*Nephrology consults*

# (Hypernatremia)

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# Introduction

- **Plasma sodium (Na) concentration >145 mEq/L**
- Usually represents a **state of hypertonicity**

- ***Hypernatremia occurs from deficit of water relative to Na.***
- Hypernatremia results from **net water loss(out patients)** or,
- more rarely, from **primary Na gain (in hospital)**

- May exist with hypo-, hyper-, or euvolemia, although hypovolemia is by far most common type

- It has been shown to be an indicator fo r **higher mortality** in critically ill patients and patients with chronic kidney disease (CKD)

***Hypernatremia will not develop if thirst mechanism is intact and water is available .***

**Hypernatremia** often occurs in **pediatric, geriatric, and critically ill** patients.

Hypernatremia induces diverse effects in **multiple organ systems**, with **short-term mortality** of approximately **50%–60%.**

**Even mild hypernatremia ([$Na^+$]<150 mEq/L) confers a 30-day mortality of >20%.**

- ***Occurs in 1% of hospitalized elderly patients***
- ***Seen in about 9% of ICU patients***
- ***. Gastroenteritis with diarrhea is the most common cause of hypernatremia in infants.***
- ***Women are at an increased risk due to decreased TBW, as compared with men.***

1 **Hypernatremic dehydration(most common)**

lack of water in the body system via:

- Inadequate fluid intake
- Unsuccessful breastfeeding
- Diarrheal disease
- Excessive urination
- Excessive sweat production
- Gastrointestinal water losses

$$\uparrow [Na^+] = \frac{Na^+(mmol)}{\downarrow Volume(L)}$$

2 **Euvolemia (salt poisoning and stable water balance)**

Excessive amount of salt entered into body system via:

- Ingestion of supersaturated salt solution
- Salt poisoning
- Mistaking salt for sugar
- Salting skin of newborns
- Salting rituals
- Salt as an emetic

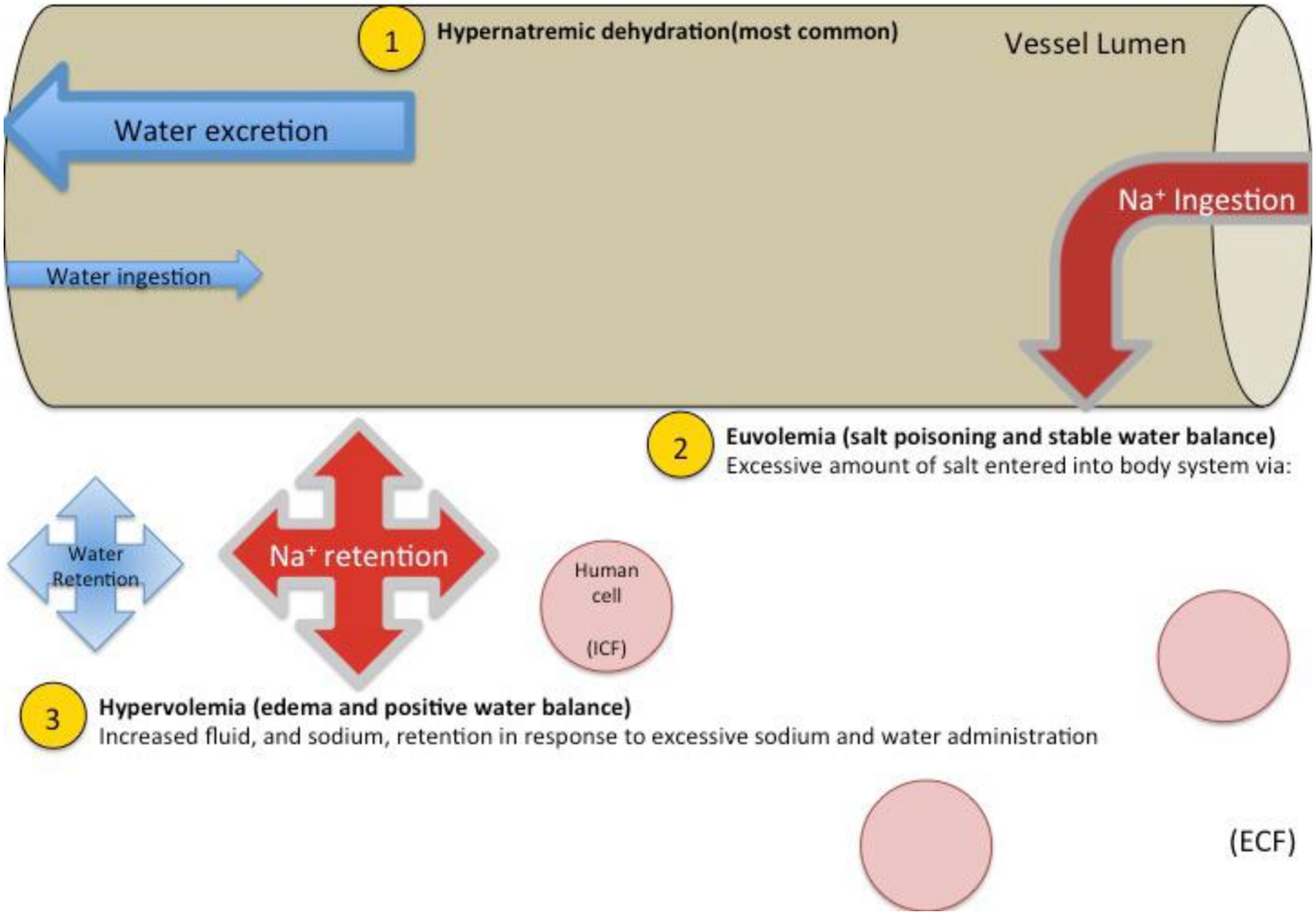
$$\uparrow [Na^+] = \frac{\uparrow Na^+(mmol)}{Volume(L)}$$

3 **Hypervolemia (edema and positive water balance)**

Increased fluid, and sodium, retention in response to excessive sodium and water administration in association with:

- Hypoalbuminemia
- Azotemia
- Excessive salt ingestion during prolonged exercise

$$\uparrow [Na^+] = \frac{\uparrow\uparrow Na^+(mmol)}{\uparrow Volume(L)}$$


1
Hypernatremic dehydration(most common)
Vessel Lumen
Water excretion
Na+ Ingestion
Water ingestion
2
Euvolemia (salt poisoning and stable water balance)
Excessive amount of salt entered into body system via:
Water Retention
Na+ retention
Human cell
(ICF)
3
Hypervolemia (edema and positive water balance)
Increased fluid, and sodium, retention in response to excessive sodium and water administration
(ECF)

## What is the underlying pathophysiology of hypernatremia?

1. **Hypernatremic dehydration(most common)**
lack of water in the body system via:
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- Unsuccessful breastfeeding
- Diarrheal disease
- Excessive urination
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2. **Euvolemia (salt poisoning and stable water balance)**
Excessive amount of salt entered into body system via:
- Ingestion of supersaturated salt solution
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**OR**

3. **Hypervolemia (edema and positive water balance)**
Increased fluid, and sodium, retention in response to excessive sodium and water administration in association with:
- Hypoalbuminemia
- Azotemia
- Excessive salt ingestion during prolonged exercise

## What is the goal of treatment?

↓ Increase plasma volume while increasing free water

↓ Remove excess $Na^+$, with or without excess water

## What is the most appropriate treatment?

↓

1. **Hypotonic fluid administration:** If circulation is stable
**or**
2. **Isotonic fluid administration:** If circulation is collapsing

↓ **Hypotonic fluid administration with or without sodium depleting diuretic**

## Causes of Hypernatremia

**Primary water deficit**

1-Reduced water intake for many days
2-Increased water loss
3-Shift of water into cells(seizure or rhabdomyolysis)

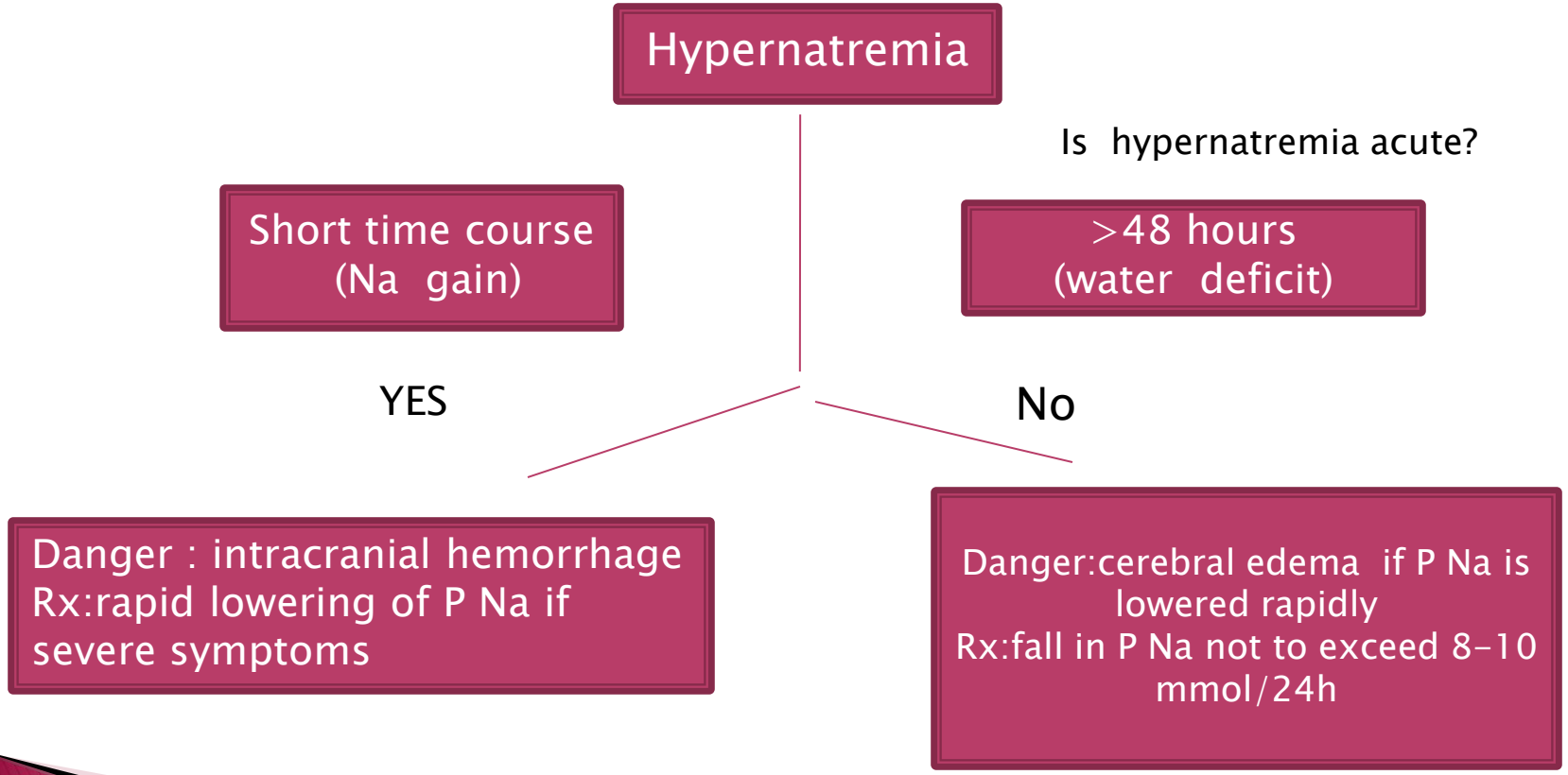
**Primary gain of Na**

**The organ that is most adversely affected is the brain**
*Focal intracerebral and subarachnoid hemorrhage*

*An adaptive regulatory vol increase,imports ionic osmolytes ( Na,k,cl)*
*a short-term fix, the ions are highly cytotoxic.*
*the osmostress evokes another set of responses via*
*tonicity-responsive enhancer binding protein (TonEBP),*
*a transcriptional factor.*
*TonEBP drives cellular accumulation of less toxic organic osmolytes (mainly myoinositol, sorbitol, betaine, and taurine) and proadaptive chaperon proteins*

# Steps in the clinical approach to the patient with hypernatremia

1-to recognize *whether there are emergencies* prior to therapy
2-to anticipate and prevent dangers that may arise during therapy
3-to proceed with therapy
4- the diagnosis of the cause of hypernatremia



**Clinical examples :**

e.g patient who has nehrogenic DI due to Li therapy, who is undergoing surgery and is given a large infusion of isotonic saline,to avoid a fall in BP

e.g patient with craniopharyngioma
During surgery,his U/o was 3litrs over 5 hours.
His plasma Na rose from 140 to 150 mmol/lit
(risk of brain edema during theapy should be reminded)!!

1-induce a negative balance of Na ions?
2-induce a positive water balance?
3-In some cases,hemodialysis may be the only opttion.

***Important !***

Oral water replacement or via NG tube
IV hypotonic fluid : half saline? Or D5W?
Because of a limited amount of glucose can be oxidized in an ill patient(about 0.25g/kg/h) ,hence only close to 0.3 L of D5W can be given to these patients per hour or as a bollous iv fluid

Anticipate and prevent danger during Rx

***There is no*** major emergency –related hypernatremia in the patient with **chronic hypernatremia**.

Overly rapid correction of plasma Na may lead to brain cell swelling ,increase in ICP ,and pssibly brain herniation.

**One should not permit the plasma Na to fall by more than 8-10 mmol/24 hour period.**

Determine the appropriate **rate** of fall in the P -Na

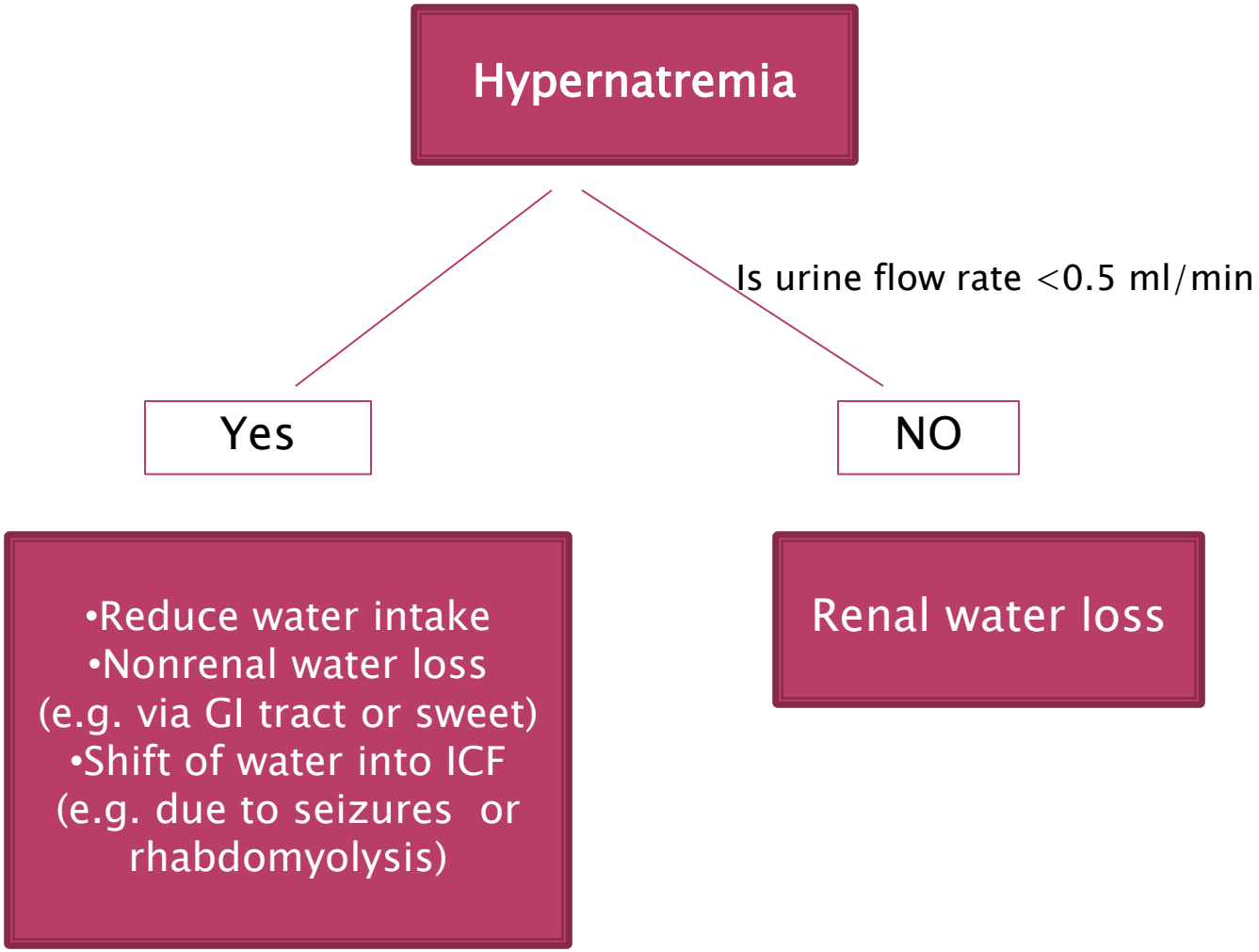
✓If hypernatremia is acute and there are significant symptoms like decrease of LOC or seizure,

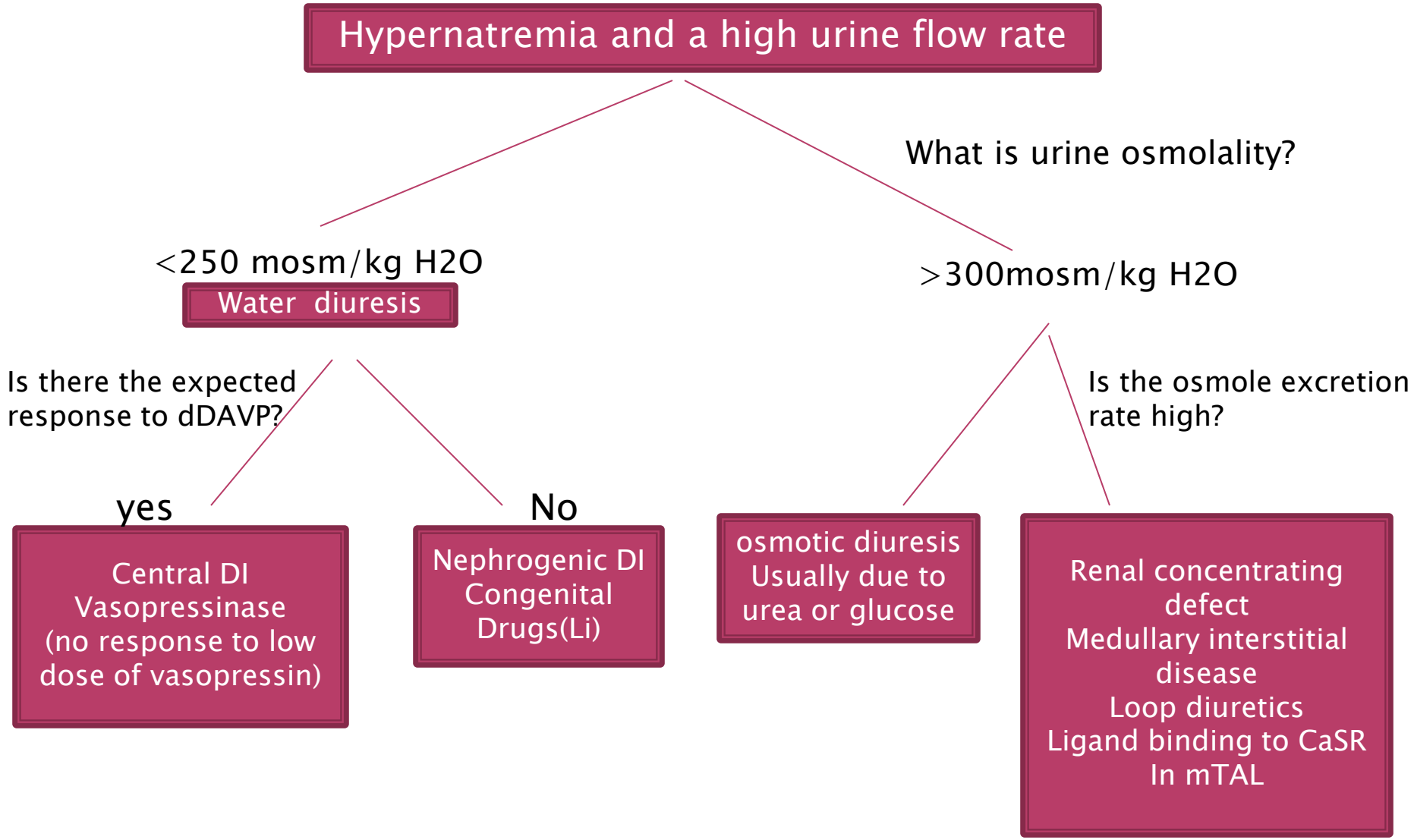
✓The plasma Na should be lowered rapidly,at least by **5%** from its current level.

✓If hypernatremia is acute but the patient is not very symptomatic,one should lower P Na more slowly(e.g. by **1-2 mmol/lit/hr**.

✓Because of cerebral adaptation,limit the fall in P Na in this setting to **12 mmol/lit** in the first 24hr.

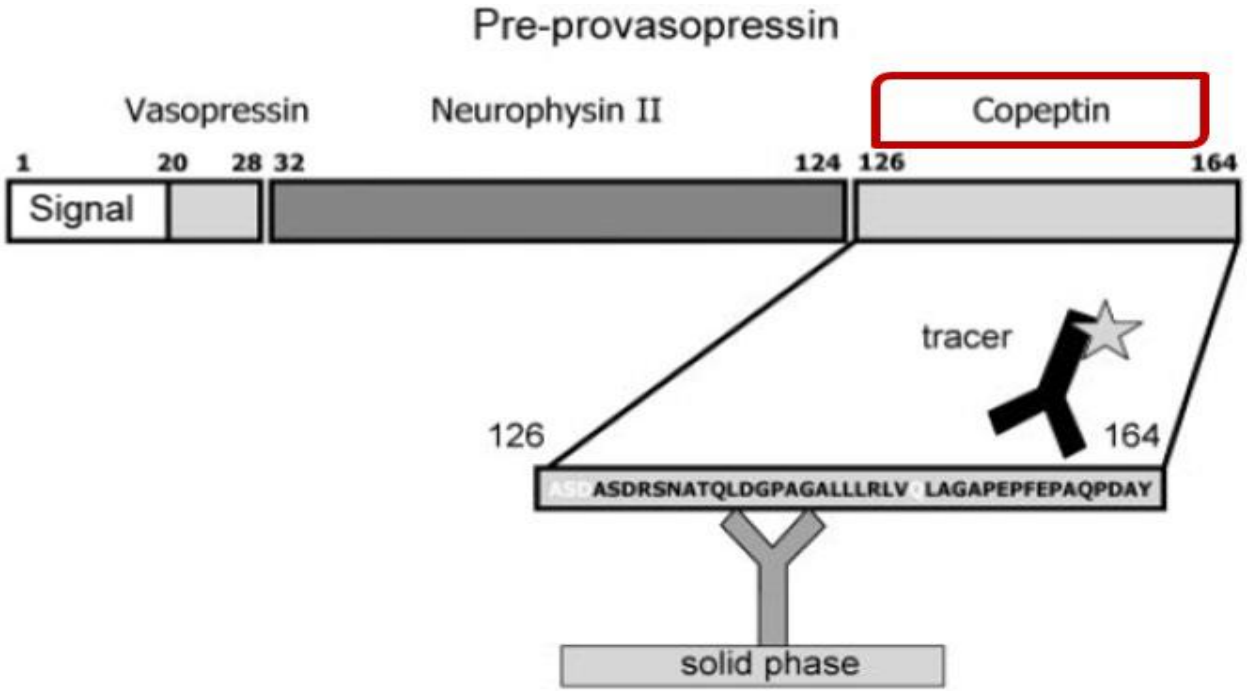
# Diagnosis the cause of hypernatremia

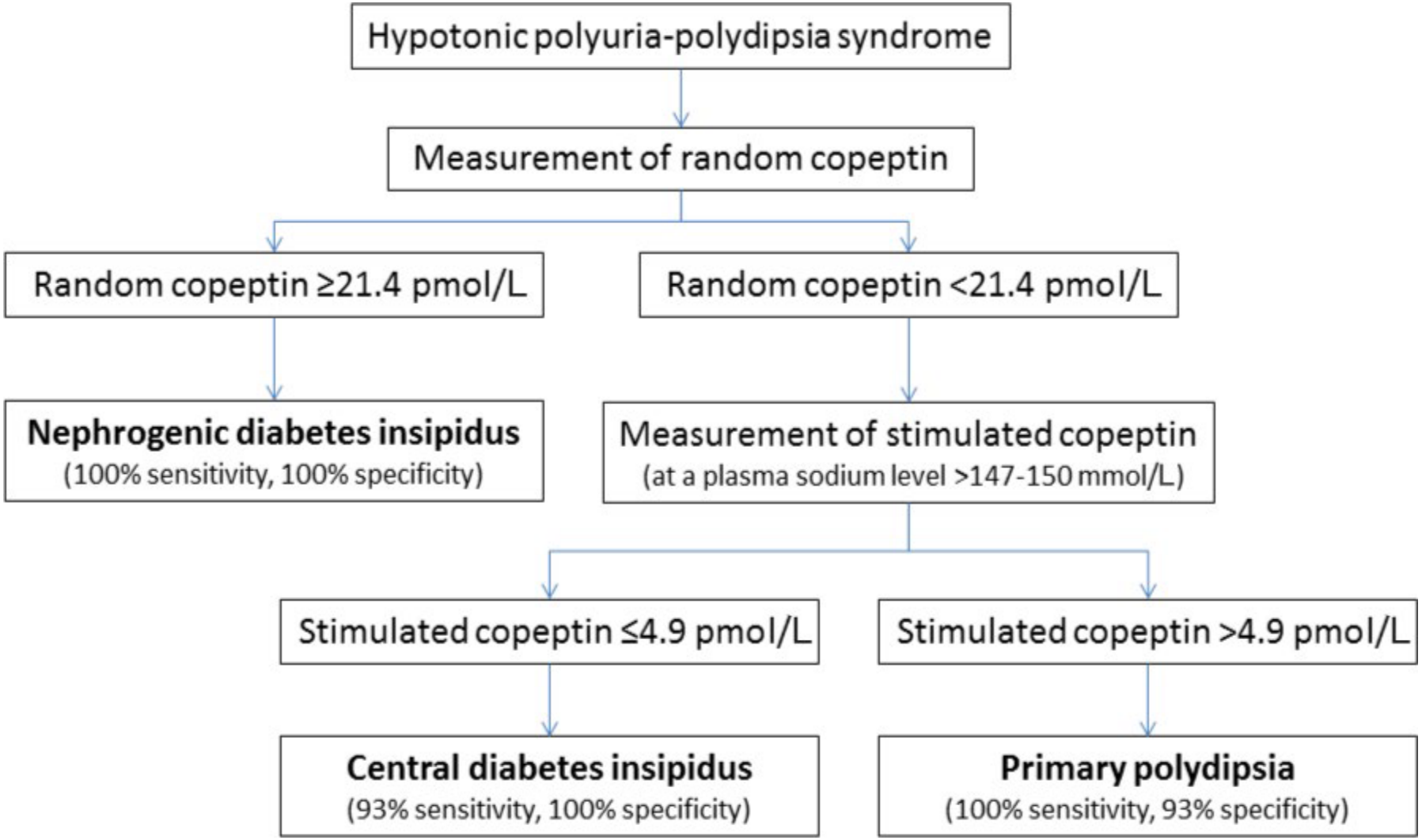



Hypernatremia and a high urine flow rate
What is urine osmolality?
<250 mosm/kg H2O
Water diuresis
>300mosm/kg H2O
Is there the expected response to dDAVP?
Is the osmole excretion rate high?
yes
No
Central DI
Vasopressinase
(no response to low dose of vasopressin)
Nephrogenic DI
Congenital
Drugs(Li)
osmotic diuresis
Usually due to urea or glucose
Renal concentrating defect
Medullary interstitial disease
Loop diuretics
Ligand binding to CaSR
In mTAL

# COPEPTIN

Copeptin is secreted in an equimolar amount to arginine vasopressin (AVP) but can easily be measured in plasma or serum with a sandwich immunoassay. The main stimuli for copeptin are similar to AVP, that is an increase in osmolality and a decrease in arterial blood volume and pressure.




Hypotonic polyuria-polydipsia syndrome
Measurement of random copeptin
Random copeptin ≥21.4 pmol/L
Random copeptin <21.4 pmol/L
Nephrogenic diabetes insipidus
(100% sensitivity, 100% specificity)
Measurement of stimulated copeptin
(at a plasma sodium level >147-150 mmol/L)
Stimulated copeptin ≤4.9 pmol/L
Stimulated copeptin >4.9 pmol/L
Central diabetes insipidus
(93% sensitivity, 100% specificity)
Primary polydipsia
(100% sensitivity, 93% specificity)

# Nephrogenic DI

1-congenital (mutations in V2R or AQP2 genes

2-Li induced NDI
The most frequent cause of NDI
Enters via ENaC….inhibits GSK3….reduces AQP2 insertion and abundance
Increase expression of PG-E2
Often becomes irreversible

3-Hypokalemia
Diminishes cAMP in response to vasopressin
Decrease density of AQP2

4-Hypercalcemia

5-renal concentrating defect

# Hypernatremia in the geriatric population

✓age-related physiologic changes such as
✓ decreased thirst drive,
✓impaired urinary concentrating ability,
✓ and reduced total body water.
✓ Medications may exacerbate this predisposition.

*Hypernatremia and dehydration occurring in nursing homes are considered indicators of neglect that warrant reporting*,

but there are other nonavoidable causes of hypernatremia, and consideration at time of presentation is essential to prevent delay in diagnosis and management

Principal causes and the underlying mechanisms Of drug-induced hypernatraemia

**A. Water loss**

1. **Renal losses**

(i) Acquired nephrogenic diabetes insipidus

Drug-induced hypokalaemia: diuretics, cisplatin, aminoglycosides, amphotericin B, penicillin derivatives

Drug-induced hypercalcaemia: lithium, vitamin A or D excess

Other drugs: lithium, demeclocycline, amphotericin B, foscarnet, colchicine, vinblastine, vasopressin V2-receptor antagonists

(iii) Other causes

Loop diuretics

Osmotic diuresis

Mannitol administration

Nutritional supplementation

Urea

Agents that cause increased production of urea: corticosteroids, high-protein supplements

2. **Gastrointestinal losses**

Osmotic cathartic agents: lactulose, sorbitol

**B. Hypertonic sodium gain**

Hypertonic sodium bicarbonate infusion

Hypertonic sodium chloride infusion

Hypertonic feeding preparation

Sodium chloride-rich emetics

Hypertonic saline enemas

Intrauterine injection of hypertonic saline

Hypertonic saline irrigation of intra-abdominal hydatid cysts

Hypertonic dialysis

*N-acetylcysteine*

NDT Plus (2009) 2: 339–346

## Clinical examples

Question

1-A 72-year-old man was admitted to the intensive care unit with pneumococcal pneumonia. He was intubated and started on mechanical ventilation. Three days later he was started on enteral nutrition with 50 ml of free water flushes down NG tube every 6 h. His sodium rose gradually from 142 mEq/l to 155 mEq/l over 3 days. How would you approach his hypernatremia?

answer

The patient is critically ill with no free access to water. Hypernatremia is commonly encountered in patients on enteral nutrition. The first action is to increase free water flushes down NG tube. If this is ineffective an infusion of D5W should be started.

Question 2.

An 85-year-old woman with advanced dementia was sent to the emergency department from a skilled nursing facility due to obtundation. Her serum sodium was 181 mEq/l. She weighs 56 kg. How should her hypernatremia be corrected?

answer

first, we utilize the water loss formula:

Water deficit=current TBW x(current serum sodium/140−1)

Water deficit=(56x 0.5)x(181/140−1)=8.2 L

Answer to question 2….continued

It would be reasonable to start D5W at 150 ml/h and to check serum sodium every 6 h.
Avoid lowering Na by more than 12 mEq/24 h. The above water deficit does not take into account ongoing water loss (for example due to urination, vomiting or diarrhea) or insensible water loss. The rate may need to be adjusted depending on serum sodium measurements.
Correcting serum sodium in this case will take about 4 days using the above guidelines: her sodium is 181-140 = 41 mEq/l above the normal range,
if we correct by10 mEq/l per 24 h period, it will take 4 days to achieve the desired target

Question 3

A 44-year-old man with manic-depressive disorder has been stable for 3 years on lithium. He is now complaining of frequent urination. A 24 h urine collection revealed a urine volume of 3.2 Liters. Urine Na 35 mEq/l, urine K 33 mEq/l, urine protein is 13 mg/24 h, urine glucose is 0, urine osmolality 180 mOsm/kg H2O. Serum sodium is 144 mEq/l. How would you manage his condition?

answer

The patient has nephrogenic diabetes insipidus due to lithium. His serum sodium is at the upper range of normal because he is able to drink, and significant hypernatremia is not expected. Urine osmolality is low, and he is polyuric (urine volume is above 3 L per 24 h).

Answer to Question 3…..continued

There is no evidence of solute (osmotic) diuresis. It would be reasonable to try amiloride in this case .

Amiloride is a weak diuretic that blocks the sodium epithelial channel (the main entry site for lithium in the principal cells of the collecting duct) and may be particularly helpful in lithium-induced diabetes insipidus.

Changing to a different agent is another option after consultation with the patient's psychiatrist.

Question -4

A 79-year-old nursing home resident with hypertension and prior strokes was admitted for decrease in mental status over 5 days. On evaluation, she was somnolent, temperature was 39.5°C, BP was 140/60 mm Hg, pulse was 102/min, and respiratory rate was 24/min (baseline weight of 56 kg). Her breath sounds were reduced; chest x-ray revealed a lobar pneumonia. Laboratory studies showed serum [$Na^+$] of 170 mEq/L, serum creatinine of 1.5 mg/dl, and urine osmolality of 780 mOsm/kg. She was given 1 L of saline *en route*

answer

Her water deficit was approximately 6 L [56×0.5×(170/140–1)]. Assuming (*1*) insensible loss to be approximately 1.2 L/d (600 ml skin and 600 ml respiratory loss) and
(*2*) urine and stool output to be zero,
to correct her [$Na^+$] to approximately 142–145 mEq/L (from 170) in 3 days, she would need approximately 9.6 L of water (6 L deficit +3.6 L insensible loss).
We thus initiated 5% dextrose water infusion at 130 ml/h (3.12 L/d). Note that these estimates do not include her future urine/stool output or potential tissue $Na^+$ mobilization, and they serve only as a starting reference.
Her [$Na^+$] was monitored closely, and the infusion rate was adjusted to keep the correction at approximately 0.4 mEq/L per hour. She reached normonatremia in 3 days and regained mental lucidity.

# Centra DI post- trans-sphenoidal surgery

Incidence ~ 20%
Only about 2% of patients require long term treatment with dDAVP.

In a small number of patients ,the clinical course fpllows **a triphasic pattern** ,in which there is
A transient initial phase of CDI,
Followed by a phase of SIADH,
Then permanent CDI.


THANKS