HYPONATREMIA

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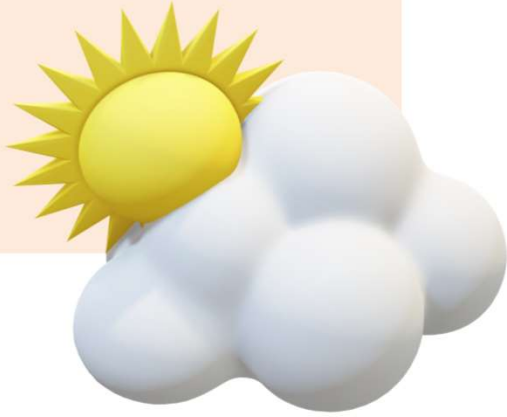
SUMS

INTRODUCTION

- Hyponatremia is a water and electrolyte abnormality frequently observed in the general population
- Hyponatremia can result from various etiologies, ranging from the most common such as (SIAD) and medication-induced hyponatremia, to the less common etiology such as salt-losing nephropathy
- It is not appropriately diagnosed or effectively treated by clinicians.
- Not only acute hyponatremia but also chronic mild symptomatic hyponatremia are associated with unfavorable outcomes.



Sodium concentration and sodium content

Two related but different concepts

- Dysnatremia occurs when electrolyte free water becomes excessive or insufficient relative to the Na content in the ECF.
- It can occur regardless of the total body Na content

Hyponatremia can develop with any ECF volume status or Na content & dysnatremia is a disorder of water balance in the body

Definition and terms

Serum sodium < 135 mq/L

severity

- Mild: Na between 130-134
- Moderate: Na between 120-129
- Severe: Na <120

duration

- Acute hyponatremia: <48 hours
- Chronic hyponatremia:>48 hours

Classification of hyponatremia

SNa concentration			
Mild	130–134 mmol/L	Mild	Mild
Moderate	125–129 mmol/L	Moderate	Moderate
Severe[a]	< 125 mmol/L	Profound	Severe
Severity of clinical symptoms			
Asymptomatic-Mild	Less pronounced	Mild	Mild
Moderate	Nausea without vomiting, confusion, headache, drowsiness, general weakness, myalgia	Moderately severe	Moderate
Severe[a]	Vomiting, stupor, seizures, coma (Glasgow Coma Scale ≤ 8)	Severe	Severe
Time of development			
Acute	< 48 hours	No difference	
Chronic	≥ 48 hours	No difference	
Serum osmolality			
Hypotonic	< 275 mOsm/kg	No difference	
Isotonic	275–295 mOsm/kg	No difference	
Hypertonic	> 295 mOsm/kg	No difference	
Clinical assessment of volume status			
Hypovolemic, euvolemic, hypervolemic		No difference	

Tonicity Vs osmolality

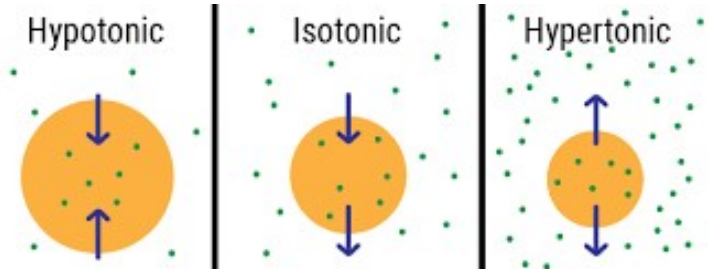
- Serum osmolality measures all osmoles in the serum (in Lab)

Calculated serum osmolality = (2 x SNa) + (Glu ÷ 18) + (BUN ÷ 2.8)

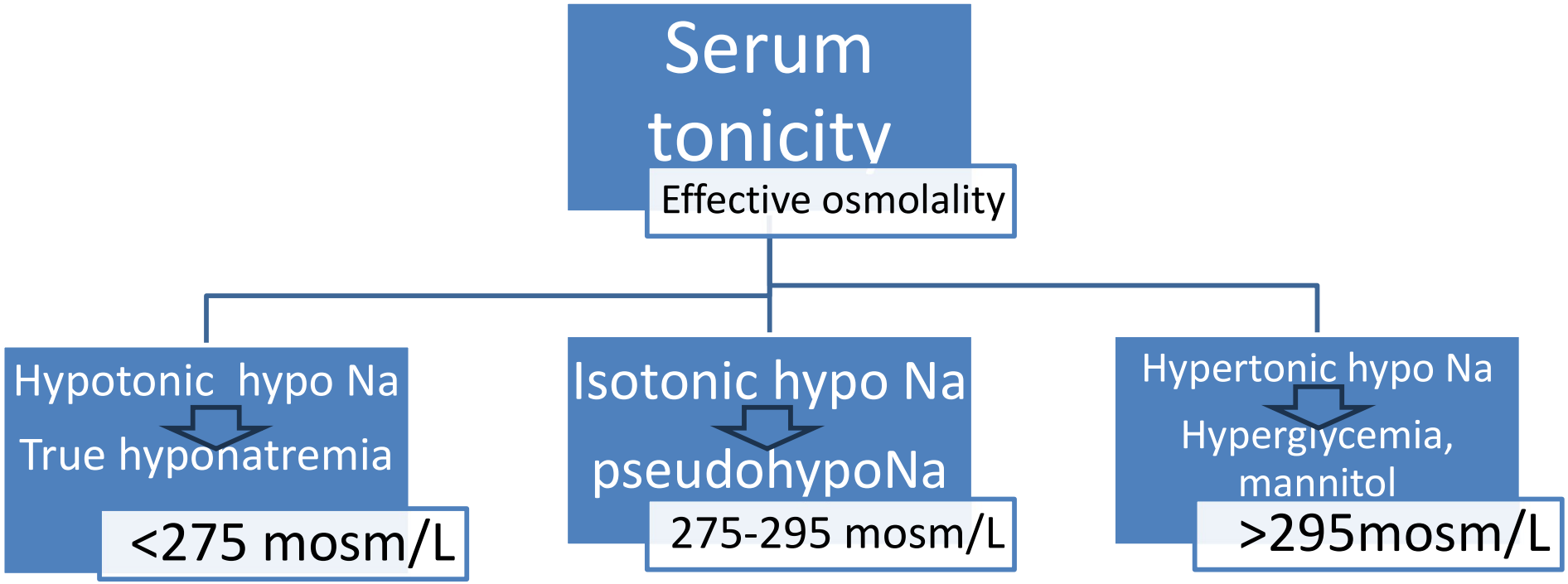
- Serum tonicity is the **effective** plasma or serum osmolality (the concentration of solutes that do not easily cross the cell membrane)

Serum tonicity = 2 × [Na] + [glucose]/18

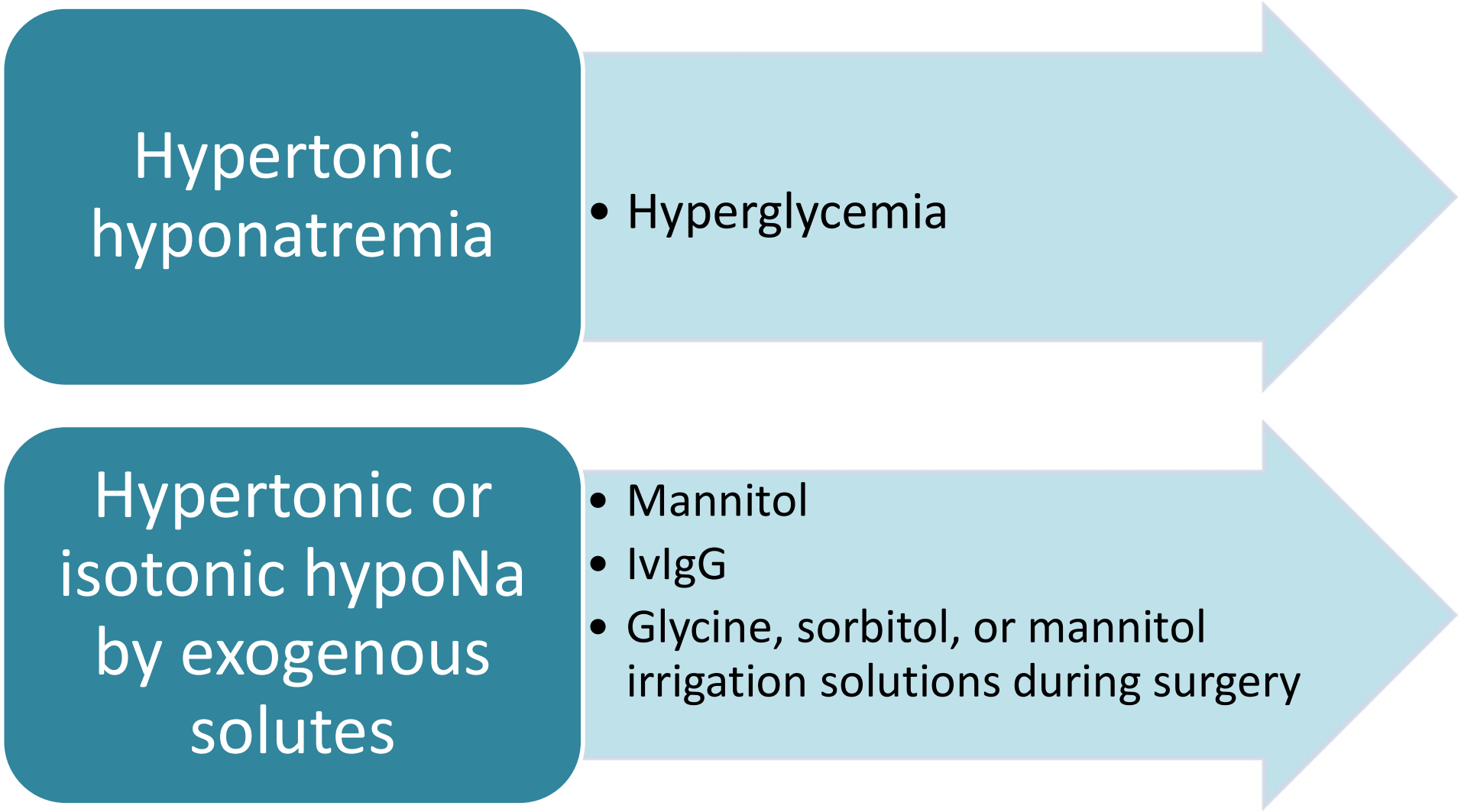
- The measured serum osmolality can sometimes be misleading, suggesting a diagnosis of hypertonic hyponatremia in patients with uremia or alcohol consumption



HypoNa and serum tonicity

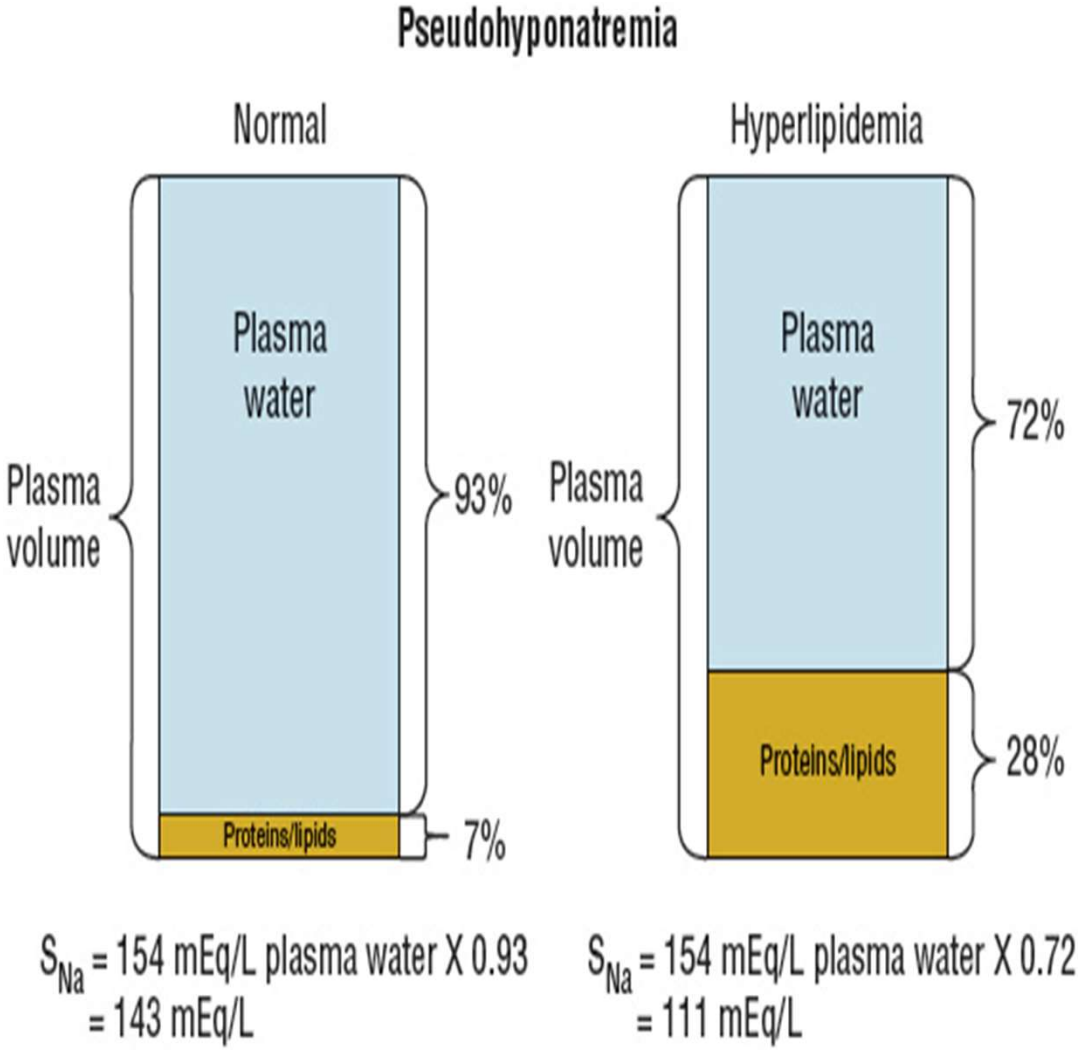


Hyponatremia without hypotonicity



Pseudohyponatremia

- Each liter of plasma contains approximately 930 mL of water
- Sodium concentration of 143 mEq/L of plasma or serum is equivalent to a concentration of 154 mEq/L of plasma water (154 x 0.93 = 143).



Causes of pseudohyponatremia

Lipemic serum

DKA

pancreatitis

Obstructive jaundice

High cholesterol

High lipoprotein X

Plasma cell dyscrasia:MM

hyperproteinemia

Evaluation of hyponatremia

History and physical exam

- ✓ **Fluid loss** (eg, vomiting, diarrhea, and diuretic therapy)
- ✓ **Anuria or oliguria** may be indicative of severe renal impairment with an inability to excrete free water
- ✓ Conditions or medications associated with **unsuppressed antidiuretic hormone (ADH) secretion** ([SIADH]) including brain injury or infection, pulmonary disease
- ✓ **Excess water intake**, especially in a child with psychiatric disease
- ✓ **Excess salt loss** can be seen in disorders with increased renal or skin loss
- ✓ **Edema and ascites with signs of reduced elective circulating volume** (ECV)
- ✓ Review medications

Basic laboratory testing

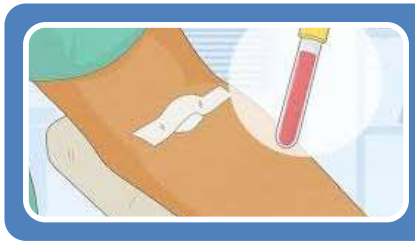
initial assessment is sufficient to determine the cause of hyponatremia in most cases

- ✓ Blood glucose
- ✓ Serum blood urea nitrogen (BUN) and creatinine
- ✓ Plasma/serum potassium
- ✓ Urine dipstick

urine osmolality of 280 mosmol/kg is equql to SG of 1.008 or 1.009.

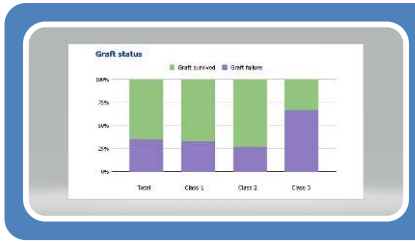
Release of ADH is associated with a urine S G ≥1.008.

Step by step diagnostic approach



STEP ONE:

- Check plasma osmolality



Step two:

Evaluate the severity of clinical symptomatic hyponatremia

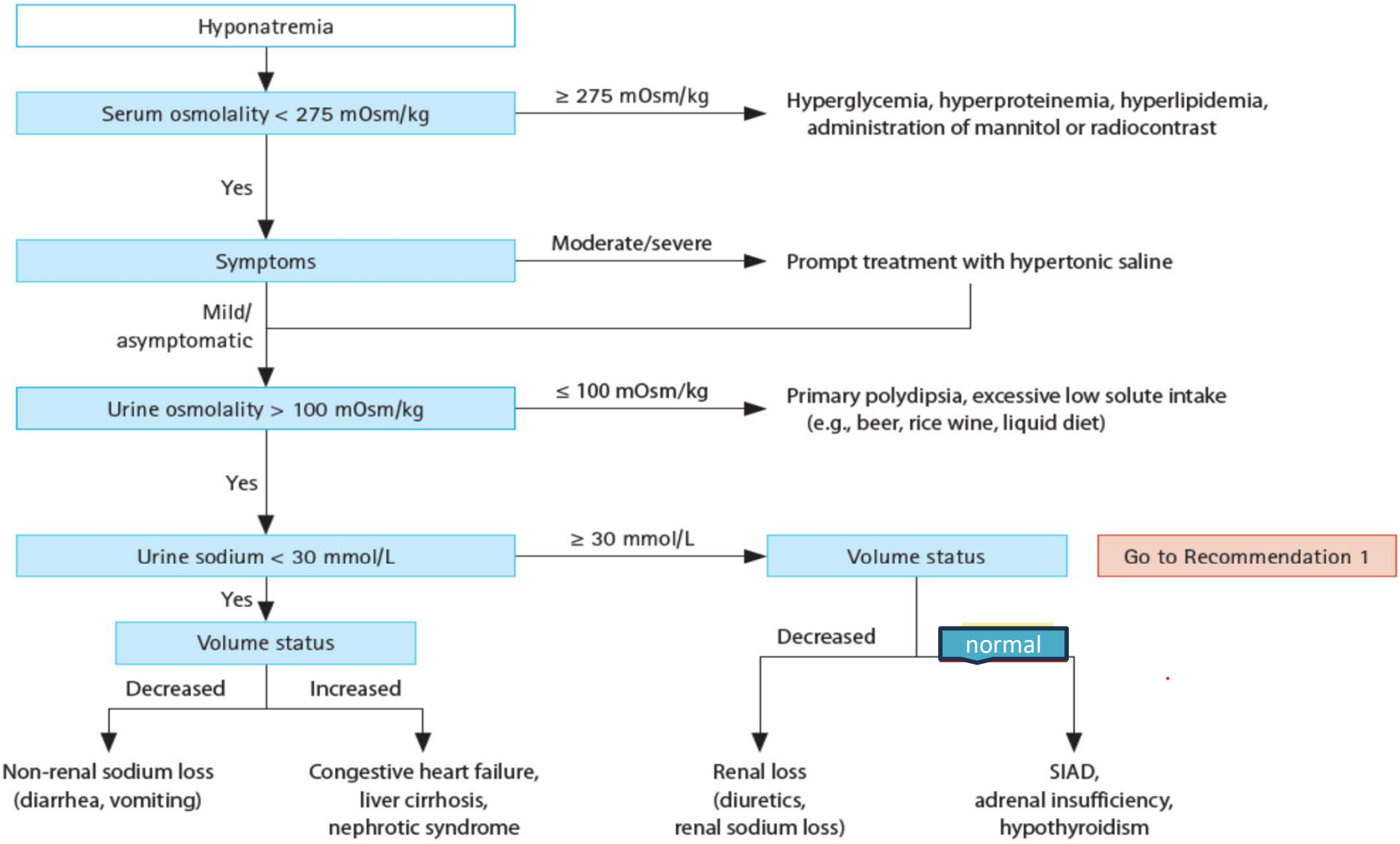
Step three:

Check urine osmolality

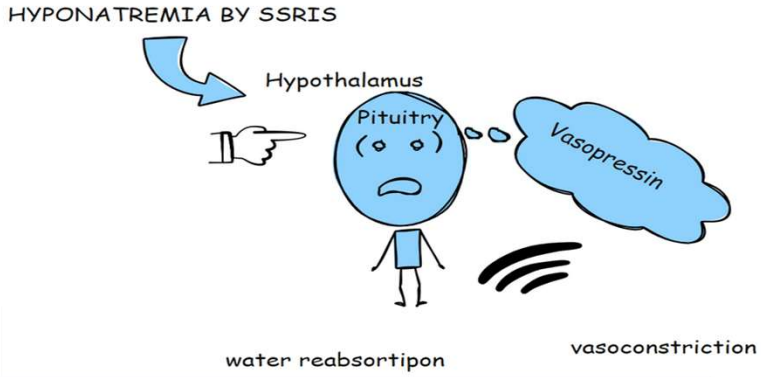
Step four:

Check urine sodium

Algorithm for diagnosis of hyponatremia



SIADH



- ✓ AVP is said to be “inappropriately” secreted
- ✓ despite the absence of osmotic stimuli and normal ECF
- ✓ central nervous system diseases, pulmonary diseases, malignancies, and medications are well-known causes of SIADH
- ✓ Serum UA of < 4 and FEUA of > 10–12% supports the presence of SIADH
- ✓ Copeptin can be used to estimate the amount of AVP secreted
- ✓ Copeptin is a hormone secreted into the blood by the cleavage of its precursor, pre-pro-vasopressin, into three peptides—AVP, neurophysin II, and copeptin

Criteria of SIADH

I. Main symptoms	No findings of ECF volume depletion
II. Laboratory data	1. Serum $[Na^+] < 135$ mmol/L
	2. $P_{Osm} < 280$ mOsm/kg H_2O
	3. Despite hyponatremia and hypoosmolality, plasma AVP concentration is not suppressed
	4. $U_{Osm} > 100$ mOsm/kg H_2O
	5. Urine $[Na^+] > 20$ mmol/L
	6. Normal renal function
	7. Normal adrenocortical function
	8. Normal thyroidal function

Definitive diagnosis: all of I and II are met

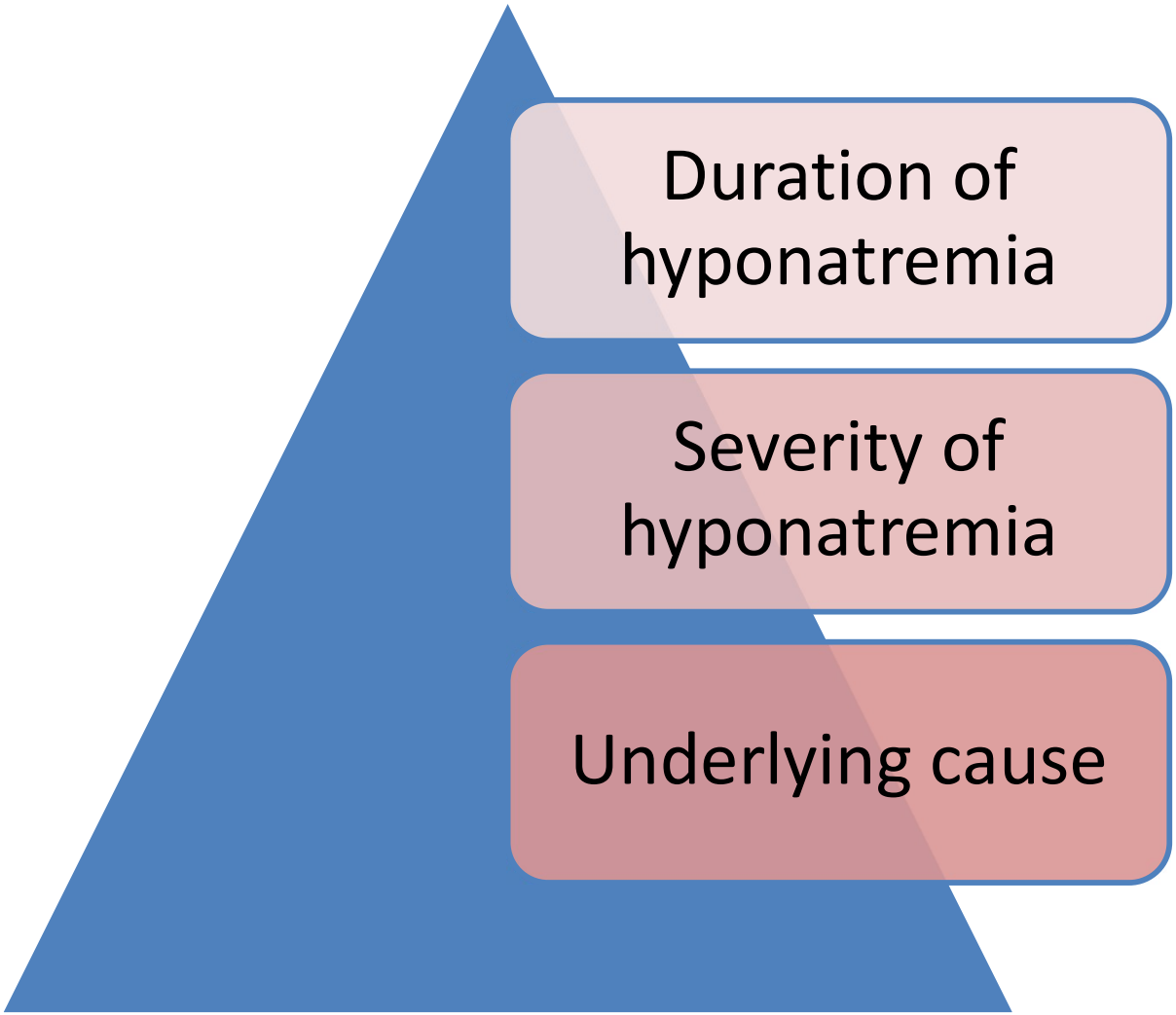
Treatment goals

Avoid too rapid correction to prevent (CNS) complications

Relieve the symptoms of hyponatremia

Prevent a further decline in sodium concentration

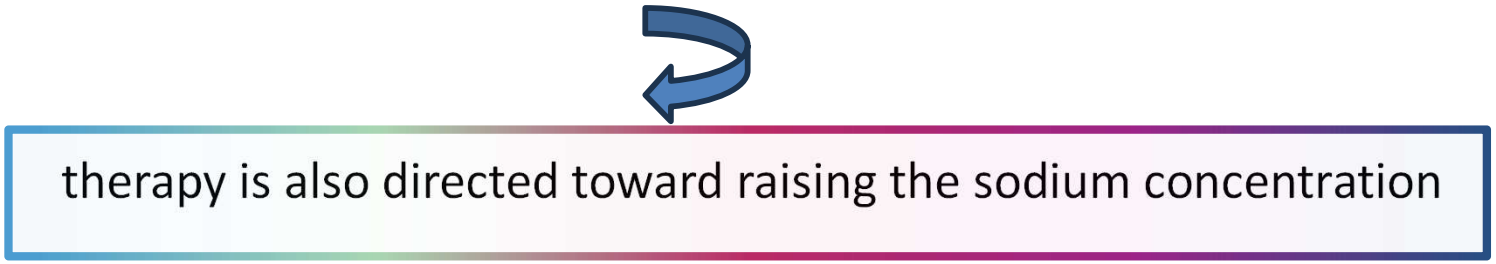
Management decision



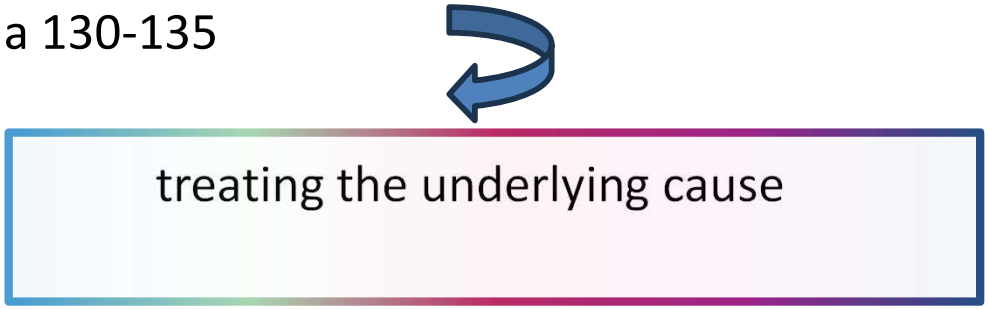
Acute hyponatremia

Severe symptoms (seizures, obtundation,coma) : Na<120

Mild to moderate symptoms :Na 120-129



Asymptomatic : Na 130-135



Chronic hyponatremia

- ✓ Cerebral cell volume adaptation has likely occurred
- ✓ Patients are less likely to be symptomatic and more importantly are at-risk for ODS if hyponatremia is corrected too quickly

- ✓ Asymptomatic or with mild symptoms

Correcting underlying cause

- ✓ Symptomatic, especially if they are severe

Directed therapy to increase serum sodium levels is provided.

Rate of correction

Depends on chronicity of hyponatremia

Acute symptomatic hyponatremia : 3 to 5 mL/kg of 3 percent saline is the suggested initial therapy, administered within 10 to 15 minutes

- Repeated two times if needed, is indicated until the seizures resolve
- **Seizures due to hyponatremia may be refractory to anticonvulsant therapy**
- Targeted goal of raising serum sodium to less than 8 to 9 mEq/L over the initial 24 hours

Acute asymptomatic hyponatremia :

- Treatment of the underlying condition
- The targeted rate of correction in this setting is 6 to 8 mEq/L over 24 hours

Chronic hyponatremia

Chronic hyponatremia with severe symptoms :

- 3 to 5 mL/kg of 3 percent saline is suggested
- Total daily correction in the 6 to 8 mEq/L per day

Chronic hyponatremia with mild to moderate symptoms

- No indication for 3 percent saline
- Total daily correction at 6 to 8 mEq/L

Chronic asymptomatic hyponatremia :

- Daily serum sodium correction should not exceed 6 to 8 mEq/L.
- Correction can be with either oral or intravenous sodium chloride

Hyponatremia and CNS diseases

Big challenge in patients with CNS disorders

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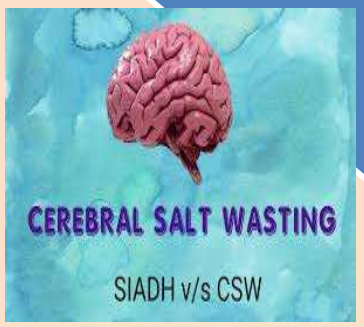
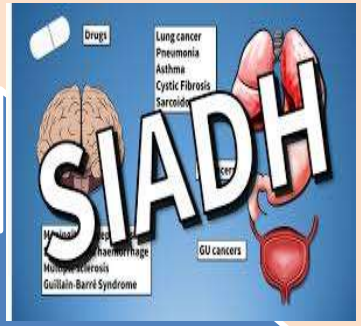
Cerebral salt wasting



SIADH



Cerebral salt wasting

Renal salt wasting and the resultant volume depletion is a protective measure, limiting extreme rises in intracranial pressure

High ICP → Impaired Symptheticc input → Decreased RAS → Na and urate wasting

High ICP → Increased BNP → BNP inhibits RAS → Na and urate wasting

CSW Vs SIADH

Hyponatremia

U Na>40mq/L

Volume expansion in SIADH

Salt wasting in CSW

Common features

High Uosm

Appropriate in CSW

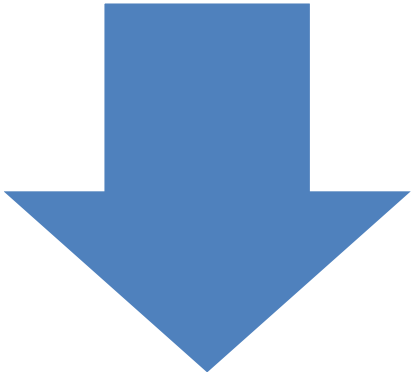
Inappropriate in SIADH

Low uric acid

Volume expansion in SIADH

High BNP in CSW

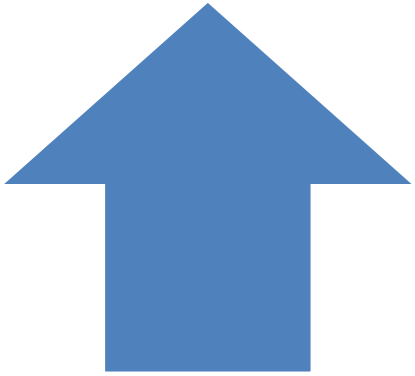
Volume status



Volume depletion in CSW

Euvolemia or mild hypervolemia

SIADH



CSW Vs SIADH

FEUA>11% in both condition

SIADH

N/S infusion

Worsen hyponatremia

After correction of hypoNa

FEUA<11%

CSW

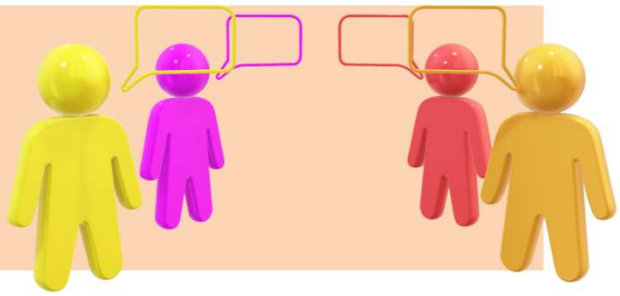
N/s infusion

Correct hyponatremia

After correction of hyponatremia

FEUA still>11%

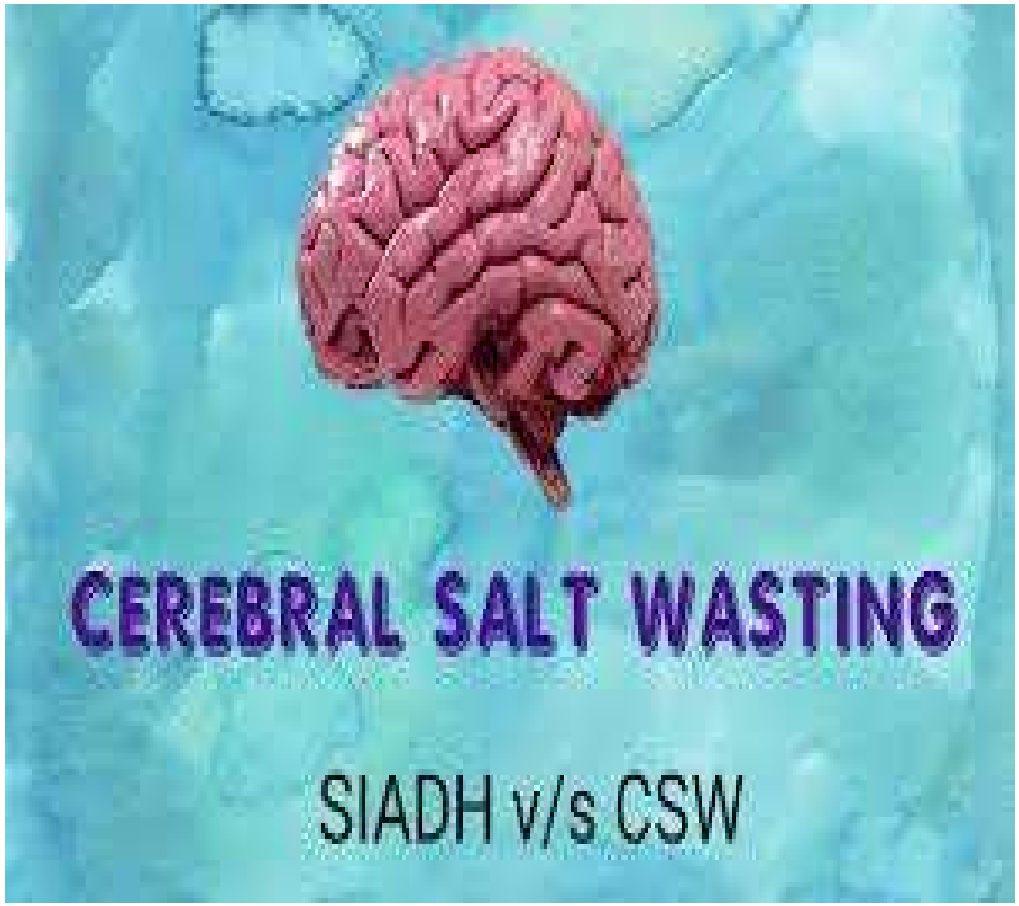
TREATMENT



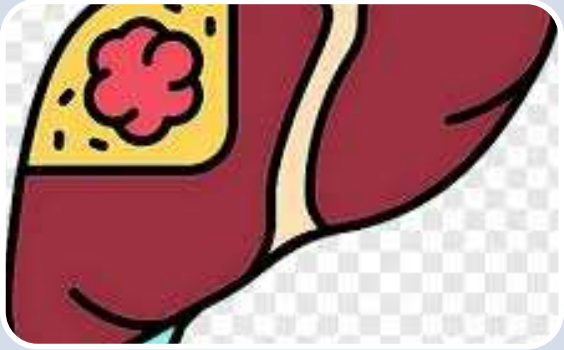
- Fluid restriction, the usual first -line therapy for (SIADH)
- All patients with active intracranial pathology (recent intracranial surgery or subarachnoid hemorrhage) should have a prompt increase in the serum sodium concentration and should avoid a decrease in ECF
- Patients with subarachnoid hemorrhage would also have SIADH in addition to CSW
- Hypertonic saline will increase the serum sodium concentration in patients with both CSW and SIADH.
- In patients with SAH, the possible administration of a mineralocorticoid, such as Fludrocortisone, to prevent volume depletion and delayed cerebral ischemia

Regardless of whether hyponatremia is caused by CSW or SIADH

Hyponatremic patients with intracranial pathology should be treated with 3 percent saline to avoid a decrease in ECF

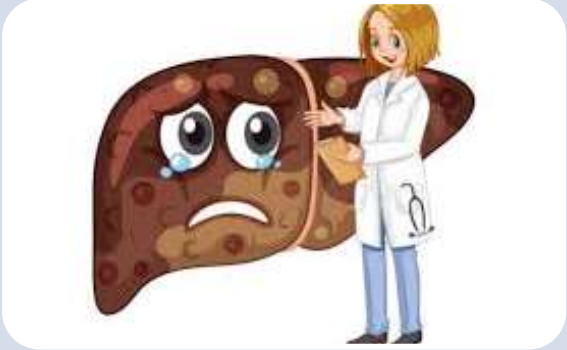


Hyponatremia and liver disease



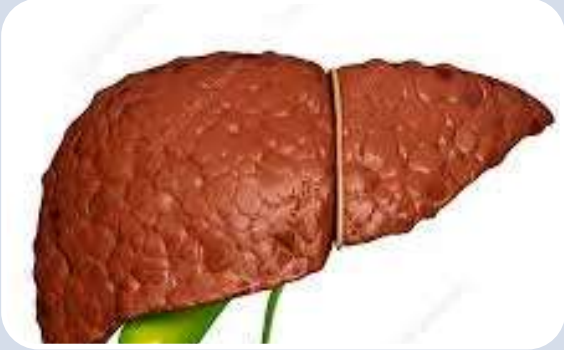
Systemic vasodilatation

by NO and PGs



Iatrogenic factors

Beta blockers

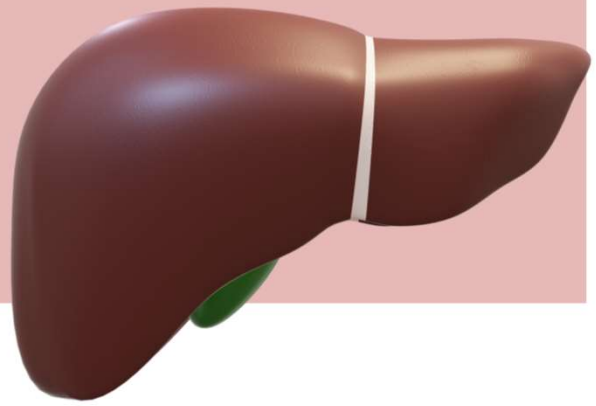


Secretion of hypovolemic hormones

ADH,RAS, sympathetic pathway

Management of hypoNa in cirrhosis

- Withdrawing beta blockers, alpha blockers, diuretics when the mean arterial pressure falls to 82 mmHg or below
- Correcting hypokalemia, if present (potassium is as osmotically active as sodium)
- Midodrine to achieve a mean arterial pressure of higher than 82 mmHg
- Hemodialysis in patients with advanced kidney function impairment who are candidates for liver transplantation

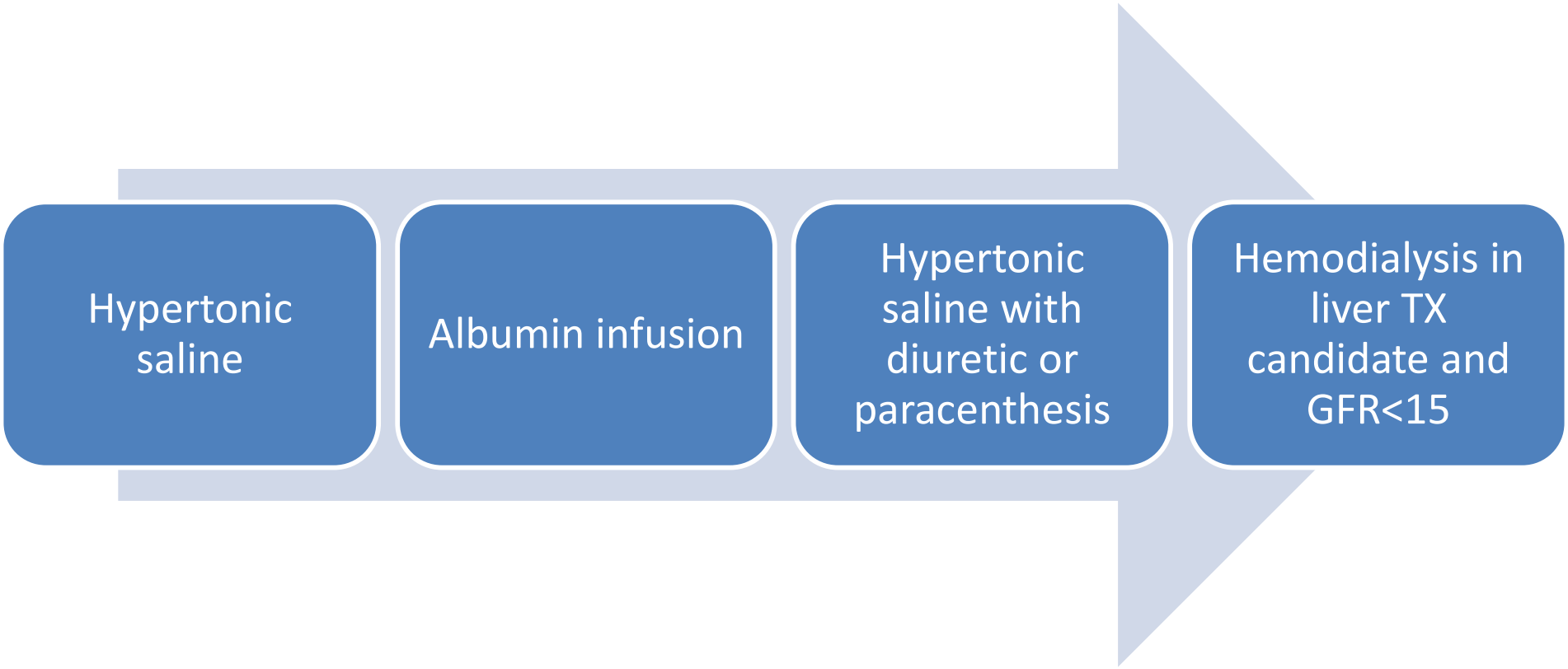


Urgent serum sodium correction

Severe symptomatic hyponatremia Na<120	Na<125 in patients undergoing imminent liver TX

Treatment of severe symptomatic hyponatremia (<120 mEq/L)

Rate of correction 4-6 mq/day

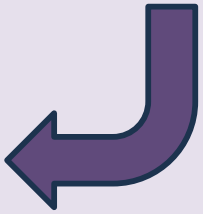


Patients undergoing imminent liver transplantation

goal of serum Na>125mq/L

- Withdrawing antihypertensive medications
- Correction of hypokalemia
- Midodrine therapy in patients with a persistent mean arterial pressure ≤82 mmHg

If not successful



- Hypertonic saline
- Albumin infusion
- Hemodialysis
- Tolvaptan (V2receptor antagonist)

ODS after liver transplantation

- ✓ Partial correction before transplantation is preferable
- ✓ Rapid correction of hyponatremia can occur after liver transplantation and is associated with neurologic complications
- ✓ The median time to onset of ODS in reported cases is five to seven days
- ✓ Large volumes of isotonic fluid administered intraoperatively are sufficient to induce rapid correction of hyponatremia

Hyponatremia in patients with heart failure

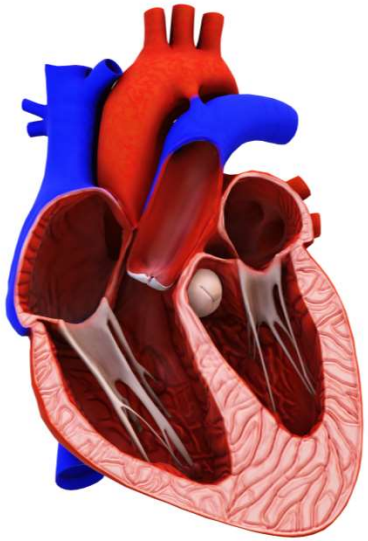
Low cardiac output

Baroreceptor in carotid and afferent arterioles

Body perceives volume depletion

Hypovolemic hormones

ADH,RAS, sympathetic pathway



Clinical manifestation

- Hyponatremia in patients with heart failure usually develops slowly
- no obvious symptoms until the serum sodium concentration falls below 120 mEq/L
- serum sodium concentration **parallel the severity** of the heart failure
- some patients with chronic moderate hyponatremia (serum sodium 120 to 129 mEq/L) have subtle neurologic manifestations (reduced scores on tests of mental, social, and physical functioning and unsteadiness and falls)

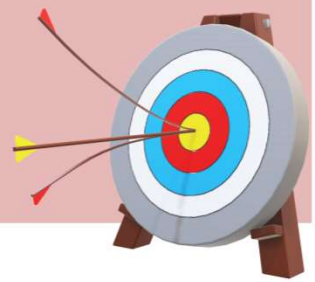
Main indication for treatment

Severe hyponatremia <120 mq/L

The presence of symptoms that might be due to hyponatremia

Concern that seemingly asymptomatic hyponatremia might predispose the patient to falls and fractures.

Treatment



Fluid restriction	ACE OR ARB	V2 receptor antagonists
• Unlikely successful	• Increase CO can decrease ADH • Increase local PGs leads to antagonize ADH effect	• Selective water diuresis(aquaresis) • When other management failed • CI in liver disease • Not more than 30 days

Medication induced hyponatremia

Keep in mind medication

Mechanism	Medications
Drugs affecting sodium and water homeostasis	Diuretics (thiazides, indapamide, amiloride, loop diuretics)
Drugs affecting water homeostasis	Antidepressants (amitriptyline, SSRIs, monoamine oxidase inhibitors)
	Antipsychotic drugs (phenothiazines, haloperidol)
	Antiepileptic drugs (carbamazepine, oxcarbazepine, sodium valproate)
	Anticancer agents (vincristine, vinblastine, cisplatin, carboplatin, intravenous cyclophosphamide, melphalan, ifosfamide, methotrexate, interferon, levamisole, monoclonal antibodies)
Potentiation of ADH	Carbamazepine, lamotrigine, chlorpropamide, tolbutamide, intravenous cyclophosphamide, NSAIDs
Reset osmostat	Venlafaxine, carbamazepine

Take home message

- Hyponatremia is a common electrolyte disorder
- Frequently exhibits a heterogeneous pathophysiology, posing difficulty in diagnosing the cause
- It is crucial to evaluate for urgency based on neurological symptoms
- It is essential to evaluate the pathophysiology of the hyponatremia in order to perform appropriate treatment