Breakout Session
Causes of Hyponatremia

I. Primary Intravascular Volume Depletion

A. Dehydration

B. Decreased "effective" intravascular volume

- Low urine sodium
- High AVP
Hemodynamic Regulation of Vasopressin

\[ P_{AVP} = 1.3e^{-0.17 \Delta VOL} \]

Dunn et al 1973 JCI
Isotonic vs. hypotonic fluid replacement in the dehydrated patient


Causes of Hyponatremia

I. Primary Intravascular Volume Depletion
   A. Dehydration
   B. Decreased "effective" intravascular volume

II. Primary Loss of Sodium Chloride
   A. Renal disorders
   B. GI disorders
   C. Cystic Fibrosis
   D. Cerebral salt wasting

Low urine sodium
High AVP
Causes of Hyponatremia

III. Primary Decreased Renal Water Excretion

A. Cortisol, thyroid hormone deficiency (may mask DI)

B. Excessive vasopressin (SIADH)
   1. Central nervous system (subarachnoid hemorrhage, meningitis?)
   2. Tumors (lung, thymus, pancreas, bladder, lymphoma)
   3. Drugs – (vincristine?, carbamazepine?, oxcarbazapine?, cyclophosphamide?, cisplatinum?)
   4. Idiopathic

C. Cerebral Salt Wasting

D. Constitutive activation of AVPR2
Nephrogenic Syndrome of Inappropriate Antidiuresis (NSIAD)

Diagnosis of Hyponatremia

- Evaluate volume status
  - Signs of dehydration
  - Routes for sodium loss
  - Peripheral edema or ascites
  - Other (e.g. positive pressure ventilation)
  - Urine sodium

- Evaluate for cortisol or thyroid deficiency

- Consider other factors which may decrease free water clearance (e.g. drugs)

- Consider SIADH
  - Blood vasopressin not useful (except for NSIAD)

- Consider cerebral salt wasting
Cerebral Salt Wasting

• First described in 1950

• Brain trauma associated with **hyponatremia** and:
  ✓ Hypovolemia due to natriuresis of NaCl
  ✓ High urine Na (>200 mEq/L)
  ✓ High levels of Atrial Natriuretic Peptide (ANP), BNP or CNP

• Treated with salt and volume replacement
Natriuretic Peptides

Heart Natriuretic

ANP

Heart Natriuretic

KRGFC-s-s-C

BNP

Diffuse Not Natriuretic

KLGFC-s-s-C

CNP

Secretion stimulated by volume expansion (atrial stretch)
Effect of Solute Load on Urine Volume at Constant Urine Osmolality

Cerebral Salt Wasting or SIADH?

- Brain injury → SIADH → Hyponatremia
- IV Saline 150 mEq/L, 4 L/day (1200 mOsm/day)
- Excrete $1200 \text{ mOsm} \times \frac{1 \text{ L}}{600 \text{ mOsm}} = 2 \text{ L}$ urine/day

Does this patient have cerebral salt wasting?

Criteria:

- Hypovolemia (studies of CWS? → normovolemic)
- High urine NaCl excretion, possibly high urine volume
- High BNP
Central DI unresponsive to AVP or too much NaCl?

- Brain injury → DI → Polyuria    Urine = 100 mOsm
- Treat with intravenous AVP (→ urine = 600 mOsm)
- IV Saline 150 mEq/L, 4 L/d (1200 mOsm/d)
- Excrete \[ \frac{1200 \text{ mOsm}}{\text{d}} \times \frac{1 \text{L}}{600 \text{ mOsm}} = 2 \text{ L urine/d, 3mL/kg/hr} \]

✓ Hypernatremia despite AVP treatment
✓ High urine volume and NaCl excretion
✓ “Patient not responding to AVP”
Emergency Treatment of Hyponatremia

• Only consider acute treatment if mental status is abnormal

• Acute onset
  ✓ 3% NaCl: 3 cc/kg, will raise serum sodium by ~3 mEq/L
  ✓ Will cause transient rise in serum sodium

• Chronic onset
  ✓ must correct serum sodium slowly, by no more than 0.5 mEq/L per hour
Central Pontine Myelinolysis
Chronic Treatment of Hyponatremia

- Correct underlying lesion
  - Rehydration
  - Attempt to treat congestive heart failure, nephrotic syndrome, cirrhosis
  - Treat cortisol or thyroid deficiency

- Water restriction

- For chronic SIADH
  - AVPR2 receptor antagonist: Aquaretics/Vaptans
  - Urea
AVP Receptor Antagonists

- **Vaptans, Nonpeptide Aquaretics**
  - Increase electrolyte-sparing water excretion
  - No effect on serum K+, Mg++, renal function

- **Tolvaptan (V2), CHF, SIADH, Oral**

- **Conivaptan (V1a, V2), CHF, IV**

- **Adults Only**
AVPR2 Antagonist in CHF

(#3) A Case of Hyponatremia

History of Present Illness

- 15-year-old previously healthy male
- 3 week-history of nausea and nonbilious, nonbloody emesis
- Denies abdominal pain
- Tonic-clonic seizure on day of admission, lasting ~5min
Review of Systems

- No increased thirst or polyuria
- Skin: Tanned but attributes it to having an outside pool at home where he has been most of the summer
Family History

- Type 1 diabetes in a paternal cousin
- Rheumatoid arthritis in the paternal grandmother
- Graves’ disease in maternal great-grandmother
Clinical Course

- Local ED: Post-ictal
- VS: HR 78  BP 84/47 R 24  T 97.6F
- Head CT without contrast: Negative for intracranial bleeding, mass or hydrocephalus
- Lab data
  - Na117 mmol/L
  - Cl 86 mmol/L
  - K 4.3 mmol/L
  - CO2 22 mmol/L
- Given normal saline, 15 cc/kg IV bolus and transported to our hospital
Clinical Course

- Local ED: Post-ictal
- VS: HR 78  BP 84/47  R 24  T 97.6F
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- Given normal saline, 15 cc/kg IV bolus and transported to our hospital
Clinical Course at Boston Children’s Hospital

- VS: HR 78   BP 95/54 R 20
  - Alert, tanned young man with normal exam

- Additional lab data
  - Na 114 mmol/L
  - BUN 22 mg/dL
  - Creatinine 0.4 mg/dL
  - Ca 9.2 mg/dL
  - Serum Osm 252 mOsm/Kg H₂O
  - Urine Osm 298 mOsm/Kg H₂O
  - Urine Na 53 mmol/L
Differential Diagnosis of Hyponatremia

- Dehydration?
  - Yes, but urine Na not low

- Decreased effective volume due to CHF, cirrhosis, etc?
  - No evidence for this by Hx or PE

- SIADH?
  - Urine Osm not very high

- Cerebral salt wasting?
  - No head injury; not polyuric, Urine Na not very high

- Other?
Differential Diagnosis of Hyponatremia (2)

- Urine Na 53 mmol/L in setting of dehydration
  - Intrinsic renal disease (normal BUN, creatinine)
  - Aldosterone deficiency
- Primary adrenal insufficiency
  - Tanned
  - Nausea, vomiting
  - Normal K
  - Cosyntropin stimulation
    - Cortisol 1.2 mcg/dL → 1.2 mcg/dL
    - ACTH 2,804 pg/mL
Hyponatremia with CNS insult

- 10 year-old male with hydrocephalus with VP-shunt. Presents to ED with headache and malaise.
- PE: agitated, HR: 56 BP: 144/76, moist mucosa, cap refill <2 secs
- Labs:
  - Na: 126 mmol/L; K: 4.4 mmol/L; BUN: 8 / Cr: 0.3
  - Serum osm: 236; Urine osm: 918; Urine Na: 86
- Diagnosis: SIADH
- Treatment: Fluid restriction to 1 L/m²/d (2/3 maintenance)