## Sodium

Drew Logan, DO  
Assistant Professor  
Internal Medicine Division of Hospital Medicine  
The Ohio State University Wexner Medical Center

### Normal Water Balance

- Approximately 9L of fluid enters GI tract daily
  - 2L by ingestion
  - 7L by secretion
  - 98% of this volume is reabsorbed
  - Fecal fluid loss ~100-200 mL/day

- Insensible water loss  
  - 500-650 mL/day

### Normal Water Balance

- Serum Na is dependent on total body Na + K and total body water: Serum Na = (TBNa + TBK)/TBW

- The body is able to maintain water balance despite variations in intake/losses by adjusting $U_{\text{osm}}$
  - Kidneys - maximally dilute urine (40-100 mOsm/kg) or maximally concentrated (900-1200 mOsm/kg) to maintain the balance

- Normal plasma osmolality 275-290 mOsm/kg

- ADH and RAAS/ANP

### Normal Water balance

- ADH synthesized within neurons of the hypothalamus
  - Distal axons project into posterior pituitary

- Osmoreceptor neurons and stretch-activated cation channels

- Osmolality >285 leads to release of ADH

- ADH acts on renal V2 receptors in the TALH and CD

- RAAS and ANP respond to changes in EAV resulting in retention or excretion of sodium in kidneys
HYPONATREMIA

- Plasma Na <135 mEq/L
- 22% of hospitalized patients
- Water in excess of kidneys' ability to excrete it (assuming normal kidney function)
  - ADH dependent mechanisms
    - If the urine osm > 100 mOsm/kg you can assume that some ADH is being released

Case

A 82 year old female presents to the Emergency Department for evaluation of a 1-day history of nausea, vomiting, weakness, confusion, and unstable gait. She has fallen several times today.

VS: 130/76, 68 without postural changes, 18, 97.2F
PE: Normal neurologic, cardiac, and pulmonary exam. No ascites or pedal edema.
Labs: Na 120, K 3.6, Cl 83, HCO3 27, Glucose 105, Serum Osm 255, Urine studies: Osm 408, K 32, Na 90

Which of the following is the most appropriate treatment?
A. 0.9% NS IVF
B. 3% saline IVF
C. Furosemide
D. Tolvaptan

Approach

- Clinical history (critical) and volume status
- Serum osmolality
- Serum glucose
- Serum uric acid
  - >4 mg/dL in hypovolemic
  - <4 mg/dL in euvolemic
- Urine Na, K, osmolality
Hypovolemic Hyponatremia

- Extrarenal losses
  - Vomiting, diarrhea, 3rd spacing, burns, pancreatitis, trauma
- Positive orthostatics, dry mucous membranes, diminished skin turgor
  - $U_{Na} < 20$
- Increase in ADH
  - Helps to preserve BP
  - Activation of V2 receptors, free water reabsorption
- Treatment
  - Isotonic saline – rapid reduction in ADH ➔ brisk water diuresis

Hypervolemic Hyponatremia

- CHF, Cirrhosis, Nephrotic syndrome
- TBW > TBNa
- Reduced EAV, increased ADH
  - $U_{Na} < 20$
- Treatment
  - Optimize tx of underlying cause
  - Urine:Plasma electrolyte ($U_{Na} + U_{K}/P_{Na}$)
    - $> 1$, aggressive fluid restriction (<500 mL/d)
    - $\sim 1$, fluid restriction (500-700 mL/d)
    - $< 1$, fluid restriction (<1000 mL/d)
- Loop diuretics
- Fluid restriction
- Tolvaptan

Euvolemic Hyponatremia

- SIADH (MC), drugs (i.e., SSRIs, NSAIDs), hypothyroid, glucocorticoid deficiency, stress/pain
- $U_{Na} > 20$
- Treatment
  - Urine:Plasma electrolyte ($U_{K} + U_{Na}/P_{Na}$)
    - $> 1$, aggressive fluid restriction (<500 mL/d)
    - $\sim 1$, fluid restriction (500-700 mL/d)
    - $< 1$, fluid restriction (<1000 mL/d)
  - Lasix 20mg PO bid + salt tabs
  - Demeclocycline (avoid)
  - Tolvaptan – V2 receptor antagonist
  - Liberalize fluid restriction
**Acute Symptomatic Hyponatremia**

- Typically develops over <48 hours
  - Thiazides, colonoscopy prep, MDMA
- Cerebral edema
  - GI complaints, lethargy, apathy, agitation, cramps, seizures, and coma
- Treatment
  - 3% saline (513 mEq/L of Na)
    - Usually started at 1-2 mL/kg/h
    - An increase in $S_{Na}$ by 5-6 mEq/L is sufficient to reverse herniation and reduce ICP by 40%

---

**Chronic Symptomatic Hyponatremia**

- Duration unknown or >48hrs
- Treatment
  - 3% saline (513 mEq/L of Na) until symptoms resolve
  - After symptom resolution, rate of correction should not exceed 0.5 mEq/L/h
    - Limit 8 mEq/L correction over 24hrs
    - Limit 18 mEq/L correction over 48hrs
  - Exceed limit, risk of osmotic demyelination syndrome (ODS)
    - D5W
    - dDAVP

---

**HYPERNATREMIA**

- Plasma sodium >145 mEq/L and osmolality >295 mOsm/kg
- Mortality rates as high as 40-60%
- Usually combined water and electrolyte deficient
  - Water loss > electrolyte loss
  - GI (osmotic, viral diarrhea) and insensible loss, osmotic diuresis, central/nephrogenic DI, hypercalcemia, hypokalemia
  - Iatrogenic
- Altered mental status, Rhabdomyolysis

---

**CASE**

An 80 year old woman presents to the Emergency Department from a nursing home for progressive lethargy. She has had constipation for 3 days and given several doses of lactulose. She subsequently developed persistent diarrhea for 24-48hrs. She has not taken any medications in 48hrs.

VS: 90/42, 117, 16, 97.7F
PE: Lethargic but arousable, dry mucous membranes, minimal skin turgor. Neuro, cardiac, pulmonary, abdominal exam otherwise normal.

Labs: Serum Na 158, K 4.1, Cl 109, HCO3 20, BUN 46, Cr 1.7, Ca 9.6, Glucose 220; Urine studies – spec gravity 1.020, osmolality 850.

Which of the following is the best initial therapy?

A. Desmopressin  
B. D5W IVF  
C. IV antibiotics  
D. 0.9%NS IVF
**Approach**

- Detailed clinical history and exam
- Serum osmolality
- Urine osmolality and electrolytes
  - Urine output <500 mL/d
  - Urine osmolality >800 mOsm/kg
- Calculate free water deficit
  - Men = 0.6 x weight (kg) x \([S_{Na}/140] – 1\]
  - Women = 0.5 x weight (kg) x \([S_{Na}/140] – 1\]

**HYPERNATREMIA**

- Treatment
  - Acute (<48hrs) vs chronic (>48hrs)
  - Estimate volume status
  - Identify and fix underlying cause
  - Free water replacement
    - PO or NG
    - IV D5W

**Hypovolemic Hypernatremia**

- Hypotonic fluid loss

**Treatment**

- Restore extracellular fluid with isotonic IVF
- Relative hypotonicity compared to plasma
- Once euvoletic, restore water deficit
- Hypotonic IVF (0.45% saline + D5 or D5W alone)

**Euvolemic Hypernatremia**

- Treatment
  - Polyuria with positive electrolyte free water clearance
  - Urine:Serum electrolyte \((U_{Na} + U_e/P_{Na})\)
    - <1, defect in urinary concentration
  - Central DI vs Nephrogenic DI
  - Central DI
    - Hx head trauma, neurosurgery, pituitary mass, evidence of anterior hypopituitarism, sarcoidism, kidney disease, medications (lithium)
    - 0.1-0.2 mg dDAVP
  - Nephrogenic DI
    - Lithium-induced - stop lithium or add amiloride if lithium continued
    - Non-drug induced – thiazide diuretic and salt restriction
Hypervolemic Hypernatremia

- Rare
- ICU setting
- TBNa > TBW
- Treatment
  - D5W + loop diuresis

References


Potassium and Calcium Disorders

Beth W. Liston, MD, PhD, FACP, FAAP
Associate Professor of Internal Medicine and Pediatrics
Director, Research and Scholarship
Division of Hospital Medicine
The Ohio State University Wexner Medical Center

Vignette #1

- You are on call for your practice group and the lab contacts you regarding a critical potassium value of 5.8. You do not know the patient, but know that you clearly need to investigate what is going on.
  - Na 141 K 5.8 Cl 99 Bicar 29 BUN 34 Cr 1.6 Glucose 166
As you prepare to review the chart, you remind yourself of the causes of hyperkalemia:
- Spurious
- Excess intake
- Medications
  - ACEi, ARB, spironolactone, Bactrim, beta blockers, NSAIDS, digoxin, heparins, calcineurin inhibitors

Renal disease, acidosis or hypoaldosteronism
- Chronic Kidney Disease
- Type 4 RTA
- Weird stuff (Addison’s, hyperkalemic periodic paralysis, tumor lysis, crush injury)

You review the chart and see this is a 62 year old male with a history of long-standing hypertension as well as a relatively new diagnosis of diabetes. Your partner had started him on a low-dose ACE-inhibitor and lasix for some lower extremity swelling.

You mentally shout AHA!
Hyperkalemia

- Treatment of hyperkalemia
  - Move it into cells
    - Albuterol, Insulin/Glucose, possibly bicarbonate
  - Renal Excretion
    - Increased renal perfusion, possibly lasix
  - GI excretion
    - Sodium Polystyrene Sulfonate

Hyperkalemia

- Ok, but is 5.8 dangerous? Do I need to call the squad?
- Shortening of QT interval, peaking of T waves
- QRS prolongation, shortening of PR interval, decreased P wave amplitude
- Onset of a wide-complex “sine-wave” ventricular rhythm
- Ultimately asystole

“ECG demonstrating hyperkalemia with absent P waves” by Ecgocardiology - Own work. Licensed under CC BY-SA 3.0 via Commons - https://commons.wikimedia.org/

Hyperkalemia

- EKG data is based on animal models
- Some correlation with higher potassium levels and EKG changes
- EKG changes are not sensitive or specific
- Our patient would be classified as mild hyperkalemia
  - Very common during initiation of ACE inhibitors


Hyperkalemia

- But this patient should be on an ACE or ARB right?
- New treatment options on the horizon:
  - Patiromer in Patients with Kidney Disease and Hyperkalemia Receiving RAAS Inhibitors
    - FDA approved Valtessa for the treatment of hyperkalemia October 15, 2015
  - Sodium Zirconium Cyclosilicate in Hyperkalemia
    - ZS-9 New drug application submitted for FDA approval July 29, 2015
Vignette #2

• You are seeing patients in an urgent care and triage has drawn labs on your next patient, who is presenting with generalized malaise. You note a K of 2.8.

• Prior to seeing the patient you review the possible causes of this finding.

Hypokalemia

• Movement into cells
  • Albuterol, insulin, alkalosis, increased cell production
  • Weird stuff (hypothermia, barium intoxication, antipsychotics, period paralysis)
• Decreased intake
  • Need only 5meq – 25 meq a day
• GI losses
  • Vomiting (alkalosis, increased aldosterone)
  • Diarrhea (direct K losses)

Hypokalemia

• Renal losses – remember the distal nephron
  • Diuretics, increased aldosterone activity
  • Polyuria, Type 1 or Type 2 RTA
  • Salt wasting nephropathies
    • (Liddle’s, Barter’s, Giddlemen’s)

Hypokalemia

• Diagnosis is almost always based on history
• EKG changes may occur
  • Complications are rare
• Check:
  • Urine potassium and acid-base status
  • TSH and cortisol
  • Oral supplementation
    • Consider magnesium
An elderly patient is brought into your office by her daughter for confusion. She is a breast cancer survivor who has largely been healthy except for some hypertension. She was in last week complaining of lower back pain.

There are no signs of infection and exam reveals a confused, dehydrated appearing lady without focal neurologic changes.

- Na 145, K 3.8, Cl 104, CO2 26, BUN 42, Cr 2.1
- Ca 12.7

“Bones, Stones, Groans, Thrones and Psychiatric Overtones”

Hyperparathyroid versus malignancy
- PTH and PTH-rp initially
  - Vitamin D levels
  - TSH, SPEP, UPEP, vit A, CXR

Hypercalcemia
- Albumin is 2.9

Corrected Ca mg/dl
- Ca mg/dl measured + 0.8(4.0 – albumin g/dl)
- 12.7 + 0.8(4 – 2.9) = 13.6 mg/dl

You recognize this as an emergency and send the patient to the hospital!

Unfortunately the ED calls you and seems confused about next steps in treatment. You gladly help them and order:

- IV hydration
  - Isotonic crystalloid boluses
  - Aggressive hydration to keep UOP > 100ml/hr
Hypercalcemia

- Calcitonin - 4 IU/kg to 8 IU/kg q6-12 hours
  - IM or Subcutaneous, intranasal less effective
  - Max effect of 2mg/dl after 4 hours
  - Tachyphylaxis after 48 hours
- Bisphosphonates
  - Zolendronic acid is most potent, 4mg IV over 15-30 minutes
- Other therapies:
  - Denosumab for refractory hypercalcemia
    - Approved in 2014
  - Prednisone if related to lymphoma or ovarian germ cell tumors
  - Cinacalcet

Future Directions:
- Infusions of PTH-rp antibodies

Vignette #4

- You are precepting a medical student who is telling you about a patient. She reports that the patient has a history of Grave’s disease and recently had a partial thyroidectomy. The patient’s main complaint is of peri-oral paresthesias. You ask the student to do additional physical exam maneuvers and check blood work:
  - Corrected calcium is 7.8 mg/dl.
  - You order PTH, creatinine, phosphate, magnesium and vitamin D levels

Hypocalcemia

- Hypocalcemia with low PTH
  - Surgical or autoimmune destruction
  - Genetic
  - Severe high or low magnesium
- Hypocalcemia with high PTH
  - Sepsis, pancreatitis
  - Vitamin D deficiency or resistance
  - PTH resistance
  - Hyperphosphatemia
Hypocalcemia

• Treatment:
  • Oral supplementation for > 7.5 if mild symptoms
  • Calcium Carbonate 1-4gm in divided doses
  • Calcitriol 0.25-0.50mcg initial
    • Titrate up to a range of 0.5mcg – 2mg for maintenance