Practical approach to disturbances in plasma sodium

Clinical case - Hyponatraemia

68 yr old female admitted with cardio-renal syndrome and pulmonary oedema

Na - 135

Rx - high dose frusemide with some effect

but.... Na -124

Why?

[Sodium]

Introduction

Normal physiology

Mechanisms

Treatment

[Sodium]

Introduction

Normal physiology

Mechanisms

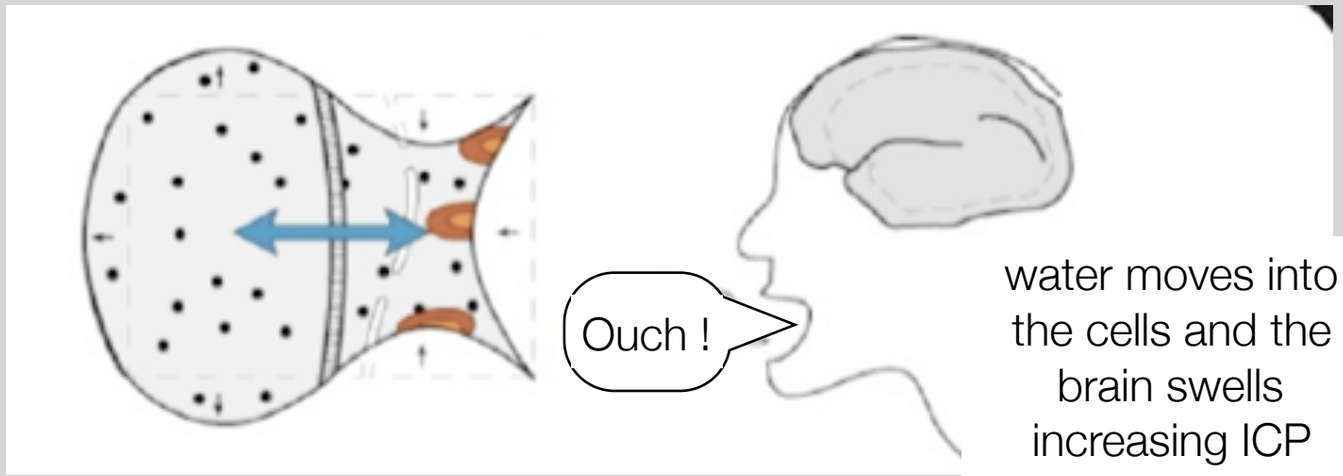
Treatment

Some basic concepts

Why care about osmolality?

- **Osmolality** = total concentration of **all particles** in a solute
- The clinically important variable is **tonicity**
- Tonicity (**"Effective osmolality"**) = osmotic gradient due to solute that do **not cross** the cell membrane

  (ex. urea is not an effective osmole)
- Sodium is the main indicator of osmolality of ECF



First....some rules of the game

- **Sodium** balance determines **volume** status.
- **Water** balance determines **tonicity** ([Na^+])
  - Hyponatremia = relative **water excess**
  - Hypernatremia = relative **water deficit**

[Sodium]

Introduction

Normal physiology

Mechanisms

Diagnosis + Treatment

Now for some physiology

Let’s get some perspective

1 L Plasma contains :

$[H^+]$ - **40** nano Moles/L (=pH 7.40)

$[Na^+]$ - **140,000,000** nano Moles/L - 140 mMol/L

$[H_2O]$ - **55.000,000,000** nano Moles/L - 55 Mol/L

H20 is the **Big** player

Some more physiology

normal serum osmolality = 285-292 mOsm/L

Maximum urine dilution

50 mOsm/L (~1/6th serum osmolality)

Maximum urine concentration

1200 mOsm/L (~ 4X serum osmolality)

What is the most water we can excrete?

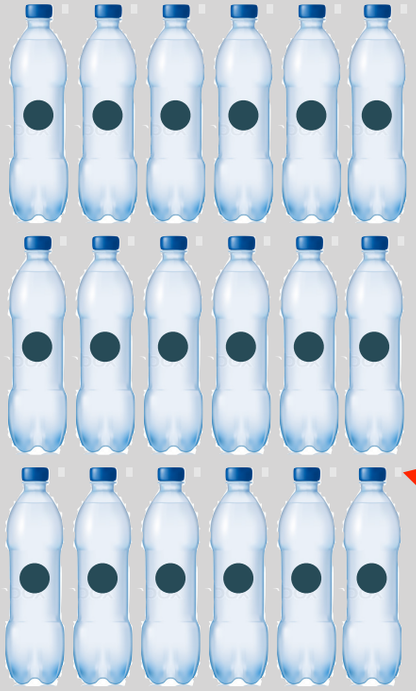
It depends on your **solute intake**

Solute intake
~900 mOsm/day

150 mOsm/day solute intake

Max. dilution
50mOsm/L
(~1/6 th plasma)

Maximum
Urine output



18 L/day

3 L/day

You can't pee pure water

Sick people are thirsty,
not hungry

Maximal concentration

Osmolality mOsm/kg

50

ADH

285

Na

H20

285

300

600

1200

1200

Isosmotic reabsorption of sodium and H20 (proximal tubule)

NaCl and KCl reabsorption **without water** (thick ascending limb)

Maximal dilution

Osmolality
mOsm/kg

50

285

285

Isosmotic reabsorption of sodium and H20 (proximal tubule)

Na
H20 H20 H20
H20 H20
ADH

300

H20
H20
H20
H20

Na
Na
Na
Na

NaCl and KCl reabsorption **without water** (thick ascending limb)

600

1200

Na
H20
H20
H20
H20
Na

50

How do we control [Na^+]

H20 intake/
H20 excretion

Often multiple causes

Ex. decreased solute intake + inability to maximally dilute urine

H20 intake - Thirst a very powerful sensation

But were you thirsty, Bear?

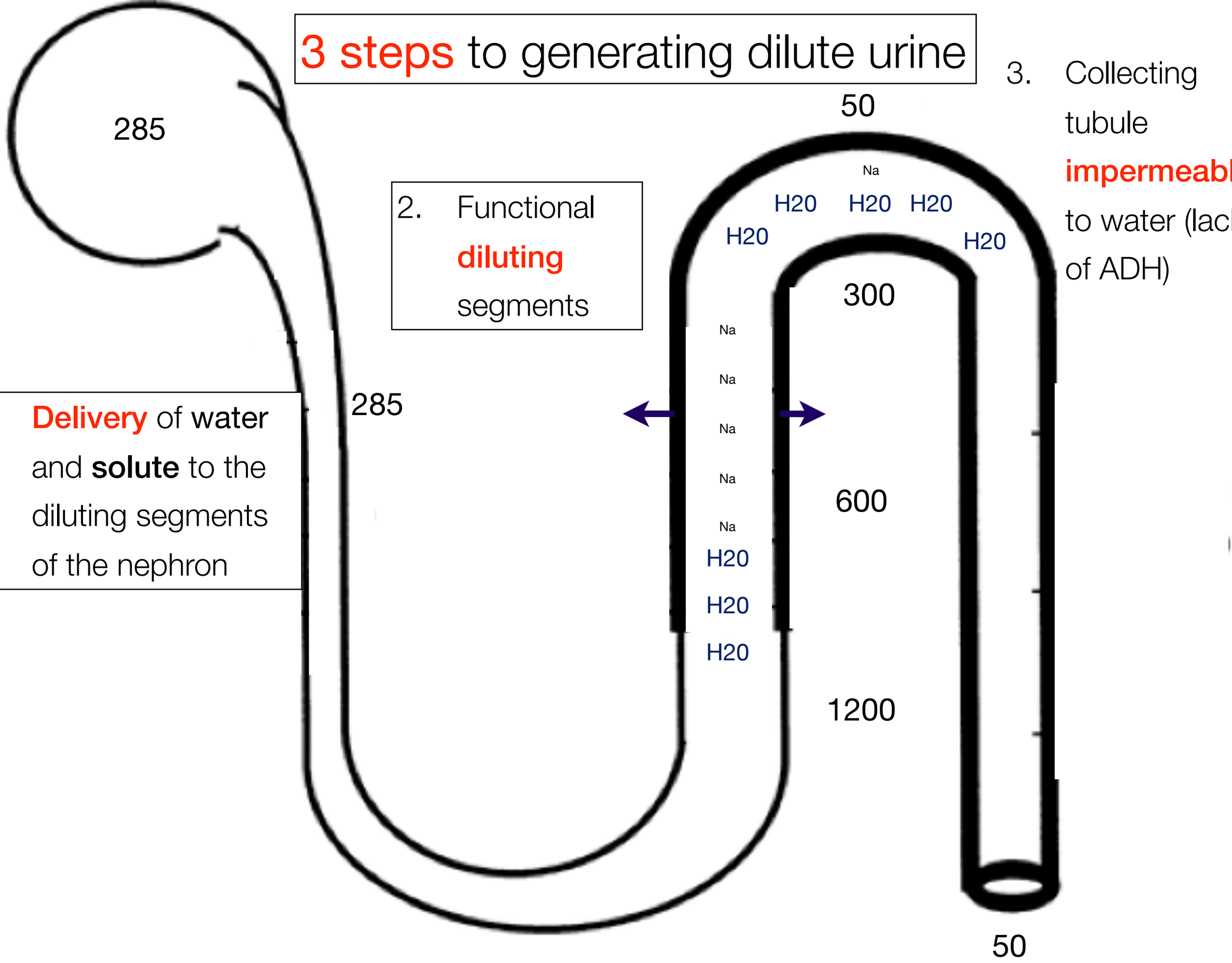
H20 excretion

3 steps to generating dilute urine

1. **Delivery** of **water** and **solute** to the diluting segments of the nephron

2. Functional **diluting** segments

3. Collecting tubule **impermeable** to water (lack of ADH)



Mechanism of low [Na]

low ADH

high ADH

Hyponatraemia - with **Low** ADH

Mechanism of low [Na]

↓ **ADH** (suppressed)

(you pee appropriately dilute but output too low **relative** to intake)

Too much **H20** (Drink, irrigation, etc)	Low **solute** (you can't pee pure H20)	**↓GFR** (not enough filtrate to pee excess H20
"Everything is working as it should, but just not enough" (dilute pee)		↑ creatinine

Hyponatraemia - with **High** ADH

Mechanism of low [Na]

↓ **ADH** (suppressed)
(you pee **appropriately** dilute but output too low relative to intake)

↑ **ADH** (concentrated pee - "**AD**ds **H**20")

Too much **H20** (Drink, irrigation, etc)

Low **solute** (you can't pee pure H20)

↓GFR (not enough filtrate to pee excess H20

↓U [Na]
U [Osmol] < Pl. [Osmol]
(dilute pee)

↑ creatinine

"Everything is working as it should, but just not enough"

ADH (“***AD****ds* ***H****20 to the body”*)

Inhibited → maximally **dilute** urine

- hypo-osmolality

Stimulated → maximally **concentrated** urine

- **hyper-osmolality**

ADH responds to 1-2% change of osmolality

- **non-osmolal stimuli**
  - ↓ in BP
  - ↓ effective circulating volume
  - “Stress”, pain, exercise, low cortisol, etc

volume takes precedent over osmolality

ADH (“***AD****ds* ***H****20 to the body”*)

works via **V2** receptors (collecting duct) -

“Opens the door” (Aquaporin) to concentrated environment in renal medulla

to retain H20 you need:

- **Concentrated medulla** - ***drives*** the process
- **ADH** - ***permits*** H20 reabsorption

Therefore kidney and ADH **saves H_20** - not Na^+ just what we give in cases of dehydration (G5%)

Mechanism of low [Na]

↓ **ADH** (suppressed)
(you pee appropriately dilute but output too low **relative** to intake)

↑ **ADH** (concentrated pee - "**AD**ds **H**20")

↓ **effective circulating volume**
("saves Na" - except renal cause)
(kidneys don't "see" enough blood flow

Too much **H20** (Drink, irrigation, etc)

Low **solute** (you can't pee pure H20)

↓**GFR** (not enough filtrate to pee excess H20

↑ creatinine

"Everything is working as it should, but just not enough" (dilute pee)

What is “Effective circulating volume”

- Effective Circulating Volume (ECV) is the volume of arterial blood effectively perfusing tissue
  - is a dynamic quantity
  - not measurable
  - ECV is about 0.7 L in a 70 kg individual

- ECV normally varies with extracellular fluid (ECF)
  - but uncoupled in some diseases (ex. CCF, cirrhosis, Sepsis)

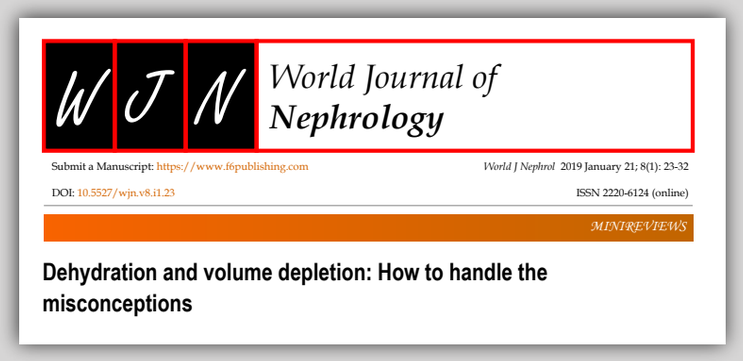
Mechanisms -↓ Effective circulatory volume

Fall in effective circulatory volume

→ 3 hypovolaemic hormones:

- *Noradrenaline* → redirects flow towards brain/heart away from kidneys
- *Angiotensin II* → enhances renal Na retention / **thirst** (increases aldosterone release)
- *ADH* → **thirst** / H20 retention

Therefore saves Na^+ and H_20 in kidneys
just what we give in volume depletion (crystalloids)



Misconceptions

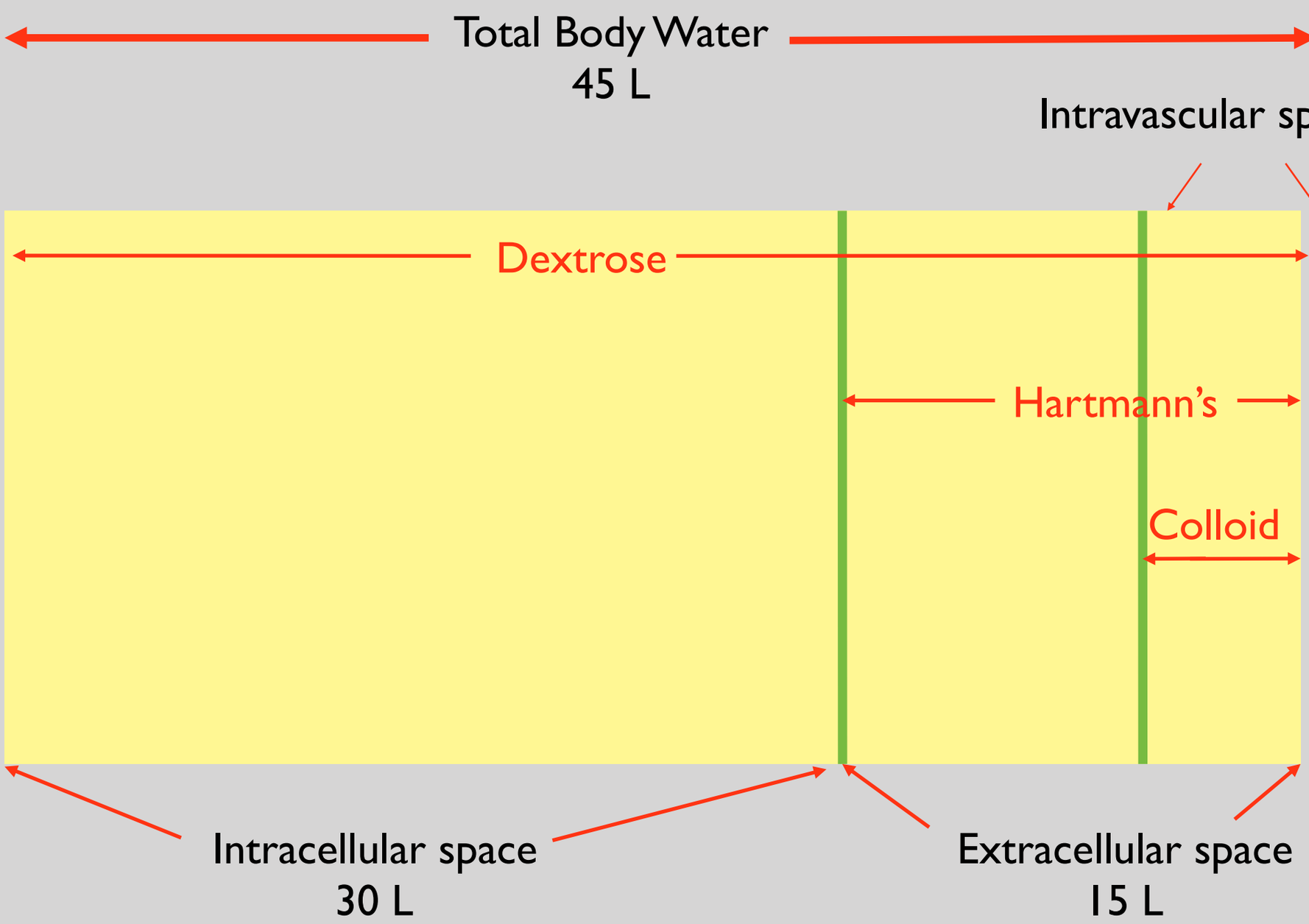
"A number of students have a misunderstanding of body fluid compartments and harbour various misconceptions"

"some physicians have insufficient knowledge of body fluids due to a lack of factual information about body fluid compartments their composition"

"misconceptions acquired from faculty members and textbooks are very difficult to eliminate from the minds of young doctors later"

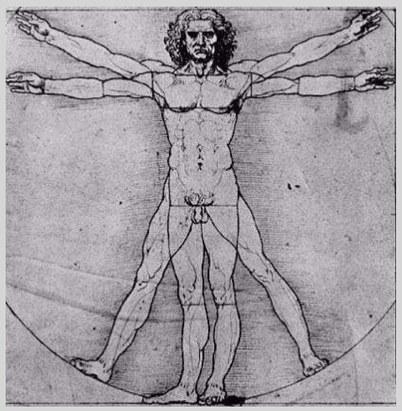
"students are generally unaware that the knowledge they possess is faulty"

All Fluids are Not Created Equal....



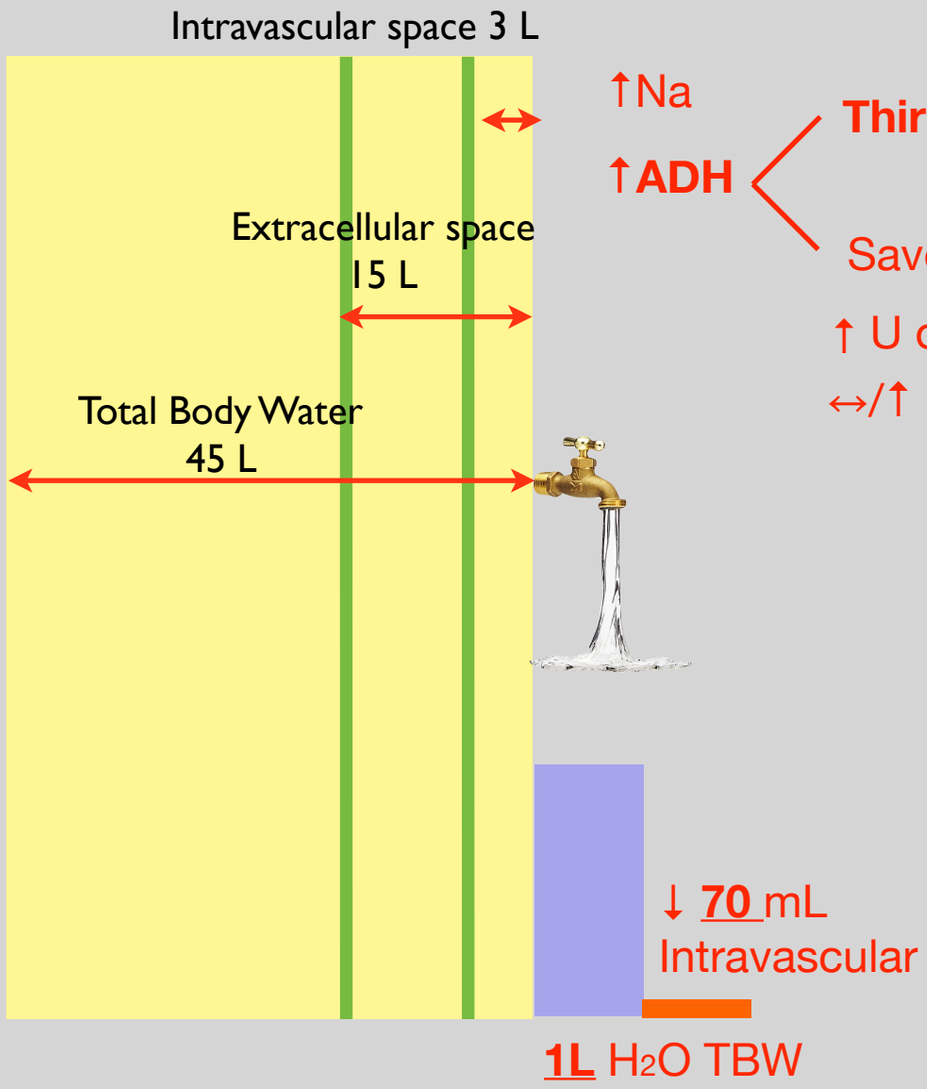
1 L infused, how much stays **intravascular ?**

- Dextrose - **70** ml
- Hartmann's - **250** ml
- Colloid - **1000** mL



Dehydration vs Hypovolaemia

Dehydration



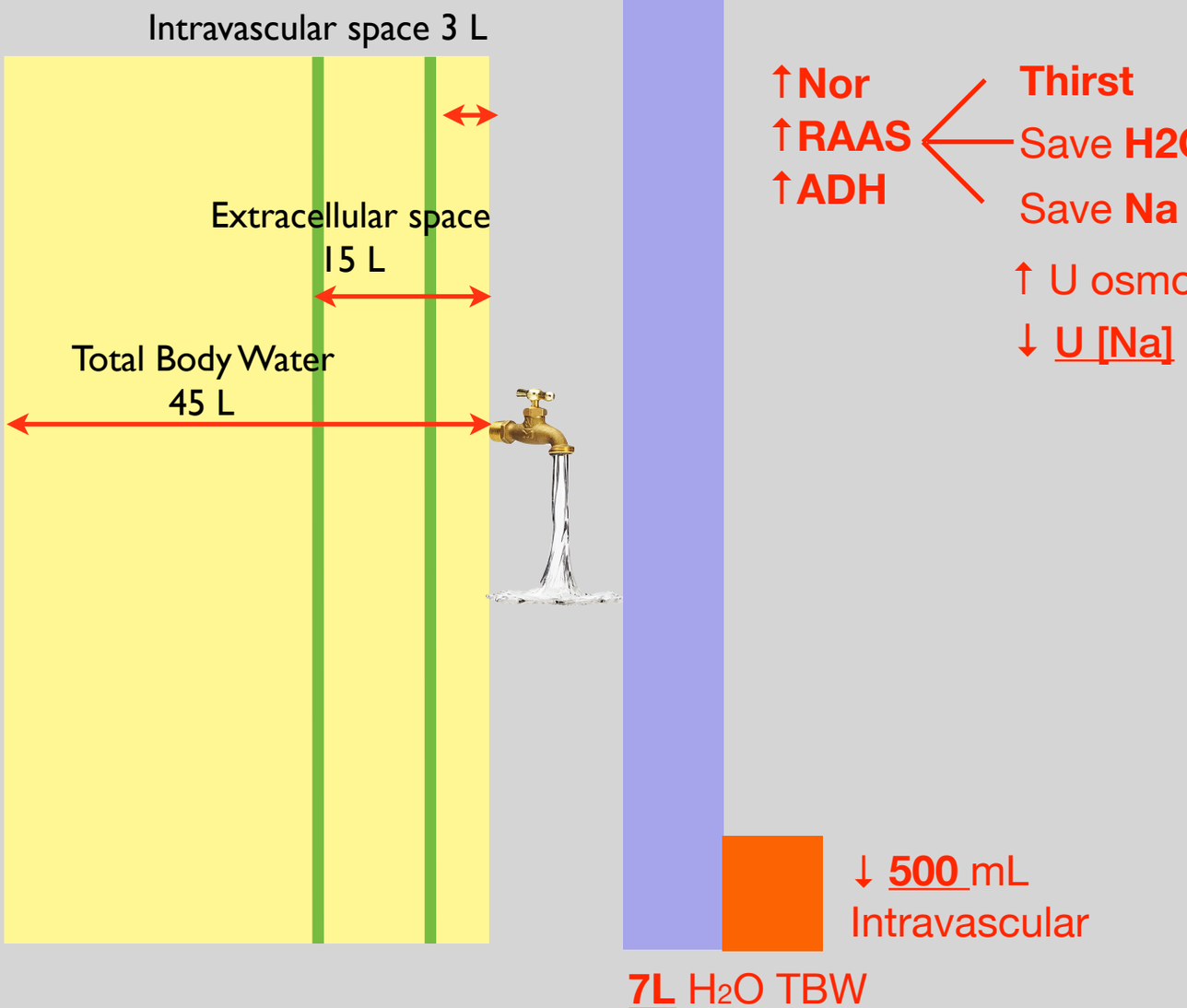
↑Na

↑**ADH** — **Thirst**; Save **H2O**

↑ U osmol.

↔/↑ U [Na]

Hypovolaemia



↑**Nor**
↑**RAAS**
↑**ADH** — **Thirst**; Save **H2O**; Save **Na**

↑ U osmol.

↓ U [Na]

Dehydration = G 5%

Hypovolaemia = Crystalloid

Mechanism of low [Na]

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"Everything is working as it should, but just not enough" (dilute pee)

↑ **ADH** (concentrated pee - "**AD**ds **H**20")

↓ effective circulating volume
("saves Na" - except renal cause)
(kidneys don't "see" enough blood flow

- **↑ ECF** (CCF, Cirrhosis, Sepsis)
- **↓ ECF**
  - **Non renal** (GI losses, bleed, etc)

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↑ ECF
(CCF, Cirrhosis, Sepsis)

↓ ECF

Non renal
(GI losses, bleed, etc)

↑ ADH in response to ↓ effective circulating volume

→ **"salt poor, concentrated pee"**

ADH raised **appropriately**

Body "perceives" ↓ECV

Volume trumps osmolality

Mechanism of low [Na]

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(CCF, Cirrhosis, Sepsis)

(↑ ADH in response to ↓ effective circulating volume → "salt poor, concentrated pee"

↓ ECF

Non renal
(GI losses, bleed, etc)

Renal Na^+ loss
(CKD,Thiazides, low steroid/thyroid)

"fixed dilution"

Some clinical examples

- Patient **unable** to achieve a urinary dilution < **300 mOsm/kg**

  “**fixed dilution**” ~ 300 mOsm/kg

  ex. Diuretics, CKD

  Ex. 900 mOsm / 300 mOsm/kg = **3 L max.**

- “Tea and toast diet”- intake **~150 mOsm / day**

  (ex. cachectic, alcoholic)

  Ex. 150 mOsm / 50 mOsm/kg = **3 L max.**

  + thirst = hyponatraemia

Mechanisms - Diuretics

Urine maximum dilution/concentration impaired

→ fixed ~ 300 mOsm/kg

Like CKD, there is an obligatory urine output - loses ability to concentrate

add thirst = hyponatraemia

- Thiazide diuretics - common
  - common cause of hyponatraemia
  - mechanism not completely understood

Mechanism of low [Na]

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(you pee appropriately dilute but output too low **relative** to intake)

- Too much **H20** (Drink, irrigation, etc)
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"Everything is working as it should, but just not enough" (dilute pee)

↑ creatinine

↑ **ADH** (concentrated pee - "**AD**ds **H**20")

- **SIADH**: "Stress, sepsis, pain, infection, malignancy,etc

↓ effective circulating volume
("saves Na" - except renal cause)
(kidneys don't "see" enough blood flow

- **↑ ECF** (CCF, Cirrhosis, Sepsis)
- **↓ ECF**
  - **Non renal** (GI losses, bleed, etc)
  - **Renal Na^+ loss** (CKD,Thiazides, low steroid/thyroid)

(↑ ADH in response to ↓ effective circulating volume → "salt poor, concentrated pee"

"fixed dilution"

U [Osm] >100 mOsm

"Diagnosis of exclusion"

"not maximally diluted"

SIADH - Diagnosis of <u>Exclusion</u>

- ADH should **not** be present when....
  - Euvolaemic/hypervolaemic
  - serum osmolality is low
- If ADH present…then it is **inappropriate**

- Diagnostic criteria
  - Hypo-osmolar hyponatraemia
  - Urine not maximally diluted
    - **i.e.** urine osmolality >**100 mOsm**
  - Normal effective circulatory volume
    - Urine [Na] >30
  - Normal renal, thyroid and adrenal function

SIADH - Causes

Medication

- Antipsychotics
- SSRI
- Narcotics
- Cyclophosphamide
- Ecstasy
- Oxytocin
- etc

Stress

- Post-surgical
- Pain
- Vomiting

Pulmonary disease

- Asthma
- Mechanical ventilation
- Pneumonia
- TB
- Tumour

Neurological disease

- Meningitis
- Tumours
- Trauma
- SAH

HIV

Mechanism of low [Na]

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SIADH

"Stress, sepsis, pain, infection, malignancy,etc

↓ effective circulating volume

("saves Na" - except renal cause)

(kidneys don't "see" enough blood flow

- **↑ ECF** (CCF, Cirrhosis, Sepsis)
  - (↑ ADH in response to ↓ effective circulating volume → "salt poor, concentrated pee"
- **↓ ECF**
  - **Non renal** (GI losses, bleed, etc)
  - **Renal Na^+ loss** (CKD,Thiazides, low steroid/thyroid)

U [Osm] >100 mOsm

"fixed dilution" "not maximally diluted"

Often <u>multiple</u> causes co-exist (thiazides, low solute intake, renal impairment, etc)

Hyponatraemia

Introduction

Normal physiology

Mechanisms

Diagnosis + Treatment

Diagnosis of hyponatraemia

- **Symptomatic**
  - Treat **aggressively** to prevent cerebral oedema
- **Asymptomatic**
  - **Slowly** (**Osmotic demyelination - O.D.)

Treatment of hyponatraemia - **Symptomatic**

- Treating cerebral oedema **urgently** takes **precedent** over O.D.
- **Reduce ICP** with
  - 1-3 boluses of 2 ml/kg 3% NaCl every 5-minutes
    - Each bolus causes a rise in pl $[Na^+]$ of about 2 mmol/l
- Cerebral symptoms should decrease when pl $[Na^+]$ increases by ~ 4 to 6 mmol/l
- **Not** 0.9% NaCl it might worsen hyponatraemia in SIADH
- Cerebral disease, hepatic encephalopathy and sedation is not worsened by slight pl $[Na^+]$ increase

Lab approach to hyponatraemia - **Asymptomatic**

Is the kidney able to concentrate ?

To test concentrating/diluting function of kidney, check urine osmolality

Is patient "perceived" to be hypovolemic?

Bodies reaction to decreased effective circulating volume is to to save Na, therefore check the urine [Na]

Lab approach to hyponatraemia - **Asymptomatic**

Is the kidney able to concentrate ?

Urine osmolality

< 100 mOsm/kg

"Everything <u>is working</u> as it should, but just not enough"

> 100 mOsm/kg

"Everything <u>isn't working</u> as it should (not max.dilute urine)

Is patient "perceived" to be hypovolemic?

U sodium

</= 30 mmol/l

Response to
↓ **effective circulating volume**
→ "salt poor, concentrated pee"

↓ECV
↓ECF

↑ pl [Na]

Not sure of volume status, try giving a saline challenge (1-2 l) Response?

> 30 mmol/l

Kidneys can't retain salt (diuretics or CKD?)

↓ECV
↓ECF

→ or ↓ pl [Na]
"the more you spend (a penny) the more you save (H20)"

SIADH

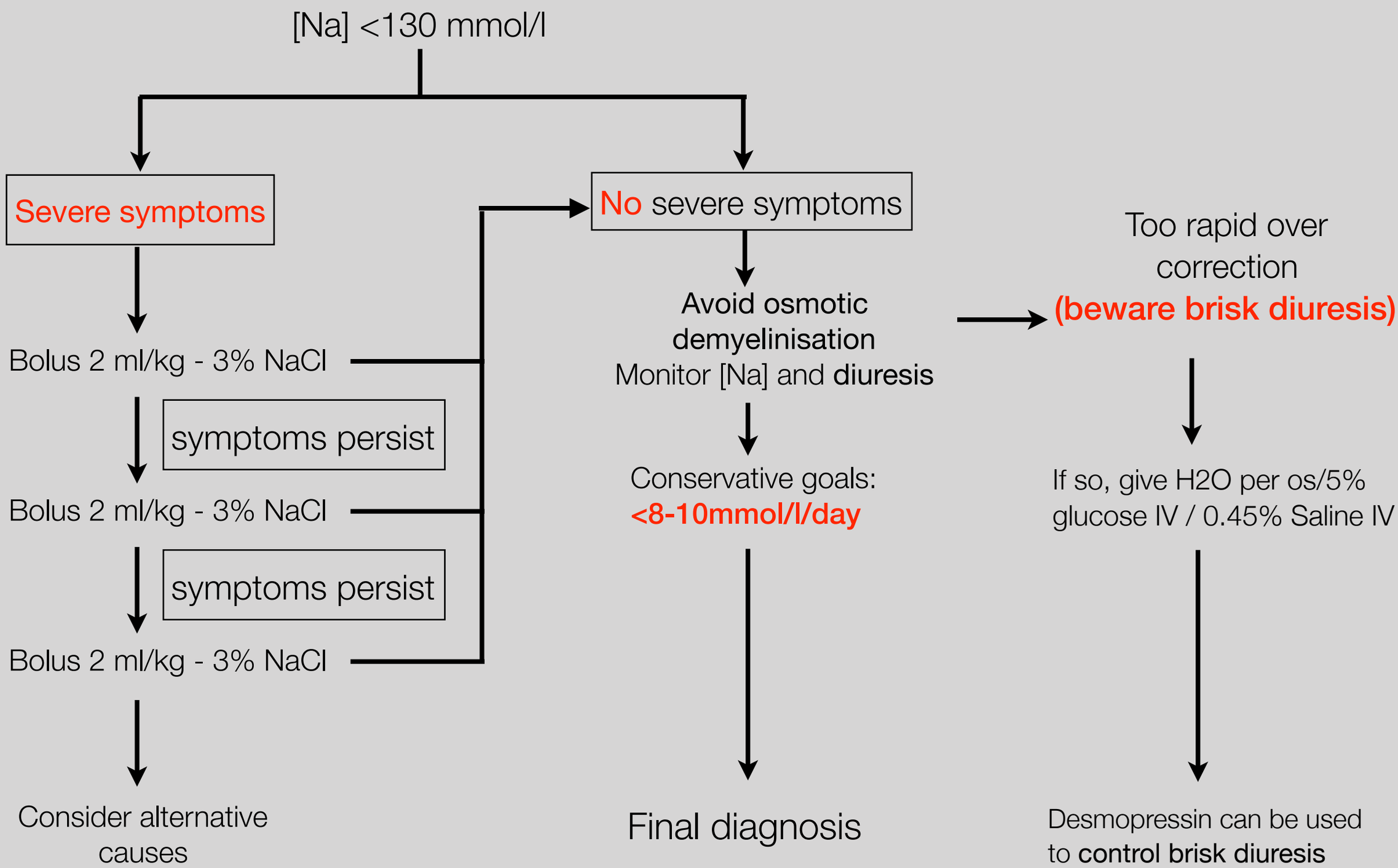
Diagnosis of **<u>exclusion</u>**

↓ECV
↑ECF

Treatment of hyponatraemia - **Asymptomatic**

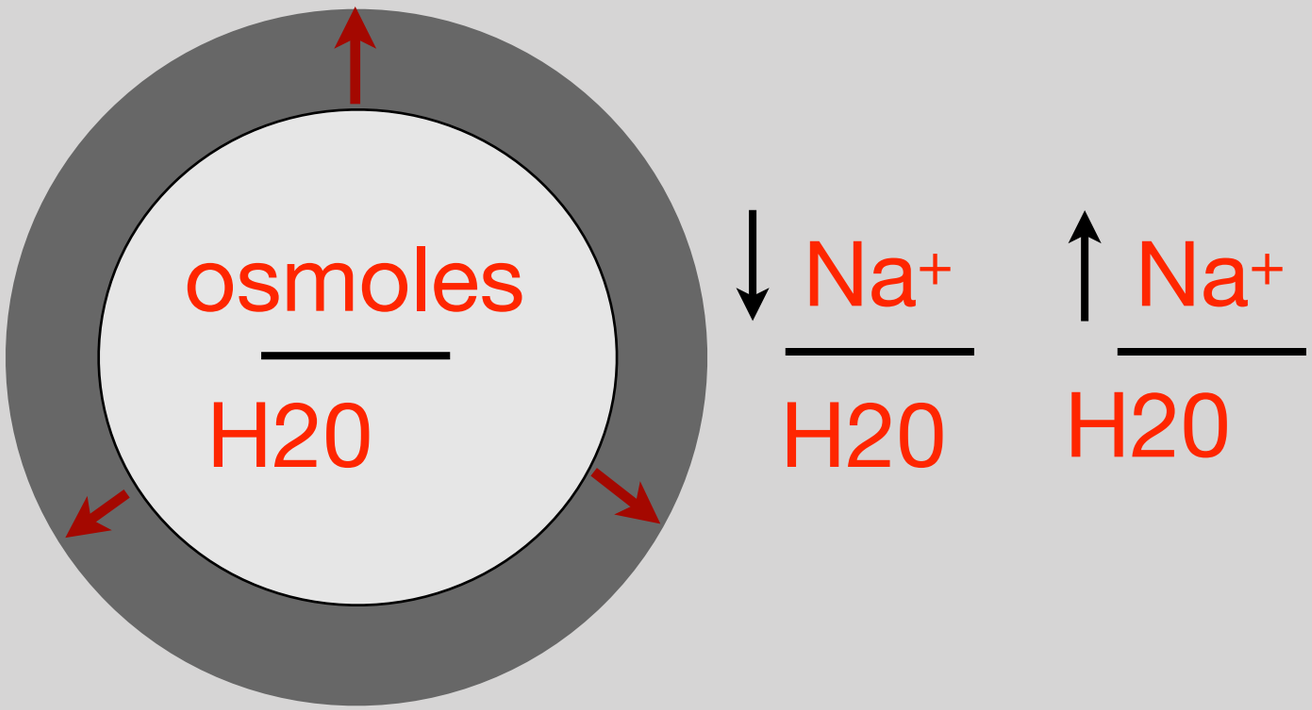
- **Avoid Osmotic Demyelinisation**
  - Correct **< 10 mMol/L/day (<0.5 mmol/l/hr)**
  - Care if Haemofiltration ***
- Despite **suppressed** ADH
  - Reduce H20 intake
  - Improve nutrition
- Thiazide diuretics
  - Stop
  - Beware over correction
- Conditions with **decreased effective circulating volumes** and **increased** ECF
  - Treat underlying condition (CCF, Cirrhosis, etc)
  - H20 restriction and loop diuretics +/- Vaptans
- Conditions with **decreased effective circulating volumes** and **decreased** ECF
  - **Hard to differentiate from SIADH**
  - **Response** to 1-2 L of 0.9% NaCl (not if symptomatic)
  - Should ↑[Na] as ECF restored and ADH stimulus is decreased

Treatment of hyponatraemia

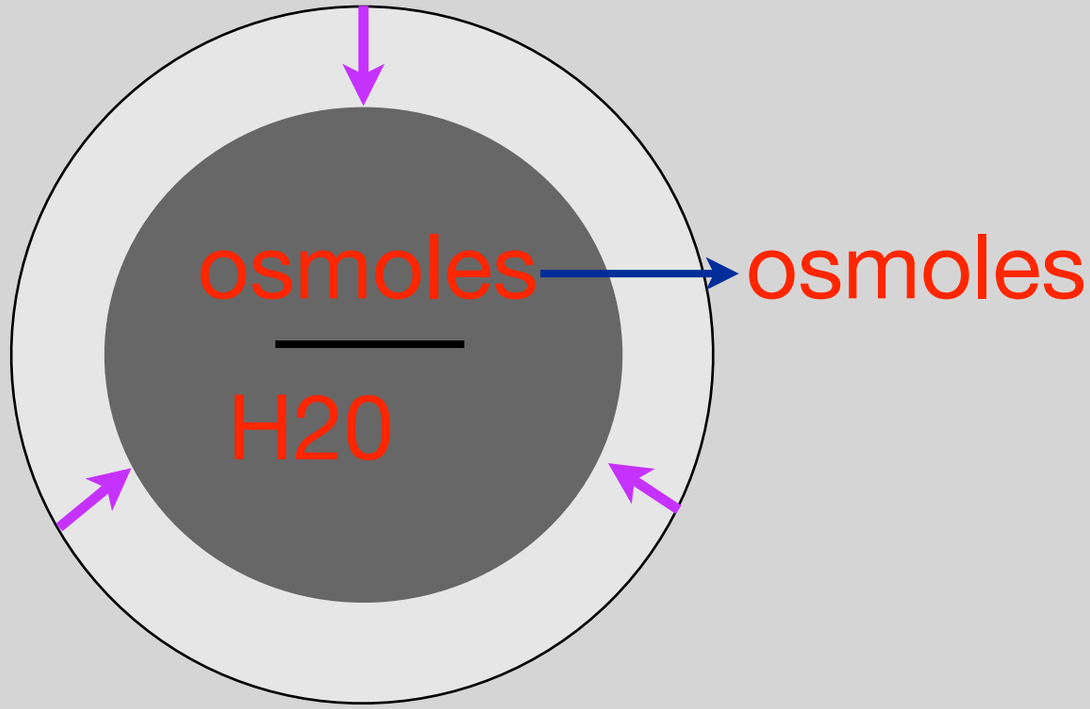


Osmotic Demyelination Syndrome

Acute hyponatraemia



Chronic hyponatraemia



Within **minutes** of hypotonicity ➙ is **swelling** of the brain

Within several **days** ➙ **normalization** of brain volume

Low osmolality in the brain persists despite the normalisation of brain volume.

Q J Med 2003; 96:935-947

Osmotic Demyelination Syndrome

- Patients with severe **chronic** hyponatraemia.

- Alcoholics, malnourished, hypokalaemia at highest risk.

- With rapid rise in [Na] (>12 mMol/L/day), mental status **improves**

  only to rapidly **deteriorate days later**

- The **prognosis** for osmotic demyelination syndrome is **poor**. In one study **only 33% recovered** completely !

RadioGraphics 2009; 29:933–938

Clinical case - Hyponatraemia

68 yr old female admitted with cardio-renal syndrome and pulmonary oedema

Na - 135

Rx - high dose frusemide with some effect

but.... Na - 126

Why?

U.Osm = 248 mOsm/kg +

+ “Tea and toast diet ~250 mOsm / day

therefore 250 mOsm / 250 mOsm/kg = **1 L**

(“**fixed dilution**” ex. diuretics, CKD “tubular injury” - fixed volume/dilution)

Recap - Hyponatraemia

- Common
- Hyponatraemia is a **WATER** problem, rarely a sodium problem
- **Symptomatic - Aggressive treatment**
- **Asymptomatic - Go Slow**
  - Beware Osmotic Demyelination Syndrome
    - <8 -10 mMol/L/24 hr
    - Watch for brisk diuresis
- “Traditional approach” - not easy in practice

???

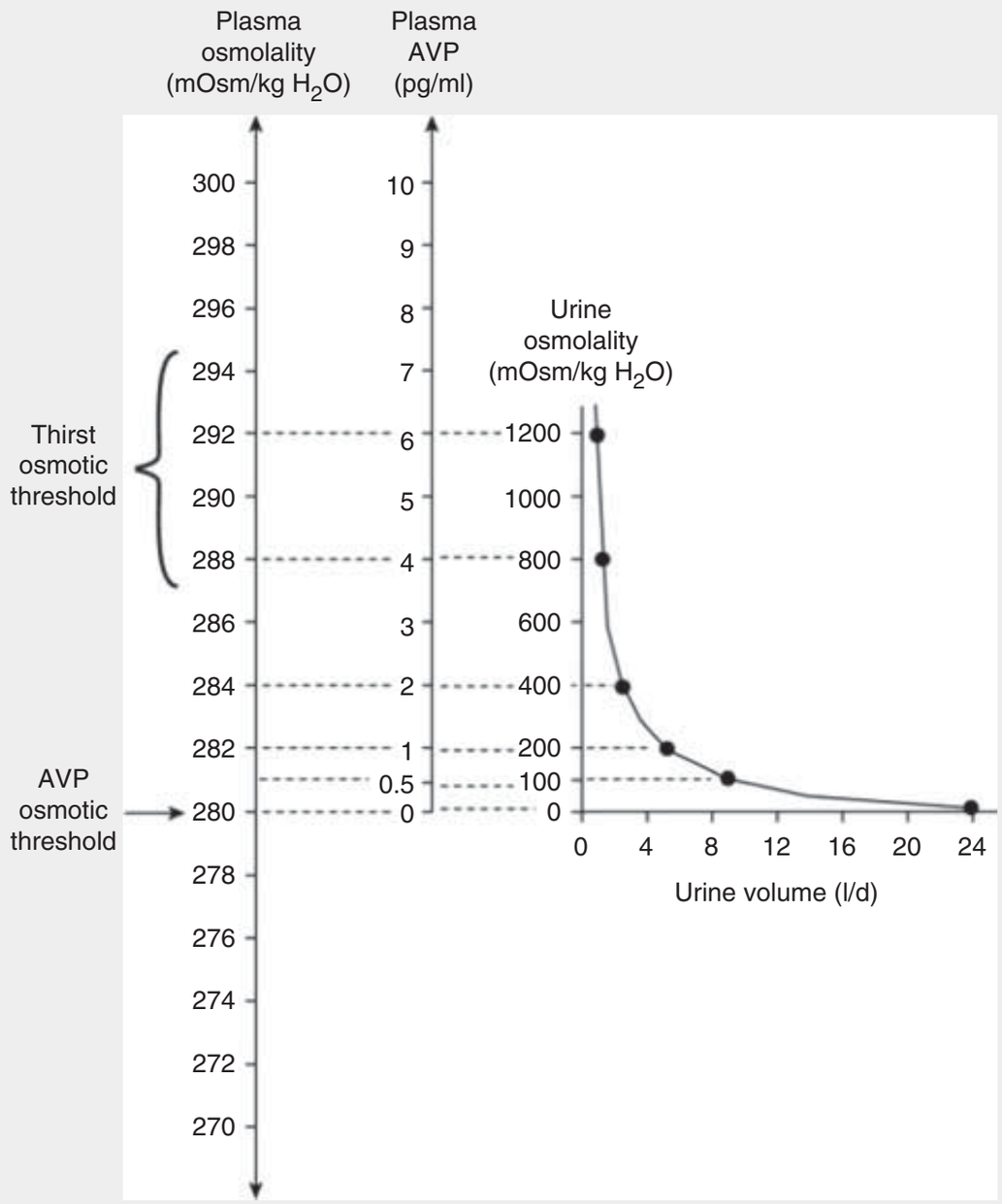
Download at

http://www.jvsmedicscorner.com

Mallory / Everest2013

New Slide?

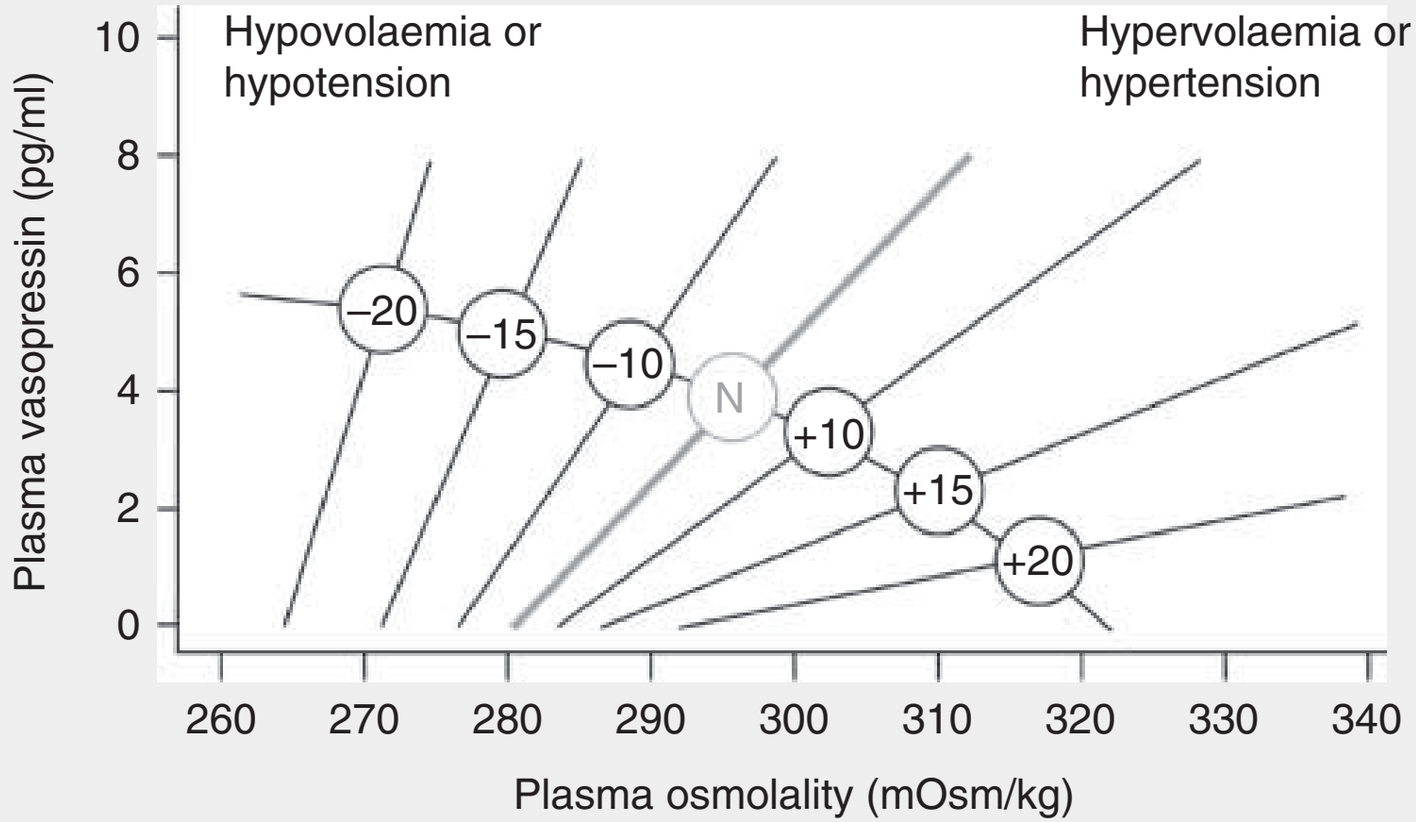
Osmotic stimulation of vasopressin release



European Journal of Endocrinology (2014) 170, G1–G47

New Slide?

Effect of hypovolaemis on osmoreceptor gain



European Journal of Endocrinology (2014) 170, G1–G47

New Slide?

XXX

In advanced kidney disease, urine osmolality is usually close to serum osmolality (isosthenuria). Free water removal is no longer regulated by vasopressin but is determined by the number of osmoles excreted in the urine (i.e. solute intake - urea and salts).

SIAD remains a diagnosis of exclusion

hypothyroidism very rarely causes hyponatraemia

Secondary adrenal insufficiency is caused by reduced or absent secretion of adrenocortico- trophic hormone, resulting in hypocortisolism. Under normal circumstances, cortisol suppresses both pro- duction of corticotrophin-releasing hormone and vasopressin in the hypothalamus. In secondary adrenal insufficiency, persistently low concentrations of cortisol fail to suppress vasopressin and hyponatraemia results from impaired free water excretion, as it does in SIAD

In primary adrenal insufficiency, hypoaldosteronism causes renal sodium loss, contracted extracellular fluid volume and hypona- traemia.

the brain needs ~48 h to adapt to a hypotonic environment, achieved mainly by extruding sodium, potassium, chloride and organic osmoles

sensitivity and specificity of clinical assessments of volume status are low

‘TURP- syndrome’. Although TURP syndrome causes isotonic hyponatraemia and hence does not cause brain oedema, neurological symptoms may develop due to accumulation of ammonia, serine or glyoxylate from the metabolism of glycine

adding 2.4mmol/l to the measured serum sodium concentration for every 5.5 mmol/l (100 mg/dl) incremental rise in serum glucose

t explains why during treatment of diabetic ketoacidosis or the hyperosmolar hyperglycaemic state a decrease in serum glycaemia leads to a ‘spontaneous’ rise in the serum sodium concentration.

The diagnostic difficulty we face with diuretics is that patients on these medications may have increased, normal or decreased extracellular and circulating volume and can have increased or decreased urine sodium concentration, depending on the timing of the most recent tablet, irrespective of their underlying volume status.

Urine sodium concentration can also be low in patients with heart failure or liver cirrhosis, due to reduced effective circulating arterial volume, even when they are taking diuretics (diuretic resistance)

urine osmolality %100 mOsm/kg on a spot urine sample always indicates maximally dilute urine.

European Journal of Endocrinology (2014) 170, G1–G47

New Slide?

XXX

Although all types of diuretics have been associated with hyponatraemia, thiazide diuretics are most commonly the culprit (39). Potassium-sparing diuretics such as miner- alocorticoid receptor blockers and amiloride may also cause hyponatraemia. It occurs less frequently with loop diuretics because they interfere with the renal concentrat- ing mechanism

Do not expect patients with severe symptoms to completely recover immediately, as it may take some time for the brain to fully recover.

Keepinmindthatifhypokalaemiaispresent,correction of the hypokalaemia will contribute to an increase in serum sodium concentration.

The estimated total body water (l) is calculated as a fraction of body weight. The fraction is 0.6 in non-elderly men and 0.5 in non-elderly women and 0.5 and 0.45 in elderly men and women respectively. Normally, extracellular and intracellular fluids account for 40 and 60% of total body water respectively.

a correction rate of 10 mmol/l during the first 24 h and 18 mmol/l during the first 48 h is probably a safe limit.

A sudden increase in urine output to O100ml/h signals increased risk of overly rapid rise in serum sodium concentration. If vasopressin activity is sud- denly suppressed, as happens when intravascular volume is restored in hypovolaemia, free water clearance can dramatically increase, resulting in serum sodium concentrations rising more rapidly than expected.

As a means of increasing solute intake,we suggest daily

intake of 0.25–0.50 g/kg urea can be used. The bitter taste can be reduced by combining it with sweet-tasting substances. The pharmacist may be asked to prepare the following as sachets: urea 10 gCNaHCO$_3$ 2 gC citric acid 1.5 gCsucrose 200 mg to be dissolved in 50–100 ml water. This will result in a more palatable, slightly sparkling solution.

it remains unclear whether hyponatraemia itself or the underlying disease explains the higher mortality risk.

avoiding increases in serum sodium concentration O10 mmol/l in the first 24 h and O18 mmol/l in the first 48 h,

Hence, the guideline development group unanimously preferred fluid restriction as first-line treatment. As a second-line treatment, we suggest an increased intake of osmotic solutes to enhance clearance of water. We agreed that oral urea might be the most practical method to achieve increased solute intake. The guideline group acknowledged the bitter taste of urea, which might reduce acceptability. However, we believed that this could be solved by combining urea with sweet-tasting substances as described in the recipe provided in the advice for clinical practice.

Although vasopressin receptor antagonists do increase serum sodium, the guideline development group judged that based on current evidence, these drugs cannot be recommended.

New Slide?

XXX

Patients with hyponatraemia and a contracted extracellular fluid volume have a combination of a true sodium and water deficit. They also have appropriate vasopressin secretion and hence diminished electrolyte- free water clearance, simultaneously resulting in dilutional hyponatraemia.

If hyponatraemia is caused by a contracted extracellular fluid volume, restoring this volume will suppress vaso- pressin secretion causing electrolyte-free water excretion to increase. Therefore, these patients are at high risk of an overly rapid increase in serum sodium concentration. Sudden increases in urine output can act as a warning signal that overly rapid correction of hyponatraemia is imminent.

Inadvertent overly rapid correction was due to documented water diuresis in 40% of cases.

The incidence of osmotic demyelinating syndrome resulting from overly rapid increases in serum sodium concentration is unknown.

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New Slide?

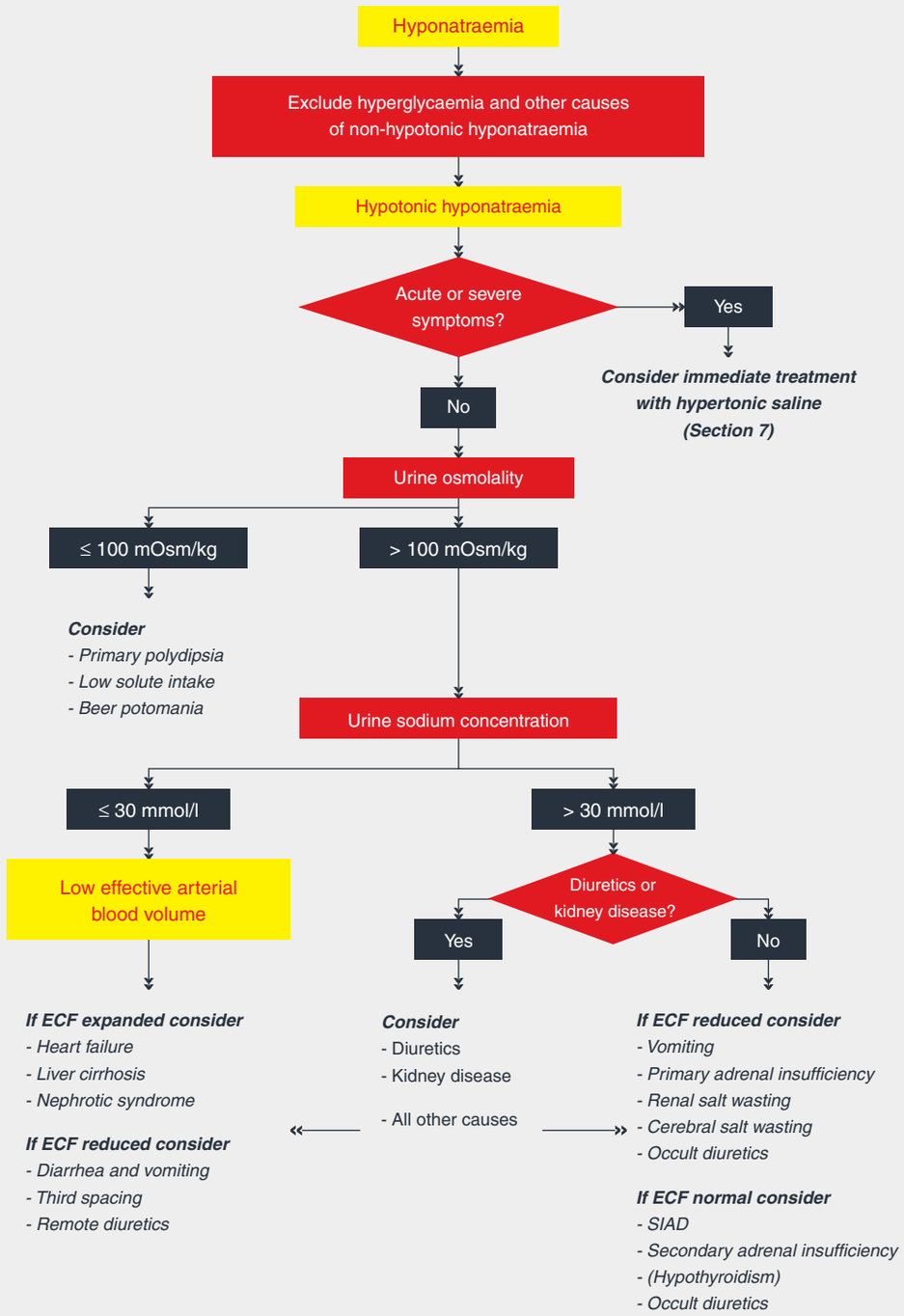
XXX

6.3. Which parameters to be used for differentiating causes of hypotonic hyponatraemia?

6.3.1.1. We recommend interpreting urine osmolality of a spot urine sample as a first step (1D).
6.3.1.2. If urine osmolality is $\leq$100 mOsm/kg, we recommend accepting relative excess water intake as a cause of the hypotonic hyponatraemia (1D).
6.3.1.3. If urine osmolality is $>$100 mOsm/kg, we recommend interpreting the urine sodium concentration on a spot urine sample taken simultaneously with a blood sample (1D).
6.3.1.4. If urine sodium concentration is $\leq$30 mmol/l, we suggest accepting low effective arterial volume as a cause of the hypotonic hyponatraemia (2D).
6.3.1.5. If urine sodium concentration is $>$30 mmol/l, we suggest assessing extracellular fluid status and use of diuretics to further differentiate likely causes of hyponatraemia (2D).
6.3.1.6. We suggest against measuring vasopressin for confirming the diagnosis of SIADH (2D).

New Slide?

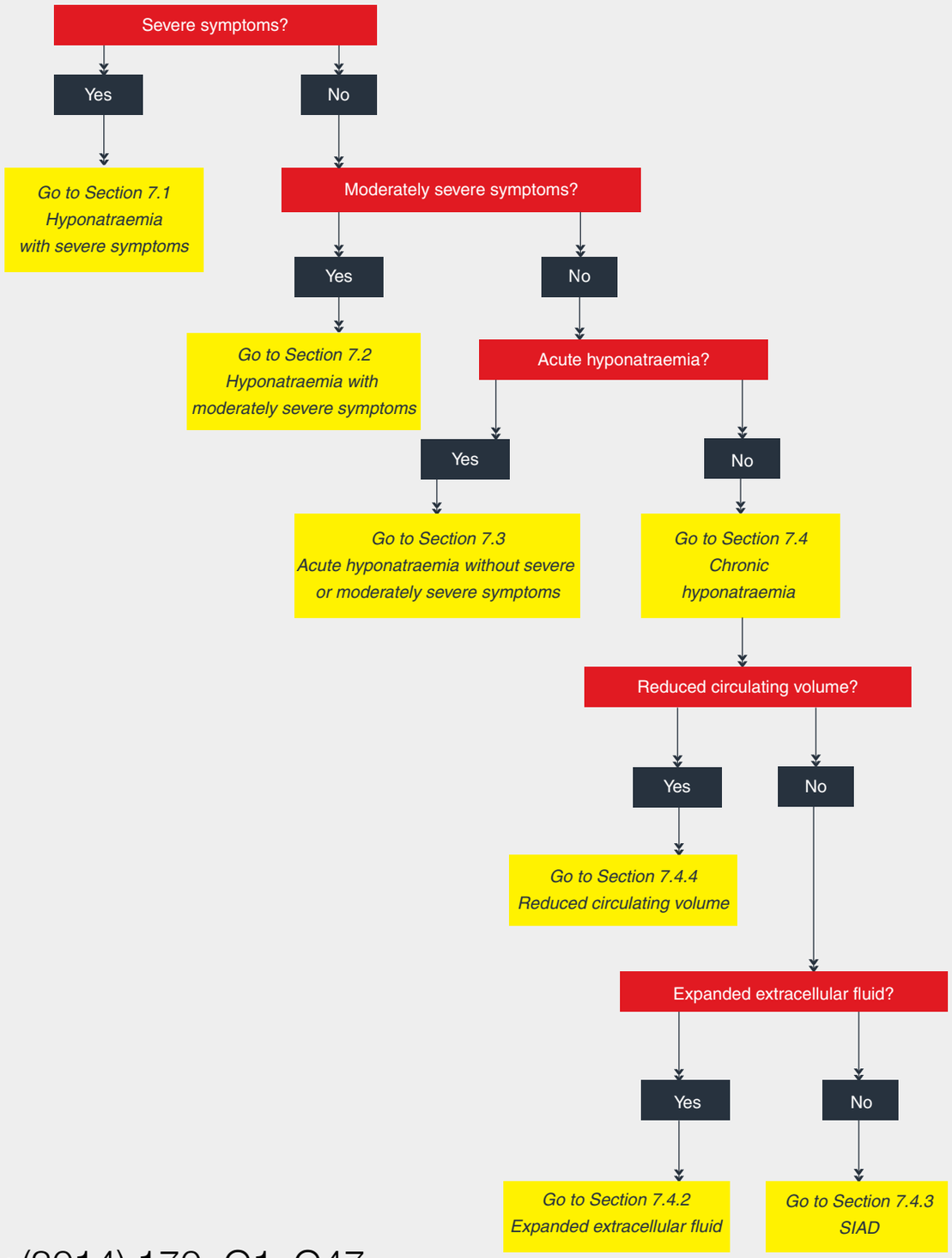
Algorithm for the diagnosis of hyponataemia



European Journal of Endocrinology (2014) 170, G1–G47

New Slide?

Algorithm for the management of hyponatraemia



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New Slide?

XXX

7.1.1. First-hour management, regardless of whether hyponatraemia is acute or chronic

7.1.1.1. We recommend prompt i.v. infusion of 150 ml 3% hypertonic over 20 min (1D).

7.1.1.2. We suggest checking the serum sodium concentration after 20 min while repeating an infusion of 150 ml 3% hypertonic saline for the next 20 min (2D).

7.1.1.3. We suggest repeating therapeutic recommendations 7.1.1.1 and 7.1.1.2 twice or until a target of 5 mmol/l increase in serum sodium concentration is achieved (2D).

7.1.1.4. Manage patients with severely symptomatic hyponatraemia in an environment where close biochemical and clinical monitoring can be provided (not graded).

New Slide?

XXX

7.1.2. Follow-up management in case of improvement of symptoms after a 5 mmol/l increase in serum sodium concentration in the first hour, regardless of whether hyponatraemia is acute or chronic

7.1.2.1. We recommend stopping the infusion of hypertonic saline (1D).
7.1.2.2. We recommend keeping the i.v. line open by infusing the smallest feasible volume of 0.9% saline until cause-specific treatment is started (1D).
7.1.2.3. We recommend starting a diagnosis-specific treatment if available, aiming at least to stabilise sodium concentration (1D).
7.1.2.4. We recommend limiting the increase in serum sodium concentration to a total of 10 mmol/l during the first 24 h and an additional 8 mmol/l during every 24 h thereafter until the serum sodium concentration reaches 130 mmol/l (1D).
7.1.2.5. We suggest checking the serum sodium concentration after 6 and 12 h and daily afterwards until the serum sodium concentration has stabilised under stable treatment (2D).

New Slide?

XXX

7.1.3. Follow-up management in case of no improvement of symptoms after a 5 mmol/l increase in serum sodium concentration in the first hour, regardless of whether hyponatraemia is acute or chronic.

7.1.3.1. We recommend continuing an i.v. infusion of 3% hypertonic saline or equivalent aiming for an additional 1 mmol/l per h increase in serum sodium concentration (1D).

7.1.3.2. We recommend stopping the infusion of 3% hypertonic saline or equivalent when the symptoms improve, the serum sodium concentration increases 10 mmol/l in total or the serum sodium concentration reaches 130 mmol/l, whichever occurs first (1D).

7.1.3.3. We recommend additional diagnostic exploration for other causes of the symptoms than hyponatraemia (1D).

7.1.3.4. We suggest checking the serum sodium concentration every 4 h as long as an i.v. infusion of 3% hypertonic saline or equivalent is continued (2D).

New Slide?

XXX

7.3. Acute hyponatraemia without severe or moderately severe symptoms

7.3.1.1. Make sure that the serum sodium concentration has been measured using the same technique used for the previous measurement and that no administrative errors in sample handling have occurred (not graded).

7.3.1.2. If possible, stop fluids, medications and other factors that can contribute to or provoke hyponatraemia (not graded).

7.3.1.3. We recommend starting prompt diagnostic assessment (1D).

7.3.1.4. We recommend cause-specific treatment (1D).

7.3.1.5. If the acute decrease in serum sodium concentration exceeds 10 mmol/l, we suggest a single i.v. infusion of 150 ml 3% hypertonic saline or equivalent over 20 min (2D).

7.3.1.6. We suggest checking the serum sodium concentration after 4 h, using the same technique as used for the previous measurement (2D).

New Slide?

XXX

7.4. Chronic hyponatraemia without severe or moderately severe symptoms

7.4.1. General management

7.4.1.1. Stop non-essential fluids, medications and other factors that can contribute to or provoke hyponatraemia (not graded).
7.4.1.2. We recommend cause-specific treatment (1D).
7.4.1.3. In mild hyponatraemia, we suggest against treatment with the sole aim of increasing the serum sodium concentration (2C).
7.4.1.4. In moderate or profound hyponatraemia, we recommend avoiding an increase in serum sodium concentration of >10 mmol/l during the first 24 h and >8 mmol/l during every 24 h thereafter (1D).
7.4.1.5. In moderate or profound hyponatraemia, we suggest checking the serum sodium concentration every 6 h until the serum sodium concentration has stabilised under stable treatment (2D).
7.4.1.6. In case of unresolved hyponatraemia, reconsider the diagnostic algorithm and ask for expert advice (not graded).

New Slide?

XXX

7.4.2. Patients with expanded extracellular fluid

7.4.2.1. We recommend against a treatment with the sole aim of increasing the serum sodium concentration in mild or moderate hyponatraemia (1C).
7.4.2.2. We suggest fluid restriction to prevent further fluid overload (2D).
7.4.2.3. We recommend against vasopressin receptor antagonists (1C).
7.4.2.4. We recommend against demeclocycline (1D).

New Slide?

XXX

7.4.3. Patients with SIAD

7.4.3.1. In moderate or profound hyponatraemia, we suggest restricting fluid intake as first-line treatment (2D).

7.4.3.2. In moderate or profound hyponatraemia, we suggest the following can be considered equal second-line treatments: increasing solute intake with 0.25–0.50 g/kg per day of urea or a combination of low-dose loop diuretics and oral sodium chloride (2D).

7.4.3.3. In moderate or profound hyponatraemia, we recommend against lithium or demeclocycline (1D).

7.4.3.4. In moderate hyponatraemia, we do not recommend vasopressin receptor antagonists (1C).

7.4.3.5. In profound hyponatraemia, we recommend against vasopressin receptor antagonists (1C).

New Slide?

XXX

7.4.4. Patients with reduced circulating volume

7.4.4.1. We recommend restoring extracellular volume with i.v. infusion of 0.9% saline or a balanced crystalloid solution at 0.5–1.0 ml/kg per h (1B).

7.4.4.2. Manage patients with haemodynamic instability in an environment where close biochemical and clinical monitoring can be provided (not graded).

7.4.4.3. In case of haemodynamic instability, the need for rapid fluid resuscitation overrides the risk of an overly rapid increase in serum sodium concentration (not graded).

New Slide?

XXX

7.5. What to do if hyponatraemia is corrected too rapidly?

7.5.1.1. We recommend prompt intervention for re-lowering the serum sodium concentration if it increases >10 mmol/l during the first 24 h or >8 mmol/l in any 24 h thereafter (1D).

7.5.1.2. We recommend discontinuing the ongoing active treatment (1D).

7.5.1.3. We recommend consulting an expert to discuss if it is appropriate to start an infusion of 10 ml/kg body weight of electrolyte-free water (e.g. glucose solutions) over 1 h under strict monitoring of urine output and fluid balance (1D).

7.5.1.4. We recommend consulting an expert to discuss if it is appropriate to add i.v. desmopressin 2 μg, with the understanding that this should not be repeated more frequently than every 8 h (1D).

Hypernatraemia

Introduction

Mechanisms

Treatment

Highest ever sodium

Fatal voluntary salt intake resulting in the highest ever documented sodium plasma level in adults (255 mmol L^{-1}):

Journal of Internal Medicine 2004; 256: 525–528

Highest survivor had a sodium of [193]

Am J Med 1985; 78: 176–8.

Hypernatraemia

Introduction

Mechanisms

Treatment

Hypernatraemia

- In almost all cases, there is loss of free water
- Persistent hypernatremia does **not** occur in healthy subjects because the ensuing rise in P_{Osm} stimulates both thirst and the release of ADH, which minimizes further water loss.
- Even patients with diabetes insipidus, with marked polyuria due to diminished ADH effect, maintain a near-normal plasma sodium by increasing water intake.
- The result is that hypernatremia occurs primarily in those patients who **cannot express thirst** normally
- A patient with a plasma sodium concentration of 150 mEq per L or more who is alert but not thirsty has a hypothalamic lesion

Rippe Textbook of Intensive Care Medicine

Hypernatraemia

- A rise in the plasma [Na^+] is a potent stimulus to **ADH** release and **thirst**
- A P_{Osm} > 295 mOsm per kg (a plasma [Na^+] ~ 145 to 147 mmol / L) generally leads to sufficient ADH secretion to maximally stimulate urinary concentration.
- The U_{Osm} in hypernatremia should exceed 700 to 800 mOsm per kg.
- The urinary sodium concentration should be **less than 20 mmol / L** when **water loss** and **volume depletion** are the primary problems
- It is > **100 mmol / L** in a **salt-overload** state
- If, the U_{Osm} is **lower** than that of the plasma, then either central (ADH-**deficient**) or nephrogenic (ADH-**resistant**) **diabetes insipidus** is present.

Fluids commonly lost	Sodium concentration (mMol/L)
Diarrhoea	40
Gastric secretions	55
Sweat	80
Frusemide diuresis	75
Pancreatic secretions	145
Small bowel secretions	145
Urine *	<10
* Varies according to daily intake	

Hypernatraemia

Introduction

Mechanisms

Treatment

Hypernatraemia - Treatment

As in hyponatremia, the cerebral adaptation in hypernatremia has **two** important clinical consequences:

1. **Chronic hypernatremia** neurologic symptoms are less likely
   Assessment of symptoms is often difficult because patients may have underlying neurologic disease, which reduces the protective thirst mechanism

2. Correct slowly (0.5 mmol /L per hour) to prevent rapid fluid movement into the brain leading to cerebral edema. .

Rippe Textbook of Intensive Care Medicine

Hypernatraemia - Treatment

1. Hypernatraemia + hypovolaemic
    - **First correct hypovolaemia**
    - Restore ECV + H20 deficit
2. Hypernatraemia + normal ECF
    - Restore H20 deficit
    - If central diabetes insipidis - add desmopressin
3. Hypernatraemia + increased total body solute
    - Diuretics
    - Replace with hypotonic fluid
    - Rarely dialysis

Slow correction

Risk of seizures from cerebral oedema

Not > 0.5 mMol/hr (<12 mMol/L/day)

Hypernatraemia - Treatment

Current TBW x current pl [Na^+] = Normal TBW x normal pl [Na^+]

Current TBW = Normal TBW x (140/current pl [Na^+])

normal TBW is ~ 60% lean body weight in men and 50% in women.

The water deficit is the **difference** between normal and current TBW

Ex. 70 kg woman has a [Na^+] 0f 160 mmol/l.

Normal TBW = 50% x 70kg = 35L

current TBW = 35 x 140/160 = 30.5 L

TBW deficit = 35 - 30.5 = 4.5 L

“I would give 1/2 this as free water per day, unless symptomatic”

???

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(Mallory / Everest2013)