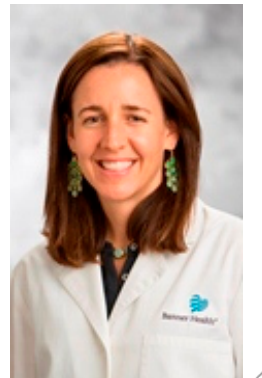


The nuts and bolts of hyponatremia in the hospital

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Disclosures

- No relevant commercial relationships to disclose.



Objectives

Recognize

Recognize the clinical significance of hyponatremia in hospitalized patients.

Become

Become familiar with a practical approach to differentiate between causes of hyponatremia in the hospital setting.

Understand

Understand the appropriate management of hyponatremia based on the etiology.



Why do we care?

- Hyponatremia is the most common electrolyte abnormality in hospitalized patients
 - Occurs in up to 10-30% of hospitalized patients
- Associated with increased morbidity and mortality as well as higher cost of hospitalization and rates of readmission
- Acute development or too rapid correction of chronic cases can have devastating outcomes



Definitions

- Plasma Na⁺ concentration <135 mEq/L
 - Mild: 130 – 134 mEq/L
 - Moderate: 120 – 129 mEq/L
 - Severe: < 120 mEq/L
- Duration of hyponatremia:
 - Acute: development within 48 hours
 - Chronic: present for > 48 hours; if duration is unclear, should be considered chronic



Key concepts

- Disorder of water balance
- Primary reasons for development of hyponatremia:
 - Water intake significant enough to overwhelm excretory capacity (rare, such as severe psychogenic polydipsia)
 - Excretion of water load taken in is impaired because of low GFR or persistent effects of ADH



Steps in evaluation

- How much time is there? (ie. is the patient symptomatic?)
- Rule out pseudohyponatremia, hyperglycemia
- Volume status?
 - Signs of volume depletion?
 - Signs of volume excess?
 - If euvolemic, reason for SIADH?
- Rule out diuretics, severe hypothyroidism, adrenal insufficiency
- Rule out poor solute intake (“beer potomania” or “tea and toast diet”)



Symptoms

Subtle symptoms	Mild symptoms	Severe symptoms
<ul style="list-style-type: none">▶ Gait abnormalities▶ Falls▶ Reduced concentration▶ Cognitive deficits▶ Increased osteoporosis and fractures	<ul style="list-style-type: none">▶ Nausea▶ Confusion▶ Headache	<ul style="list-style-type: none">▶ Vomiting▶ Cardiorespiratory distress▶ Abnormal and deep sleep▶ Seizures▶ Coma



Serum osmolality

- Determine serum osmolality
 - Normal (280 to 285 mOsm per kg) *RARE
 - Isotonic (pseudo) – hyperlipidemia or hyperproteinuria
 - High (>285 mOsm per kg)
 - Hypertonic – hyperglycemia most common
 - Low (< 280 mOsm per kg)
 - Hypotonic – most common; now assess volume status...



Pseudohyponatremia and hypertonic hyponatremia

- Vast majority of cases are hypotonic, but don't forget about isotonic and hypertonic...
- Pseudohyponatremia (isotonic)
 - Hyperlipidemia
 - Hyperproteinemia (ie. Multiple myeloma)
- Hypertonic hyponatremia
 - Hyperglycemia – calculate corrected Na
 - $\text{Measured Na} + 0.024 \times (\text{serum glucose} - 100)$, or
 - $\text{Measured Na} + 0.016 \times (\text{Serum glucose} - 100)$
 - Mannitol, sorbitol use or recent radiocontrast media



Hypotonic

- Volume status assessment, not always easy...
 - Consider vital signs, checking orthostatics, assess JVP, skin turgor/mucous membranes, peripheral edema, BUN levels
- Then check urine osmolality and urine sodium levels to help determine etiology



Hypotonic hyponatremia

Classification by volume status

Hypovolemia

- Total body water ↓
- Volume (total body sodium) ↓↓

Euvoolemia

- Total body water ↑
- Volume (total body sodium) ↔

Hypervolemia

- Total body water ↑↑
- Volume (total body sodium) ↑



Hypotonic hyponatremia

Hypovolemia

Extrarenal losses:

- Vomiting
- Diarrhea
- Pancreatitis
- Sweating
- Small bowel obstruction

Renal losses:

- Osmotic diuresis
- Cerebral salt wasting
- Salt-losing nephritis
- Diuretics
- Addison disease

Euvoemia

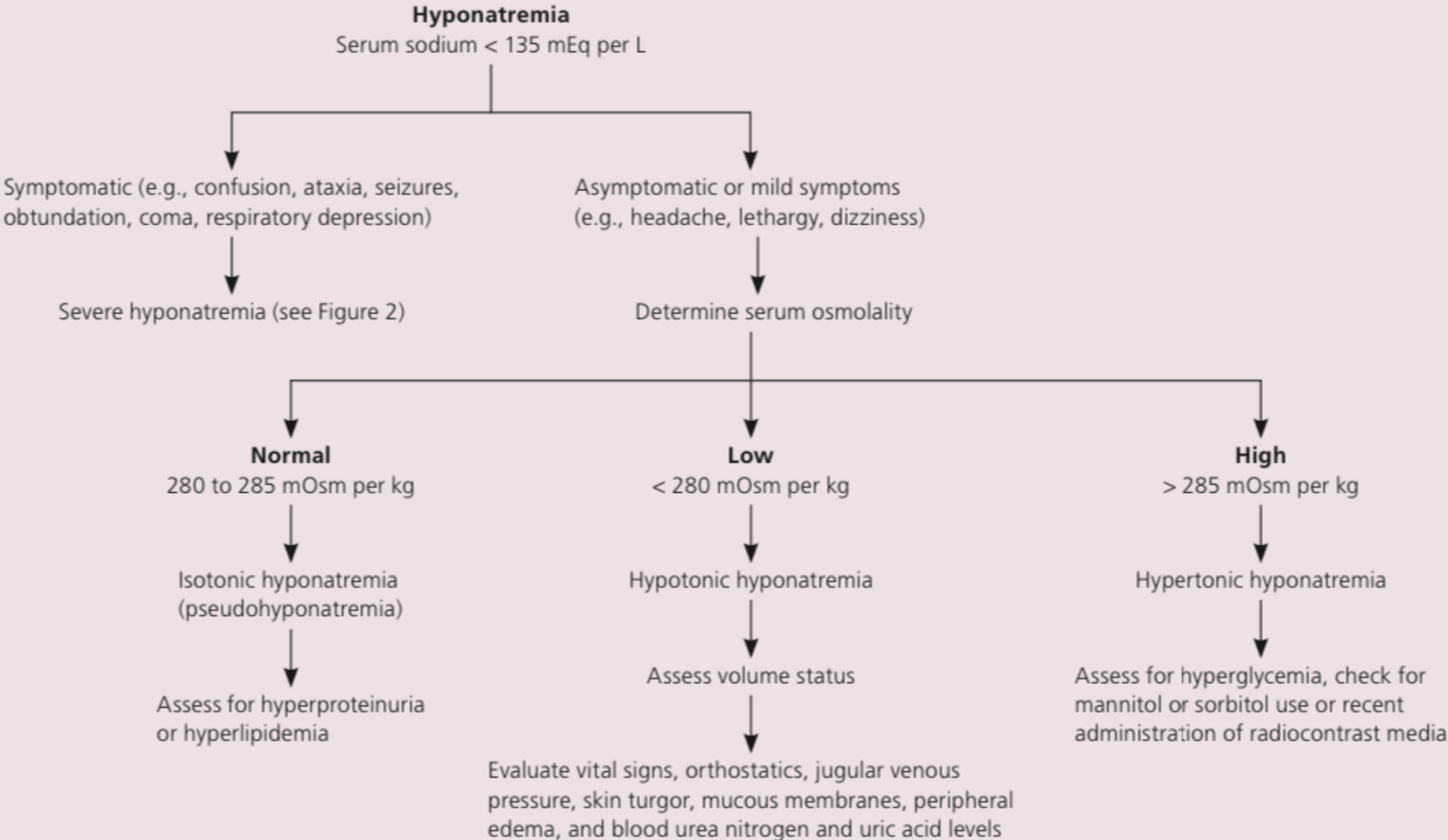
- Primary polydipsia
- Decreased solute excretion
- Diuretics
- Hypothyroidism
- Cortisol deficiency
- Syndrome of inappropriate antidiuretic hormone secretion

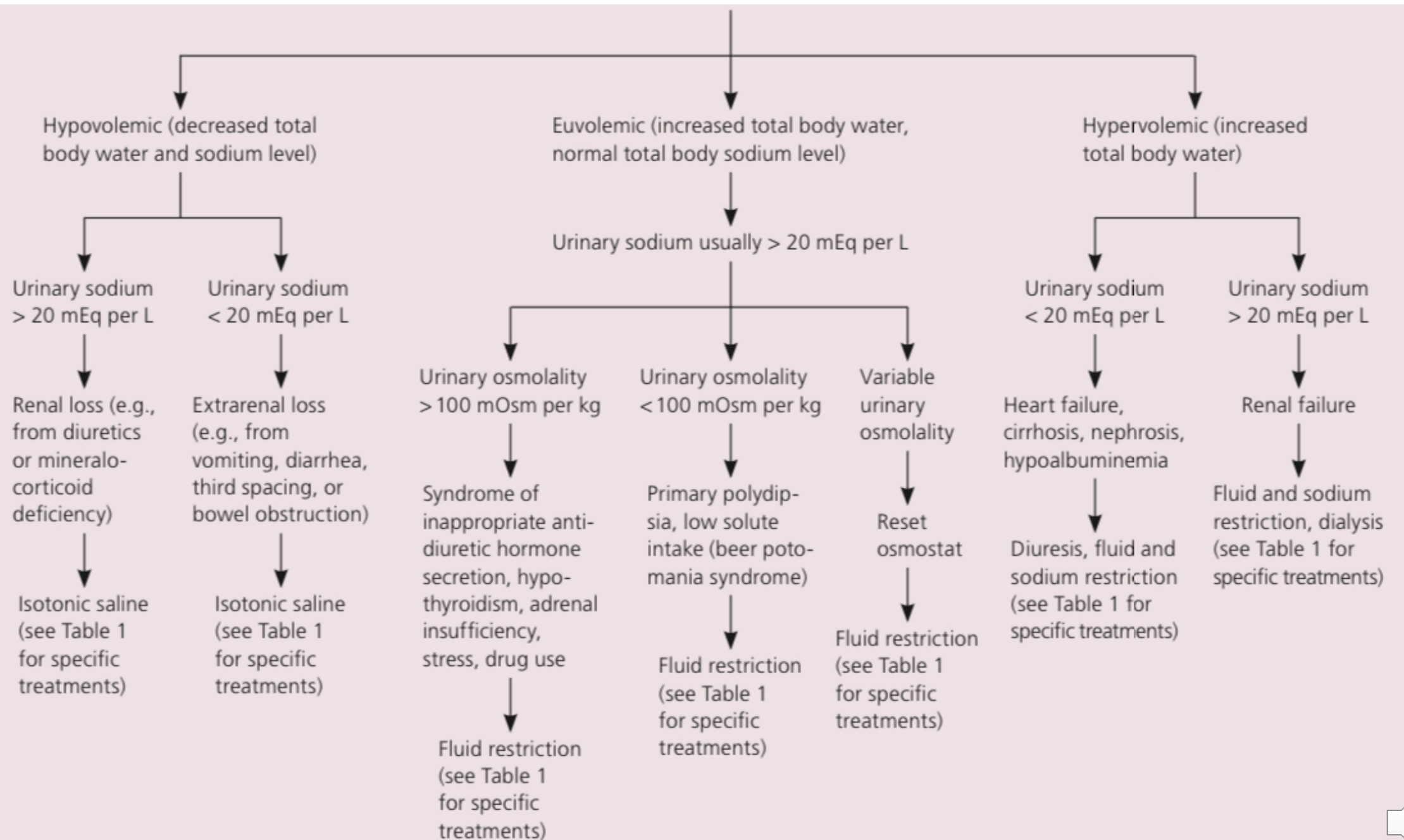
Hypervolemia

- Heart failure
- Cirrhosis
- Nephrotic syndrome
- Chronic kidney disease



Evaluation of Hyponatremia





Case #1

- 62 y/o F w/ PMH of hypothyroidism presents w/ 1 week of URI symptoms along w/ nausea and vomiting. PO intake has been minimal. She was brought in by family for worsening confusion.
- VS: BP 100/54, HR 101, confused, no edema, dry mucous membranes
- Labs at noon: Na 118 mEq/L, K 3.4 mEq/L, Serum Osm 250, BG 130, TSH wnl; urine Na 15 mEq/L
- Pt was bolused 2L NS in ED at noon
- Admitting hospitalist called by ED for admission ~5pm; orders stat BMP, asks night team to f/u as shift ends at 7pm



Case #1

- The patient was kept in the ED until 3am due to bed availability and the next Na level was not drawn until 4am morning labs, Na is 136
- Patient feels better, “back to normal”
- RN states patient has put out “liters of urine” and asks if she can be discharged today
- Are you concerned? What are the risks?



Osmotic demyelination syndrome (ODS)

- Brain edema is the concerning manifestation of hyponatremia
- Too rapid of correction of Na levels can result in ODS
- Na typically < 120 mEq/L at presentation
 - Additional RF: cirrhotic, OLTx patient, DI patient who has developed hyponatremia related to desmopressin and then desmopressin suddenly stopped, malnutrition, alcoholism, concurrent hypokalemia
- Current rate of correction recommendations:
 - Less than 6-8 mEq/L in 1st 24h and 18mEq/L in 1st 48h



Reversal of Na overcorrection

- With rapid overcorrection, therapeutic re-lowering of the plasma Na recommended if plasma Na <120 mEq per L, chronic (>48 hours) or unknown duration of hyponatremia particularly if RFs for osmotic demyelination syndrome
- Goal is to bring the plasma Na just under the correction limit
- Best accomplished by the coadministration of desmopressin and D5W
 - Desmopressin is given at a dose of 2–4 mcg IV or subcutaneously every 6–8 hrs
 - Halts further water diuresis
 - D5W IV infusion at a rate of 3 ml/kg per hr; will decrease plasma Na by ~ 1 mEq/L per hr



Case #2

- 58 y/o M with hx of HTN, HLP and ongoing tobacco use (35 pack year smoking history) presents with cough and occasional hemoptysis recently treated for community acquired pneumonia but without improvement in his symptoms.
- In the ED he was tachycardic and with O2 sat 90% on RA
- Concern for PE prompted a CTA chest which was negative for PE but revealed a hilar mass. He was admitted for work-up of lung mass.
- CBC, CMP were unremarkable aside from a Na level of 126.



Case #2

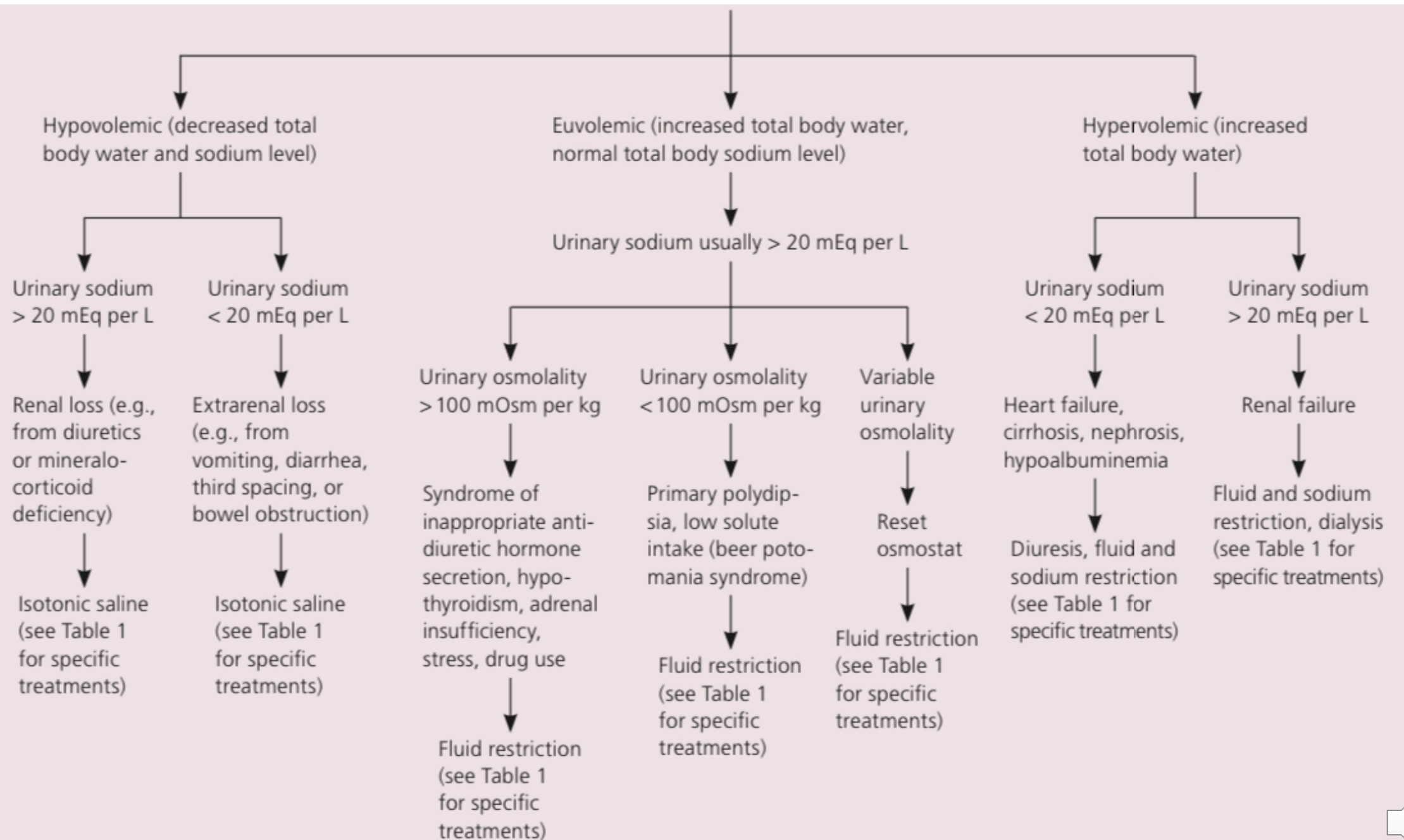
- You admit the patient and consult pulmonology to perform bronchoscopy for diagnosis.
- How do you manage the low sodium?



Case #2

- 1. Assess for symptoms
- 2. Look for prior lab values to see if this is new vs. chronic; has it been worked up previously?
- 3. Orders:
 - Serum osmolality – 275 mOsm per kg
 - Urine osmolality – 380 mOsm per kg
 - Urine sodium – 50 mEq/L
 - You also check TSH and am cortisol which are both wnl





SIADH

- CNS disturbances (but, don't forget cerebral salt wasting...)
 - CVA, hemorrhage, infection, trauma, psychosis
- Malignancies
 - Small cell lung CA, head and neck CA, extrapulmonary small cell CA
- Drugs
 - Chlorpropamide, carbamazepine, oxcarbazepine, cyclophosphamide, SSRIs
- Surgery
 - Potentially pain-mediated, transsphenoidal pituitary surgery
- Other: pulmonary disease (pneumonia), HIV, hereditary



SIADH

- 1. Treat the underlying disease
 - Hormone replacement for hypothyroidism or adrenal insufficiency
 - Treat infectious trigger
 - Stop offending drugs
- 2. Initial therapy to raise serum Na
 - Fluid restriction (<800 mL/day); *** except in setting of SAH (3% saline)
 - Oral salt tabs
 - Urea powder
 - Vasopressin receptor antagonists – tolvaptan – though with caution
- 3. Prolonged therapy with persistent SIADH



Case #3

- A 28 y/o F with brought to the ED because of confusion. She reportedly took 3,4-methylenedioxymethamphetamine (ecstasy) at a party. She reportedly has no medical problems and was previously well. On physical examination, the patient is confused and difficult to arouse. She mumbles her name.
- Lab work-up reveals: Na 118 mmol/L, K 3.5 mEq/L, Cr 0.8 mg/dL, bicarb 21 mmol/L, blood glucose 88 mg/dL
- What are your next steps?



Case #3

- Management of severe, symptomatic hyponatremia
 - IV bolus of 100 mL of 3% saline over 10 minutes, can be repeated with 2 additional 100 mL boluses if symptoms persist
 - Certainly the treatment for severe symptoms: seizure, coma, respiratory arrest; but some recommend giving for any symptoms that may be related to increased ICP (headache, nausea, vomiting)
 - Goal is to rapidly increase serum Na by 4-6 mEq/L over a few hours to relieve symptoms and prevent herniation
 - Once symptoms improve, the basal rate can be calculated with a goal rate of sodium correction of 6 to 8 mEq/L in 24 hours or 12 to 14 mEq/L in 48 hours
 - Several case studies showed osmotic demyelination syndrome can be avoided with this cautious rate of correction



Take home points

- Rule out hyperglycemia
- Look for symptoms
 - If symptomatic and severe, act fast with 3% saline
- If symptoms are mild, determine etiology
 - Volume down -> give volume
 - Volume up -> diurese
 - Check **urine osm** and **urine Na** to help determine cause
 - Rule out hypothyroidism, adrenal insufficiency
 - Don't correct too fast, and if you do, fix it



References

- Williams DM, et al. The clinical management of hyponatremia. *Postgrad Med J* 2016;92:407–411. doi:10.1136/postgradmedj-2015-133740
- Henry, D. In the clinic: hyponatremia. *Annals of internal medicine* 2015.
- *Braun M, Barstow, C, Pyzocha N.* Diagnosis and Management of Sodium Disorders: Hyponatremia and Hypernatremia *Am Fam Physician*. 2015 Mar 1;91(5):299-307.
- *Kumar S, Berl T: Diseases of water metabolism. In: Atlas of Diseases of the Kidney, Vol I, Schrier RW [ed]. Philadelphia, Current Medicine, Inc, 1999*

