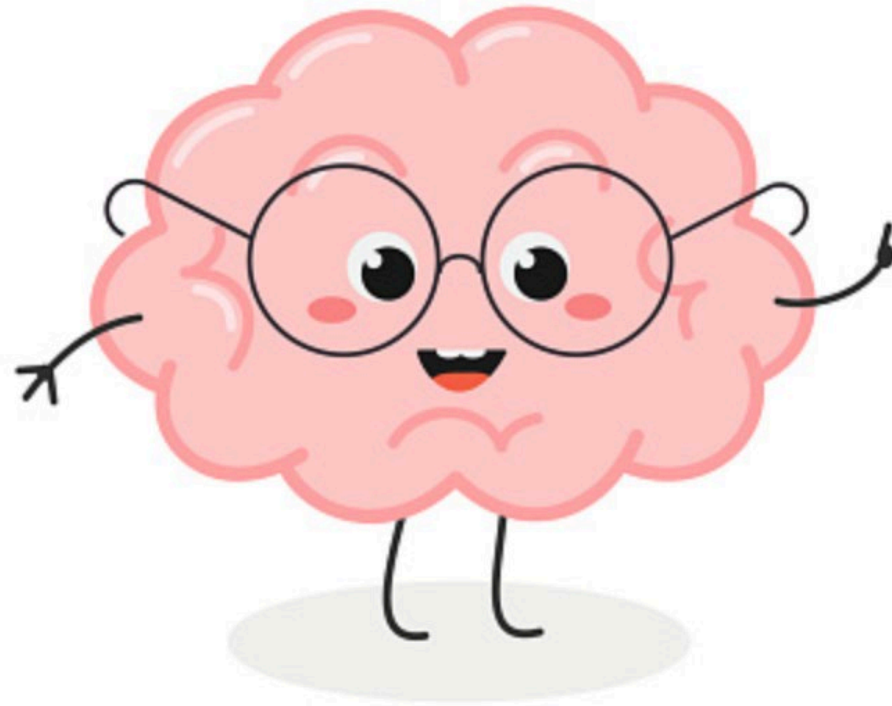
- Risk Factors: stroke, infection, neoplasm, TBI
- Failure of the brain to adapt to osmotically driven forces
- Treat it as you would any cerebral edema: increase serum sodium
 - Increases in plasma sodium by 5-6mEq/L will decrease the intracranial pressure by 5 to 10 mmHg
 - 100mL bolus of 3% over 10 minutes, plus 2 additional boluses if symptoms persist
- Ongoing debate regarding the rate and method of sodium correction in the setting of cerebral edema → need more data

For Acute Severe Symptomatic:

- $\uparrow$ Na by 4-6 mEq/L can reverse impending herniation or stop seizure activity
- US: 100 mL 3% bolus over 10 minutes
 - Repeat twice more if required for symptom management



YOU DO NOT NEED A CENTRAL LINE!!!



To Review....

Duration

- Acute
- Chronic



Severity of Hyponatremia

- Mild
- Moderate
- Severe



Severity of Symptoms

- Asymptomatic
- Mild-moderate
- Severe



Initial Goals

- Make sure you collected the data
- Prevent further decline
- Prevent brain herniation
- Relieve Symptoms
- Avoid Overcorrection

Acute Hyponatremia: the first 6 hours

1. **Symptomatic:** 100 mL bolus of 3% saline infused over 10 minutes
2. **Asymptomatic:** 50 mL bolus of 3% saline over 10 minutes **unless** there is evidence of autocorrection (increasing output of dilute urine and/or evidence that serum sodium concentration is increasing without treatment)
3. Goal: ↑ increase serum sodium by 4 to 6 mEq/L over a few hours.
4. Stop all other IVF
5. Seizing: 100ml bolus of 3, if response is delayed give lorazepam 4mg IV
6. Still symptomatic: two additional 100 mL doses of 3% saline may be given
7. Repeat sodium q1-2h
8. Monitor urine output.

Chronic Hyponatremia: the first 6 hours

- Mild (130-134)
 - Identify cause and treat
 - Limit further intake of water
- Moderate (<130)
 - Asymptomatic patients with intracranial pathology still get treated with 3%
- Severe (<120)
 - 3% 15-30ml/hr vs 100ml boluses q6h

4-6 mEq/L in 24hrs

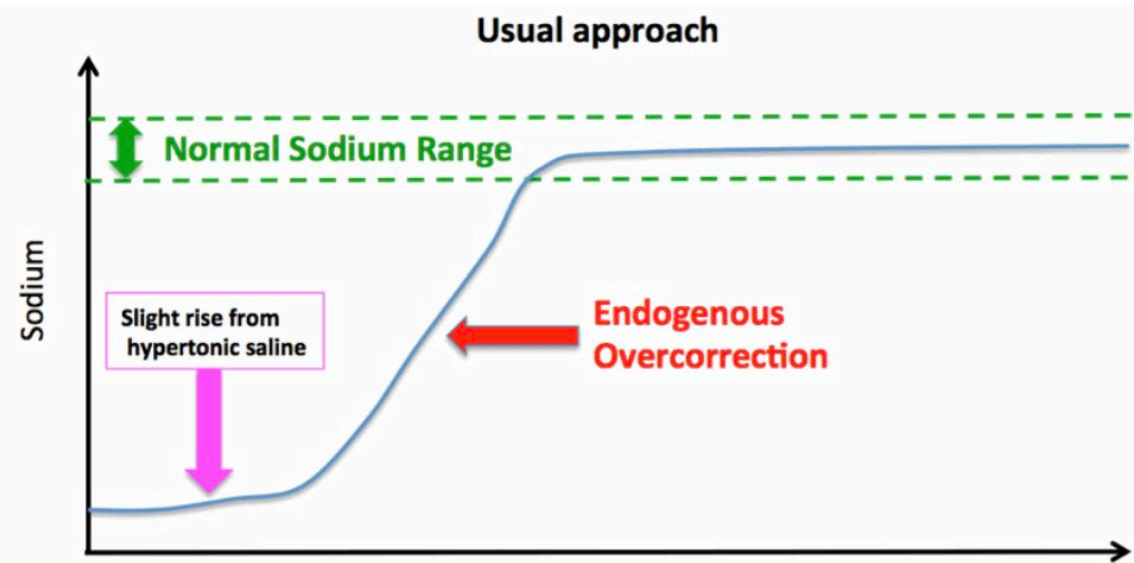
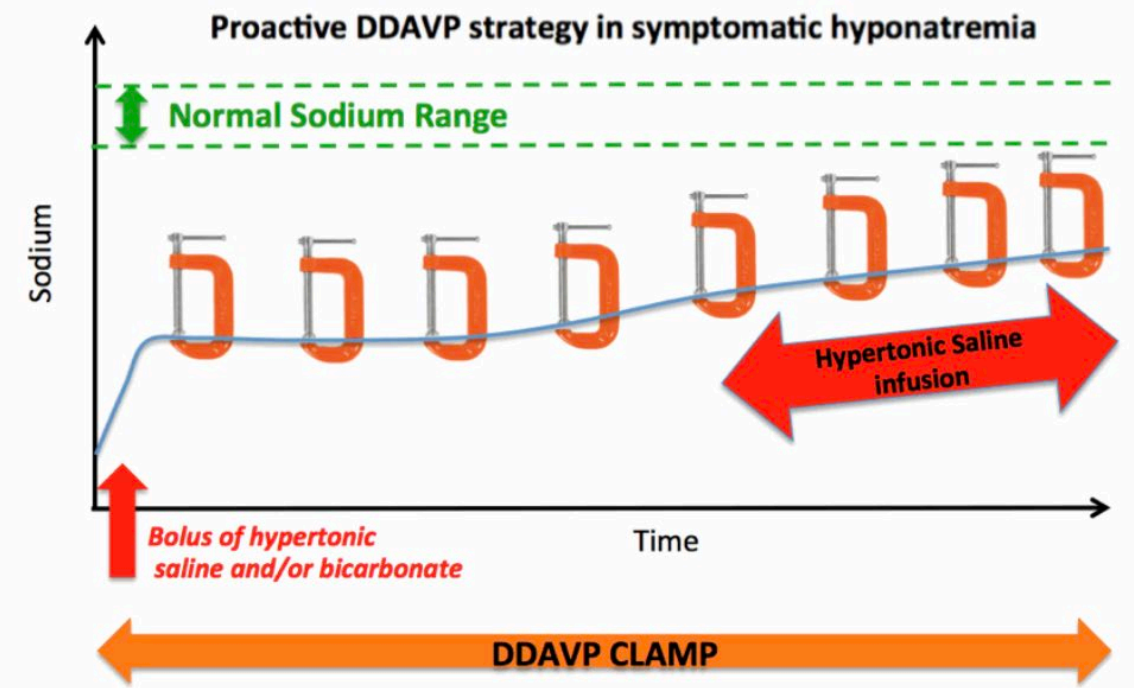


Proactive DDAVP Strategy

- DDAVP is started upon admission (2mcg IV q8h) and continued until sodium is close to normal
- Sodium is correct with hypertonic saline
- Oral intake is controlled/restricted

Sodium will be increased by the infused solution and not waiting on the kidney to let go of water.



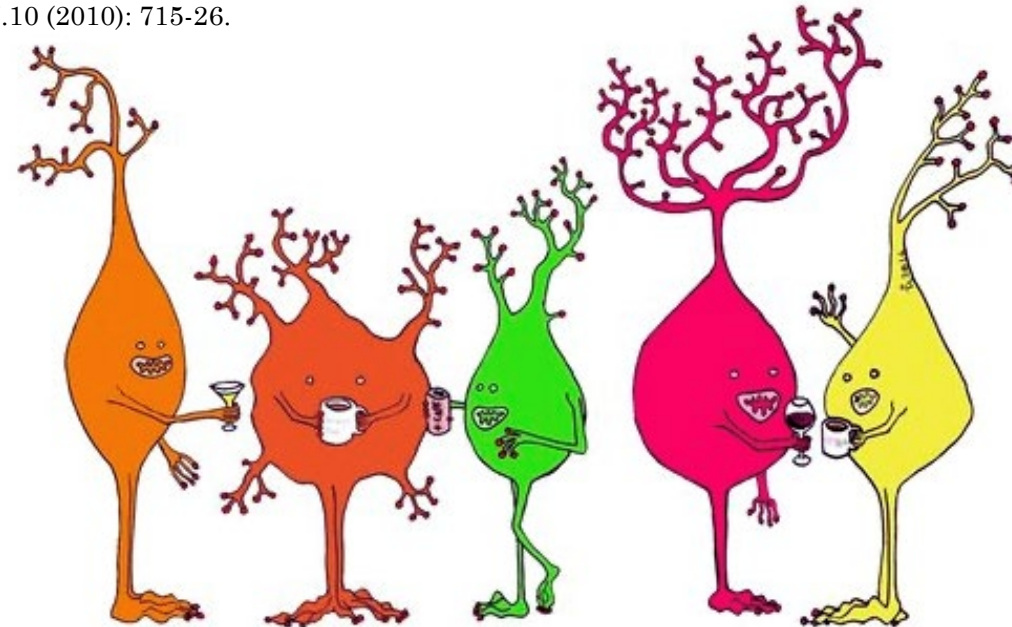


Thank you!



References:

- Adrogué HJ, Tucker BM, Madias NE. Diagnosis and Management of Hyponatremia: A Review. *JAMA*. 2022 Jul 19;328(3):280-291. doi: 10.1001/jama.2022.11176. PMID: 35852524.
- Barkas, Fotios, et al. "A step-by-step guide for the diagnosis and management of hyponatraemia in patients with stroke." *Therapeutic Advances in Endocrinology and Metabolism* 14 (2023): 20420188231163806.
- https://www.uptodate.com/contents/osmotic-demyelination-syndrome-ods-and-overly-rapid-correction-of-hyponatremia?search=osmotic%20demyelination%20syndrome&source=search_result&selectedTitle=1%7E38&usage_type=default&display_rank=1#H7
- https://www.uptodate.com/contents/overview-of-the-treatment-of-hyponatremia-in-adults?search=hyponatremia%20treatment&source=search_result&selectedTitle=1%7E150&usage_type=default&display_rank=1
- Lerner, David P., Starane A. Shepherd, and Ayush Batra. "Hyponatremia in the neurologically ill patient: a review." *The Neurohospitalist* 10.3 (2020): 208-216.
- Vaidya, Chirag, Warren Ho, and Benjamin J. Freda. "Management of hyponatremia: providing treatment and avoiding harm." *Cleve Clin J Med* 77.10 (2010): 715-26.



NEURAL NETWORKING