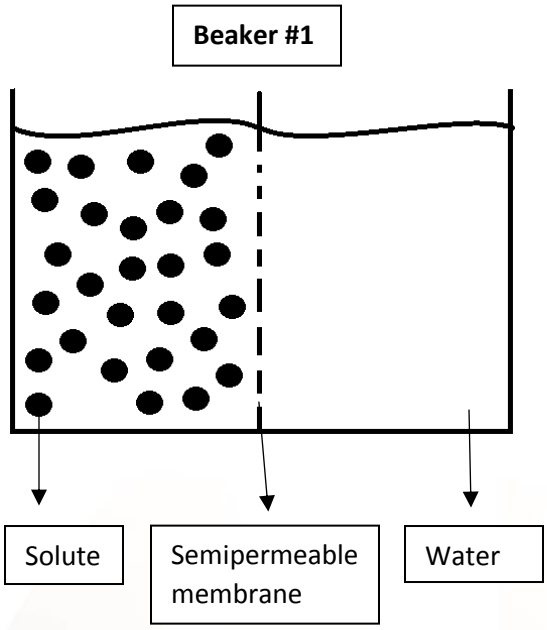
Hyponatremia AHD – Facilitator Guide
November 14th, 2019

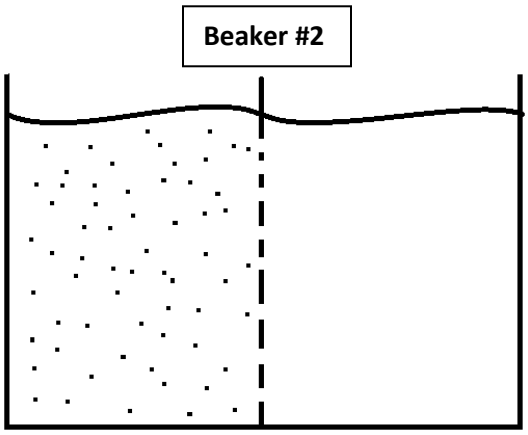
What is the difference between tonicity and osmolality?

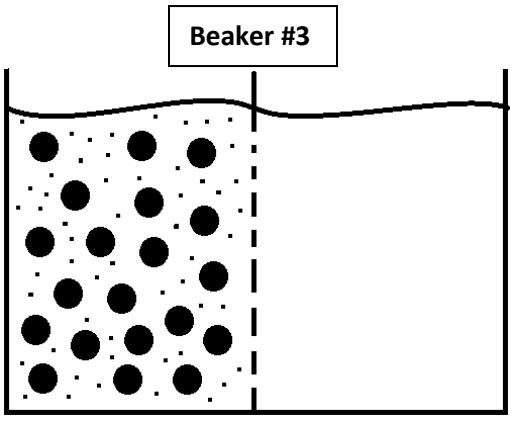
- Osmolarity simply depends on the concentration of all solutes
- Tonicity depends on the concentration of EFFECTIVE OSMOLES. These are solutes that cannot cross the semipermeable membrane and can cause a shift in water.

Let's explore this difference by taking a look at some examples. There are three beakers below, and each has two compartments separated by a semipermeable membrane that only allows small solutes to pass. A solute has been added to one compartment of each beaker.

Is the compartment on the left hyper-, iso-, or hypotonic relative to the compartment on the right? Is it hyper-, iso-, or hypo- osmolal? Predict how the solutes and water will shift in each example.







Beaker 1 – Hypertonic AND hyperosmolar, water will shift from right to left
Beaker 2 – Isotonic, hyperosmolar, solute will diffuse from left to right, but no shift of water
Beaker 3 – Hypertonic, hyperosmolar. Water will shift from right to left, and small solute will also diffuse

What are the main solutes present in serum? How do you calculate serum osmolality?

- Main solutes are sodium salts (NaCl, NaHCO3), glucose, and urea.
- Can get an approximation of serum osmolarity if we limit our calculation to those three solutes
- Calculated serum osm = 2 x [Na^+] (in mmol/L) + [glucose]/18 (in mg/dL) + [BUN]/2.8 (in mg/dL)
- Normal range is 275 – 295 mosmol/kg

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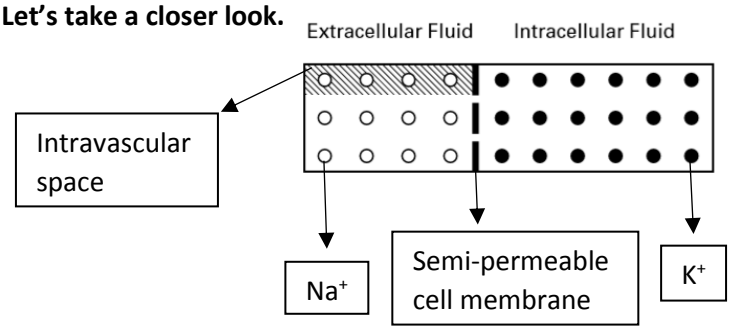
Are sodium, glucose, and urea effective osmoles? In other words, can differences in the concentrations across cell membranes cause a shift of water?

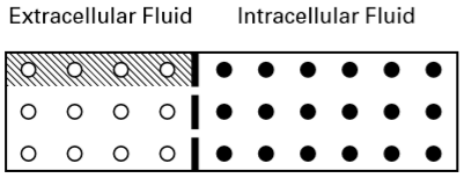
- Sodium and glucose are effective osmoles because cell membranes are relatively impermeable to these solutes. Urea can easily diffuse across cell membranes, thus it will not cause shifts of water.

Why the focus on tonicity? Hypotonic vs. hypertonic hyponatremia have different etiologies and different potential complications. Let's take a closer look.

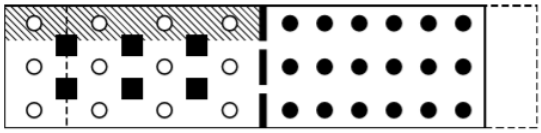
To the right is a patient with a normal renal panel. Glucose and urea are omitted in the diagram.



Scenario #1: What will happen if this patient's glucose is 800 instead of <100? Add ■ to the diagram to represent glucose. Will there be any other shifts?



- Extracellular fluid will become hypertonic
- Water will shift from intra- to extracellular space
- Dilutional hyponatremia results
- **HYPERTONIC HYPONATREMIA**

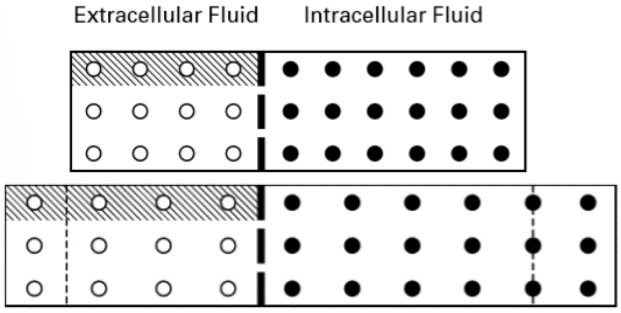


Will this patient be at risk for cerebral edema?

- No, water has flowed OUT of cells, not in. This is a significant difference between hypotonic vs. hypertonic hyponatremia.

Scenario #2: What will happen if a patient develops SIADH? Draw shifts onto the diagram

- Excess free water will dilute extracellular space making it hypotonic, and consequently water will shift into intracellular space.



Will this patient be at risk of cerebral edema? Yes

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The brain adapts to chronic hypotonicity (>48 hours) by losing intracellular solutes to approach the tonicity of serum. What will happen with rapid correction of chronic hyponatremia in brain cells?

- Water will shift out of cells. Cell will shrivel/shrink, and can develop osmotic demyelination syndrome.
- Overly rapid correction of HYPOTONIC hyponatremia can lead to osmotic demyelination

Is the patient in scenario #1 at risk of osmotic demyelination syndrome? How about scenario #2?

- Scenario #1 – No, cells never needed to adapt to hypotonicity, thus not at risk for ODS
- Scenario #2 – Yes, probably has chronic hyponatremia

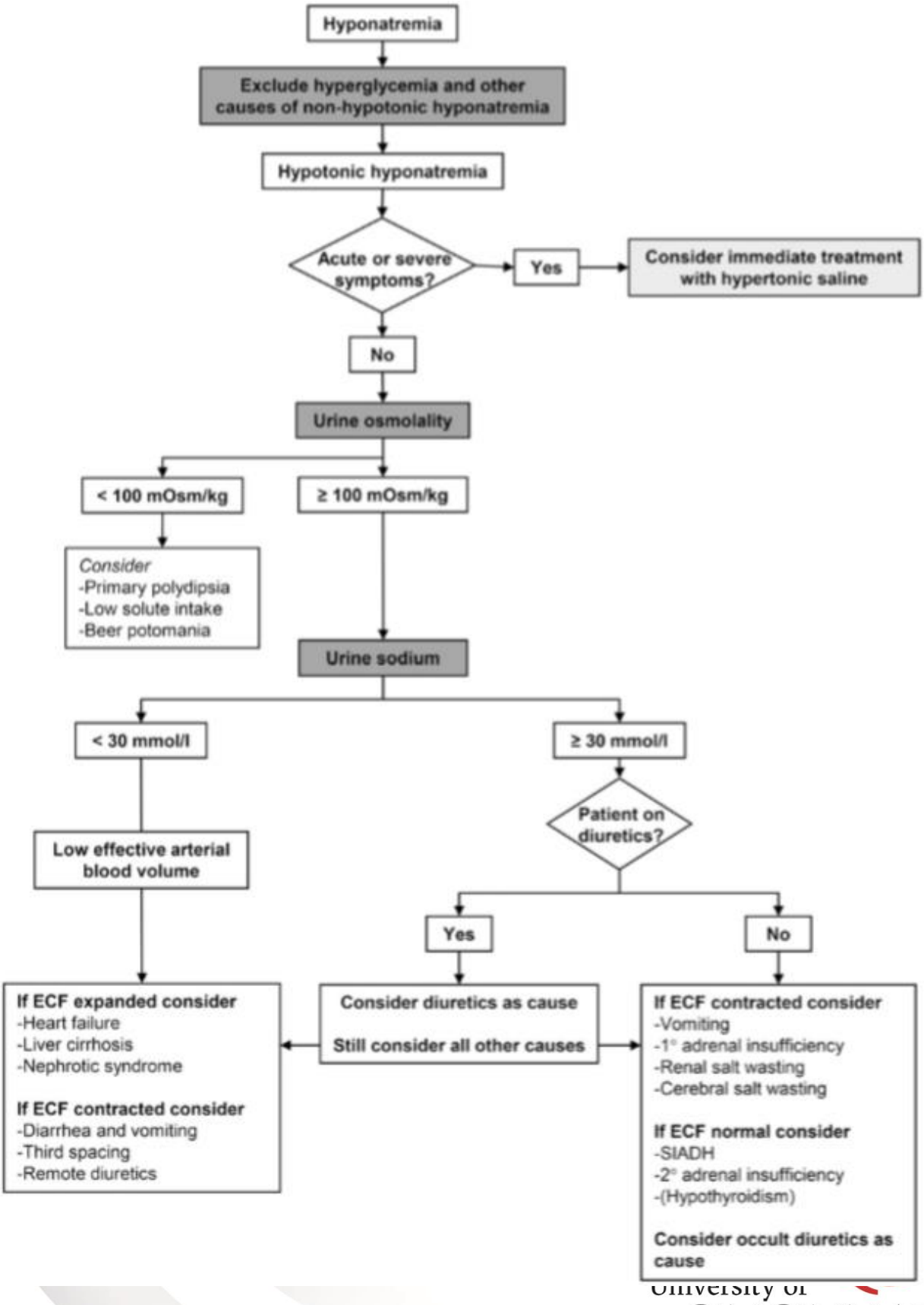
You've likely seen different algorithms to workup HYPOTONIC hyponatremia. While there may be slight variations (one on the next page), these algorithms usually include the following: exam findings, urine osmolarity, and urine sodium. Lets discuss how does each of those factors help you determine the etiology of hyponatremia.

- **Physical exam**
  - Edema, ascites? -> hypervolemia -> "low effective arterial blood volume" states such as heart failure, cirrhosis, and nephrotic syndrome
  - Orthostasis? Dry mucous membranes? Poor skin turgor -> hypovolemia
- **Urine osmolality**
  - Gives us insight into ADH activity
  - Urine Osm < 100 in the setting of hyponatremia -> appropriately suppressed AHD and production of dilute urine.
  - Urine Osm > 100 hints ADH activity greater than would be expected. The stimulus for this excess ADH activity may be "appropriate" such as in hypervolemia or hypovolemia or frankly "inappropriate" such as in SIADH.

- **Urine sodium**
  - Surrogate for volume
  - Tells us what the kidneys are "seeing." Low urine sodium (< 20-30) suggests the kidneys are trying to retain sodium in response to perceived hypovolemia/hypotension. This could be due to true hypovolemia or "low effective arterial blood volume" such as in HF.

In what instances is the urine sodium unreliable?

- Diuretics
- CKD (impaired ability to reabsorb sodium)
- Low sodium diet



Case #1

A 60 yo male with a PMH significant for HTN and CAD presents with nausea, vomiting, and abdominal cramps for 3 days. He also reports weakness and dizziness. He has been babysitting his granddaughter who has been home from preschool with similar symptoms. Medications include ASA, metoprolol, and simvastatin.

Vitals: T 98.9, BP 98/69, P 103, RR 18, SaO2 98% on RA.
General: Appears ill
HEENT: dry mucous membranes
Cardiac: regular rhythm, normal heart sounds
Abd: Diffuse tenderness without rebound or guarding. No distension
Msk: No peripheral edema.

Labs:

126 | 85 | 42 < 98 8.8 \ 16.3/ 383
3.6 | 26 | 1.6 /48.9

What type of hyponatremia is this? Why do you think this patient is hyponatremic?

- Hypotonic hyponatremia – [Na] + [glucose] + [BUN] = 272 mosmol/kg
- Although this may seem close to normal range, azotemia will raise osmolality without affecting tonicity
- Patients with AKI and azotemia may have a normal calculated serum osmolality but have hypotonic hyponatremia
- Hypovolemia secondary to viral gastroenteritis stimulating ADH release leading to free water reabsorption is etiology of hyponatremia

What do you predict this patient's urine osmolality and urine sodium will be?

- Urine osm > 100 mosm/kg due to stimulus for ADH release
- Urine Na < 20 due to hypovolemia

How will you treat this patient? How often will you check labs?

- General principals of treatment of hyponatremia
    - Goal to increase Na by 4-8 mEq/L MAX per day regardless of acuity
    - Try to achieve this in several hours if acute hyponatremia. Can achieve correction more slowly over 24 hours if chronic
    - < 48 hours – acute
    - > 48 hours – chronic
- Volume expansion with normal saline will treat hypovolemia and stop stimulus for AHD release
- Lab frequency likely ~q6h to start

Is this patient at risk for cerebral edema?

- Yes, but risk is overall low because his hyponatremia is moderate (120-129) and chronic

Is this patient at risk for osmotic demyelination syndrome if Na is corrected too quickly?

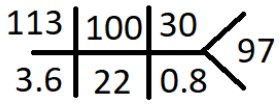
- Technically yes because he has hypotonic hyponatremia to which his brain is adapting, but overall risk is low because his hyponatremia is moderate

Case #2

A 68 yo man is brought in to the ED by his family for 3 days of worsening confusion and lethargy. He was brought in today because his family can hardly wake him up. He has no significant PMH, doesn't take any meds, and doesn't see any doctors. He has an 80 pack year history of smoking. His family notes that he has recently been coughing a lot, and at times coughs up blood. They also feel like he has lost a lot of weight and has had a poor appetite.

Vitals: T 98.9 BP 143/88 HR 88 RR 22 SpO2 98% on room air

HEENT: Moist mucous membranes
Cardiovascular: Regular rhythm, pulses normal, heart sounds normal
Pulmonary: Unlabored breathing. Wheezing in the right upper lobe, otherwise clear lung sounds
Abdomen: Soft, non-tender, non-distended.
Msk: No peripheral edema
Neuro: He requires physical stimuli to awaken, is oriented to self only, follows commands, but quickly becomes very drowsy without continued stimulus.



Urine osmolality 400, urine Na 32

What kind of hyponatremia does this patient have? What's on your differential?

- Hypotonic hyponatremia, calculated serum osm = 242
- Labs consistent with SIADH. History consistent with small cell lung cancer and subsequent SIADH. Additional differential includes hypothyroidism, and glucocorticoid deficiency

What do you predict would happen if this patient received 1 liter of normal saline in the ED?

- Remember that due to SIADH this patient will retain excess free water
- Handling of sodium in kidneys is regulated by aldosterone
- This patient has excess SIADH so free water from bolus would be retained while NaCl is excreted by the kidneys
- HYPONATREMIA WOULD LIKELY WORSEN
- With SIADH, administered fluid must be MORE CONCENTRATED than urine. Otherwise hyponatremia will worsen.
- Osmolality of normal saline is = 2 x 154 mEq/L = ~300 mosm/kg. This is less concentrated than the urine this patient is producing, administration would worsen hyponatremia

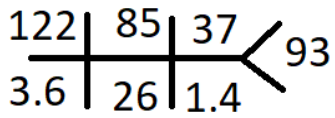
How do you treat this patient's hyponatremia?

- Emergently! – patient is having severe symptoms of hyponatremia which include obtundation.
- Given severe hyponatremia (Na < 120) and symptoms, high risk of seizure or herniation.
- Again goal is to raise Na 4-8 mEq total in first 24 hours, but for this patient the increase should occur within a few hours
- Boluses of hypertonic saline would be used (osmolality is ~1000 mosm/kg)

Case #3

A 65 yo male with a PMH significant for CAD s/p CABG 5 years ago presents with increasing dyspnea, fatigue, PND and edema.

Vitals BP 101/60 HR 100 RR 20 SaO2 88% on RA.
General: In no acute distress, but slightly tachypneic
Cardiac: regular rhythm, S3 present. Elevated JVD. 2+ pitting edema to mid-thigh bilaterally.
Pulmonary: Slightly tachypneic, speaks in full sentences. Bibasilar crackles
Abdomen: Soft, non-tender, non-distended.



How would you characterize this type of hyponatremia?

- **Chronic, hypotonic, hypervolemic**
- **Calculated osm = 262 mosm/kg**

Why this patient is hyponatremic. What do you predict this patient's urine osmolality and urine Na to be?

- Hypervolemia 2/2 HF
- Urine osm - >100 due to ADH stimulation due to low effective arterial blood volume
- Urine Na - < 20 due to the kidneys "seeing" hypovolemia/hypotension and attempting to augment volume

Etiology	What is happening here?
CHF	Decreased CO → Dec effective circulating volume → Dec GFR → Body perceives hypovolema → Inc ADH → Inc plasma free water
Cirrhosis	Peripheral vasodilation → Dec effective circulating volume → Dec GFR → Body perceives hypovolema → Inc ADH → Inc plasma free water
Nephrotic syndrome	Hypoalbuminema → Dec oncotic pressure →Dec. ECV → Dec GFR → Body perceives hypovolema → Inc ADH → Inc plasma free water
Advanced renal failure	Dec ability to adequately reabsorb sodium and moreso dec ability to excrete free water

What is the appropriate treatment?

- Free water restriction
- Mobilize excess sodium and water with loop diuretics

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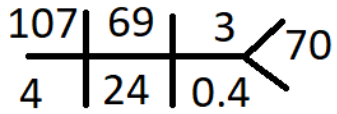
Case #4

A 52 yo male with a PMH significant for alcohol use disorder is brought in by his family because he has been confused and drowsy for the past 3 days. His family reports that the patient has had a problem with alcohol for years, and while he has had periods of sobriety, he has been drinking 30 cans of beer daily for weeks leading up to presentation. Patient reports abdominal pain, but it is difficult to get much more out of him.

Vitals: T 101.8 F BP 143/88 HR 99 RR 22 SpO2 98% on room air
General: Jaundiced. Disheveled, drowsy, malnourished
Cardiac: Regular rhythm, normal heart sounds, no edema
Pulmonary: Unlabored breathing, clear lungs
Abdomen: Soft, +hepatomegaly, right upper quadrant tenderness, non-distended
Msk: No peripheral edema
Neuro: He requires physical stimuli to awaken, is oriented to self only, follows commands, but quickly becomes very drowsy without continued stimulus.



AST 277	**WBC 14**	**urine osm 77 mosm/kg**
ALT 122	**Hgb 11**	**urine Na 15 mEq/L**
T bili 5	**Plts 113**	**Prothomrbin time 20 (normal = 12)**

What is on your differential?

- Learners should recognize this patient has the classic features of alcoholic hepatitis (fever, jaundice, appropriate LFT pattern, abdominal pain). Many other items, especially infectious etiologies may be reasonable.

How would you categorize this patient's hyponatremia? Why do you think this patient is hyponatremic?

- Hypotonic hyponatremia (calculated serum osm is 219 mosm/kg)
- Low urine osm + clinical history suggests low solute intake as etiology of hyponatremia

What is the treatment for this patient's hyponatremia?

- Emergently! – patient is having severe symptoms of hyponatremia which include obtundation.
- Given severe hyponatremia (Na < 120) and symptoms, high risk of seizure or herniation.
- Again goal is to raise Na 4-8 mEq total in first 24 hours, but for this patient the increase should occur within a few hours
- Boluses of hypertonic saline would likely be used

What additional treatment may this patient require?

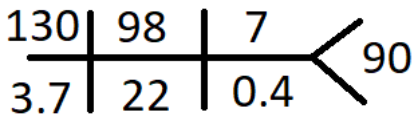
- Can calculate Maddrey discriminant function (42 for this patient), >=32 indication for steroids

Case #5

A 61 yo female presents for follow up 2 weeks after initiation of a medication for hypertension. She has no complaints and ROS is negative.

Vitals: Temp 98F BP 115/70 HR 83 sitting, RR 18 SaO2 98% RA
Examination is unremarkable

A renal panel is obtained:



What are the symptoms of hyponatremia we should ask this patient about?

- Generally non-specific – headache, malaise, nausea, lethargy.
- Severe symptoms would include altered mental status and seizures

Does this patient need to be hospitalized?

- Hospitalization usually recommended acute, severe, or symptomatic hyponatremia
- This patient's hyponatremia can be managed as an outpatient
- Mild- Na 130-134
- Moderate 120-129
- Severe < 120

What medication had you most likely prescribed this patient?

- Hydrochlorothiazide – thiazides are associated with hyponatremia

What do you think the urine Na is?

- Elevated due to diuretic use

How do you treat this patient's hyponatremia?

- Discontinue HCTZ

Sources

Adrogué, Horacio J., and Nicolaos E. Madias. "Hyponatremia." *New England Journal of Medicine* 342.21 (2000): 1581-1589.

Hoorn, Ewout J., and Robert Zietse. "Diagnosis and treatment of hyponatremia: compilation of the guidelines." *Journal of the American Society of Nephrology* 28.5 (2017): 1340-1349.