sODIUM

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Normal Water Balance

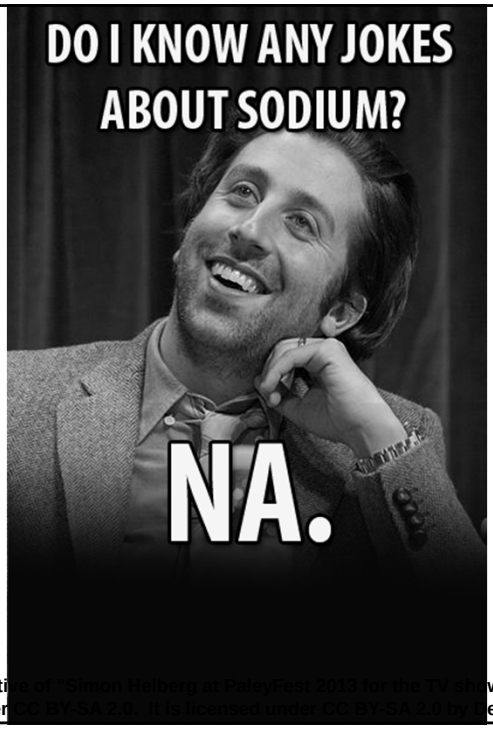
- **Approximately 9L of fluid enters GI tract daily**
  - **2L by ingestion**
  - **7L by secretion**
  - **98% of this volume is reabsorbed**
  - **Fecal fluid loss ~100-200 mL/day**
- **Insensible water loss**
  - **500-650 mL/day**

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_{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
- Osmorecepter 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



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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

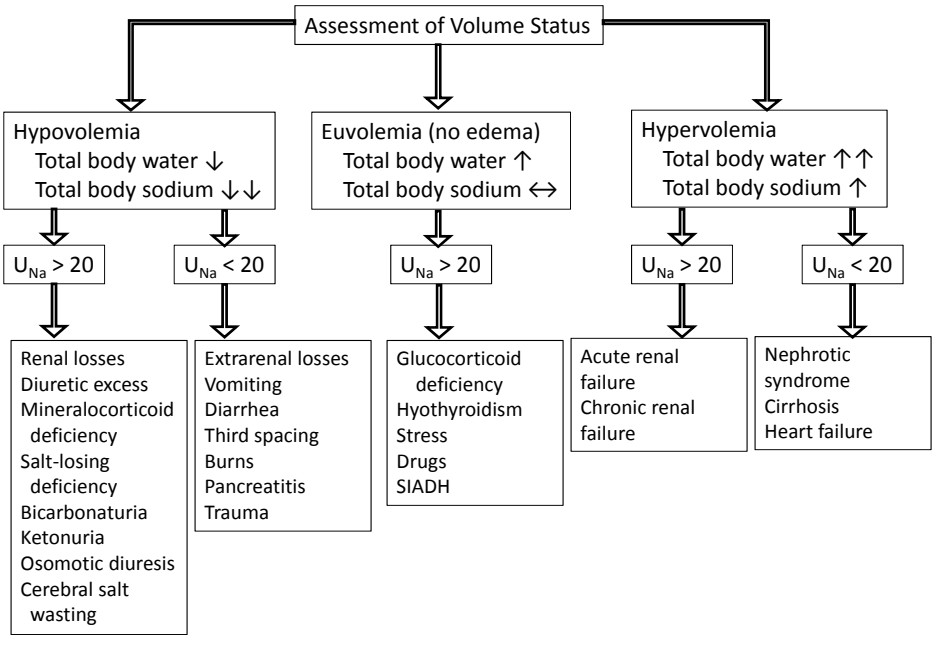
- **Extrarenal losses**
  - **Vomiting, diarrhea, 3rd spacing, burns, pancreatitis, trauma**
- **Positive orthostatics, dry mucous membranes, diminished skin turgor**
  - **U_{na} <20**
- **Increase in ADH**
  - **Helps to preserve BP**
  - **Activation of V2 receptors, free water reabsorption**
- **Treatment**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

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)**
    - **~1, fluid restriction (500-700 mL/d)**
    - **<1, fluid restriction (<1000 mL/d)**
  - **Lasix 20mg PO bid + salt tabs**
  - **Demeclocycline (avoid)**
  - **Tolvaptan – V_2 receptor antagonist**
    - **Liberalize fluid restriction**

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)**
    - **~1, fluid restriction (500-700 mL/d)**
    - **<1, fluid restriction (<1000 mL/d)**
  - **Loop diuretics**
  - **Fluid restriction**
  - **Tolvaptan**



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 euvolemic, 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_K/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

- **D.B. Mount et al. (eds.), *Core Concepts in the Disorders of Fluid, Electrolytes and Acid-Base Balance*, DOI 10.1007/978-1-4614-3770-3_2, © Springer Science+Business Media New York 2013**
- **Mount DB. Fluid and Electrolyte Disturbances. In: Kasper D, Fauci A, Hauser S, Longo D, Jameson J, Loscalzo J. eds. *Harrison's Principles of Internal Medicine, 19e*. New York, NY: McGraw-Hill; 2015. http://accessmedicine..mhmedical.com/content.aspx?bookid=1130&Sectionid=79726591.Accessed January 02, 2016.**

Potassium and Calcium Disorders

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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**

Hyperkalemia

- 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

Hyperkalemia

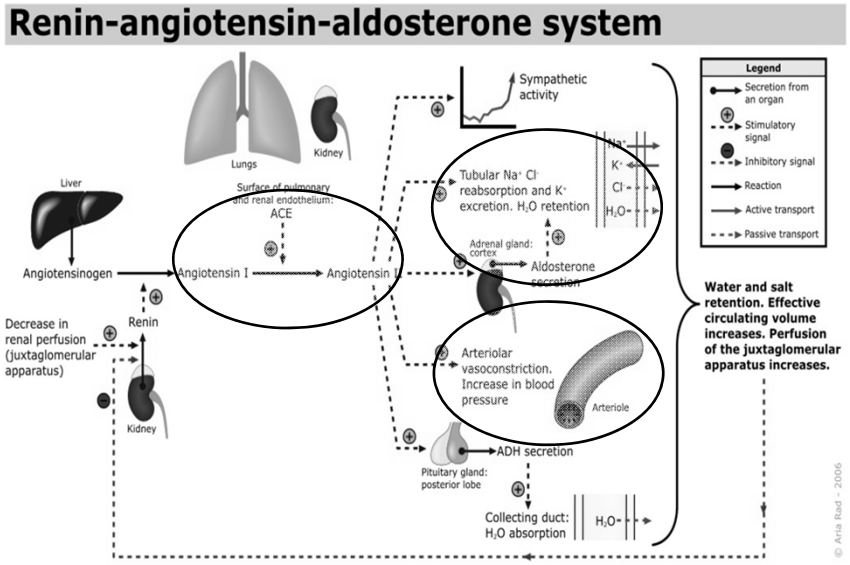
- Renal disease, acidosis or hypoaldosteronism
  - Chronic Kidney Disease
  - Type 4 RTA
- Weird stuff (Addison's, hyperkalemic periodic paralysis, tumor lysis, crush injury

Hyperkalemia

- **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



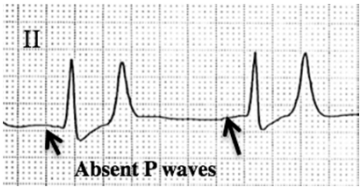
"Renin-angiotensin-aldosterone system" by A. Rad. Licensed under CC BY-SA 3.0 via Commons - https://commons.wikimedia.org

Hyperkalemia

- Treatment of hyperkalemia
  - Move it into cells
    - Albuterol, Insulin/Glucose, possibly bicarbonate
      - Batterink et al. Pharmacological interventions for the acute management of hyperkalaemia in adults. Cochrane Database Syst Rev. 2015 Oct 27;10:CD010344
  - Renal Excretion
    - Increased renal perfusion, possibly lasix
  - GI excretion
    - Sodium Polystyrene Sulfonate
      - Harel Z, Harel S, Shah PS, Wald R, Perl J, Bell CM. Gastrointestinal adverse events with sodium polystyrene sulfonate (Kayexalate) use: a systematic review. Am J Med. 2013 Mar;126(3):264.e9-24.

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 Ecgtocardiology - 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 intitiation of ACE inhibitors

- Montague, B, Ouellette, J, and Buller, G. Retrospective Review of the Frequency of ECG Changes in Hyperkalemia Clin J Am Soc Nephrol. 2008 Mar; 3(2): 324–330.

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
    - Wier, et al. N Engl J Med. 2015 Jan 15;372(3):211-21
    - FDA approved Valtessa for the treatment of hyperkalemia October 15, 2015
  - Sodium Zirconium Cyclosilicate in Hyperkalemia
    - Packham, et al. N Engl J Med 2015; 372:222-231
    - 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

Vignette #3

- **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**

Hypercalcemia

- **"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!**

Hypercalcemia

- **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 15-30minutes

Hypercalcemia

- 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

- Mirrakhimov AE1.Hypercalcemia of Malignancy: An Update on Pathogenesis and Management. N Am J Med Sci. 2015 Nov;7(11):483-93.
- Sternlicht H, and Glezerman IGHypercalcemia of malignancy and new treatment options. Ther Clin Risk Manag. 2015; 11: 1779–1788

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**