

# Advances in the understanding & management of hyponatraemia

John Newell-Price

[j.newellprice@sheffield.ac.uk](mailto:j.newellprice@sheffield.ac.uk)



The  
University  
Of  
Sheffield.

# Lecture outline

## Case based

- Acute symptomatic (emergency) hyponatraemia
- Chronic hyponatraemia
- Hyponatraemia in patients needing chemotherapy

# Case 1

- 29 year old male
- very fit but recently taken up fell running
- 18 mile race with 2200m of ascent in morning of hottest day of the year
- Regular water throughout race and all afternoon after - witnessed
- That evening - found at home drowsy and confused, evidence of urinary incontinence
- Ambulance to A+E

# Case 1

O/E

- GCS 10, agitated
- BP 118/70, Pulse 56, not dehydrated
- No focal neurology
- CT head normal
- ABG - no acid/base disturbance
- O<sub>2</sub> sats on air 100%

# Case 1

## Investigations

Na+	122 mmol/L
K+	4.1 mmol/L
Urea	2.6 mmol/L
Creat	79 $\mu$ mol/L
Glucose	4.6 mmol/L
Plasma osmolality	249 mOsmol/kg
Urine osmolality	220 mOsmol/kg
Urine sodium	30 mmol/L

# Case 1

## Investigations

Na+	122 mmol/L
K+	4.1 mmol/L
Urea	2.6 mmol/L
Creat	79 $\mu$ mol/L
Glucose	4.6 mmol/L
Plasma osmolality	249 mOsmol/kg
Urine osmolality	220 mOsmol/kg
Urine sodium	30 mmol/L

How would you classify his hyponatraemia?

# Classification of Hyponatraemia

## Biochemical

- Mild 130-135mmol/l
- Moderate 125-129mmol/l
- Severe <125mmol/l

# Classification of Hyponatraemia

## Biochemical

- Mild 130-135mmol/l
- Moderate 125-129mmol/l
- Severe <125mmol/l

## Symptoms

- Mild
- Moderate
- Severe



# Classification of Hyponatraemia

## Biochemical

- Mild 130-135mmol/l
- Moderate 125-129mmol/l
- Severe <125mmol/l

## Symptoms

- Mild
- Moderate
- Severe

## Aetiology

- Hypovolaemic
- Euvolaemic
- Hypervolaemic

# Classification of Hyponatraemia

## Biochemical

- Mild 130-135mmol/l
- Moderate 125-129mmol/l
- Severe <125mmol/l

## Symptoms

- Mild
- Moderate
- Severe

## Aetiology

- Hypovolaemic
- Euvolaemic
- Hypervolaemic

## Acuity of onset

- Acute < 48 hours
- Chronic > 48 hours

# Classification of Hyponatraemia

15-22% of all hospitalised patients

## Biochemical

- Mild 130-135mmol/l
- Moderate 125-129mmol/l
- Severe <125mmol/l

## Symptoms

- Mild
- Moderate
- Severe

## Aetiology

- Hypovolaemic
- Euvolaemic
- Hypervolaemic

## Acuity of onset

- Acute < 48 hours
- Chronic > 48 hours

# Hyponatraemia

## General

- Stop hypotonic fluids
- Review drug card – long list - PPI etc.

## Specific

- Plasma and Urine Osmolality
- Urinary Na<sup>+</sup>
- glucose
- TFT's
- +/- Assessment of Cortisol
- Assessment of underlying causes eg chest imaging

# Symptomatic Hyponatraemia

**No or Mild  
Symptoms**

**Moderate  
Symptoms**

**Severe  
Symptoms**

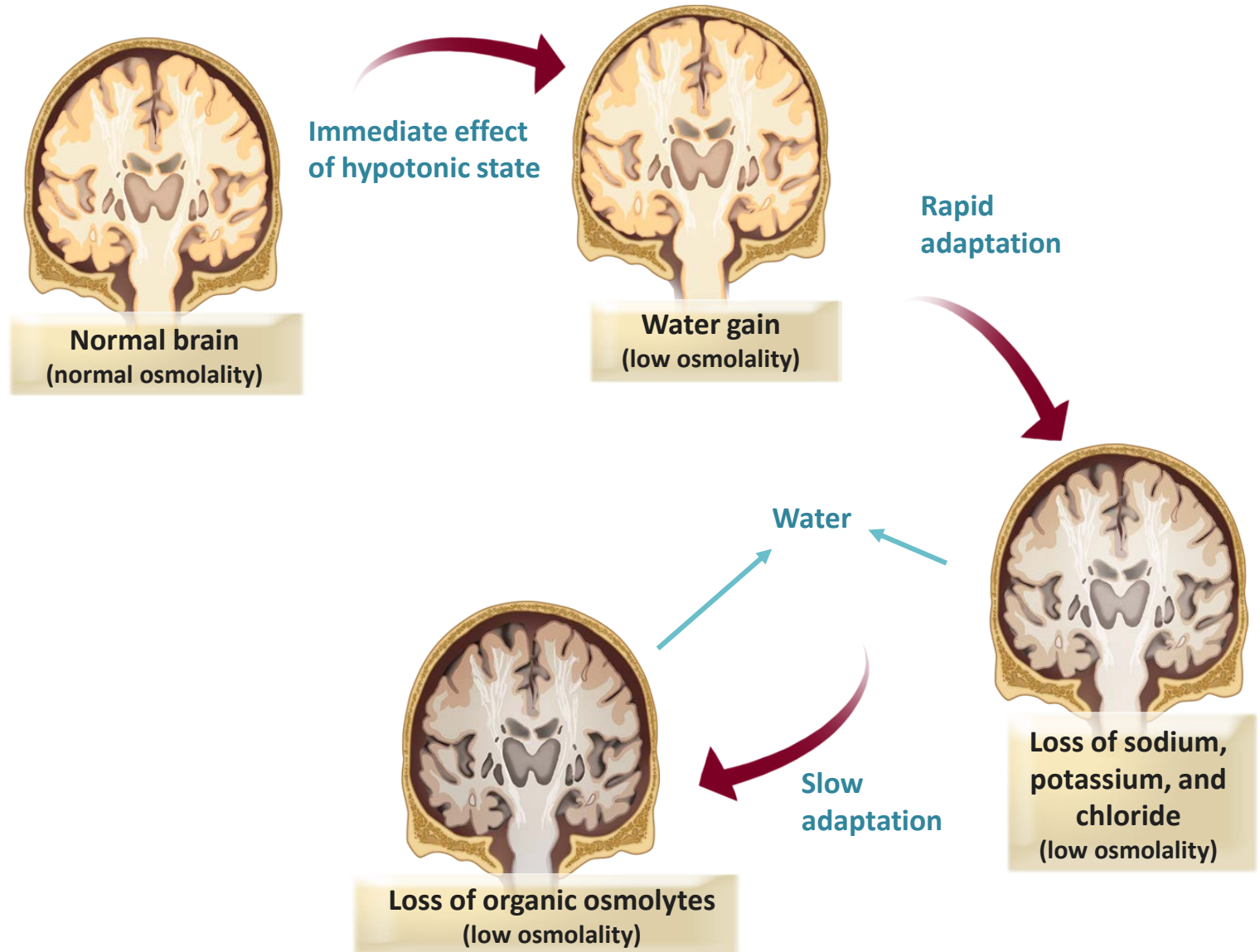
USUALLY CHRONIC

ACUTE OR CHRONIC

- Headache
- Irritability
- Nausea / vomiting
- Mental slowing
- Unstable gait / falls
- Confusion / delirium
- Disorientation

- Stupor / coma
- Convulsions
- Respiratory arrest

# The brain undergoes volume adaptation in response to gradual-onset hyponatraemia



Adroque HJ, Madias NE, *NEJM*. 2000; 342: 21: 1581-1589.

# Case 1

- Acute severe symptomatic (emergency) hyponatraemia
- *NO* time to wait for all the biochemical results – (TSH, cortisol etc)

SOCIETY FOR ENDOCRINOLOGY  
ENDOCRINE EMERGENCY GUIDANCE



# Emergency management of severe symptomatic hyponatraemia in adult patients

**Stephen Ball<sup>1</sup>, Julian Barth<sup>2</sup>, Miles Levy<sup>3</sup> and the Society for Endocrinology  
Clinical Committee<sup>4</sup>**

<sup>1</sup>Department of Endocrinology, Central Manchester University Hospitals Foundation Trust,  
Manchester Royal Infirmary, Manchester, UK

<sup>2</sup>Leeds General Infirmary, Leeds Teaching Hospitals NHS Trust, Blood Sciences, Leeds, UK

<sup>3</sup>Department of Endocrinology, University Hospitals of Leicester, Leicester Royal Infirmary, Leicester, UK

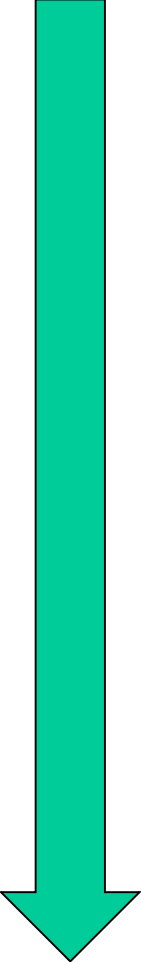
<sup>4</sup>The Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol, UK

2016

Correspondence  
should be addressed  
to S Ball  
**Email**  
[s.ball@manchester.ac.uk](mailto:s.ball@manchester.ac.uk)



# Management of acute severe symptomatic hyponatraemia



1. iv 150ml of 3% Saline or equivalent over 20 mins

2. Check serum Na<sup>+</sup>

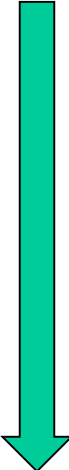
3. Repeat twice until **5mmol/L increase Na<sup>+</sup>**

4. **After 5mmol/L increase**  
Stop hypertonic saline  
Establish diagnosis  
Na<sup>+</sup> 6 hourly for 1<sup>st</sup> 24 hours  
Limit increase to 10mmol/l first 24 hour

# Case 1

Initial Na<sup>+</sup> 122 mmol/L

Treatment:

- 
- 1.8% N/saline 300ml over 20 mins
  - More alert after 30 mins
  - Repeat serum Na<sup>+</sup> 124 mmol/L
  - Further bolus 1.8% N/Saline 300ml
  - Much more alert 1 hour later
  - Repeat serum Na<sup>+</sup> 127 mmol/L – able to converse

# Case 1

- diagnosis = high vasopressin (ADH) secretion - intense exercise, *and* excessive hypotonic fluid intake
- rapid fall – no reason to think Na<sup>+</sup> not normal before
- as rapid fall rapid correction permissible

## Case 2

- 84 yr old lady
- Admitted with back pain and abdo pain
- Poor appetite
- Recent chest infection
- Independent and self caring
- No oedema
- Not dehydrated

## Case 2 - Drugs

- Theophylline 175mg OD
- Isotard XL 90 mg OD
- Nicorandil 5mg OD
- Diltiazem 120 mg OD
- Aspirin 75 mg OD
- inhalers

## Case 2

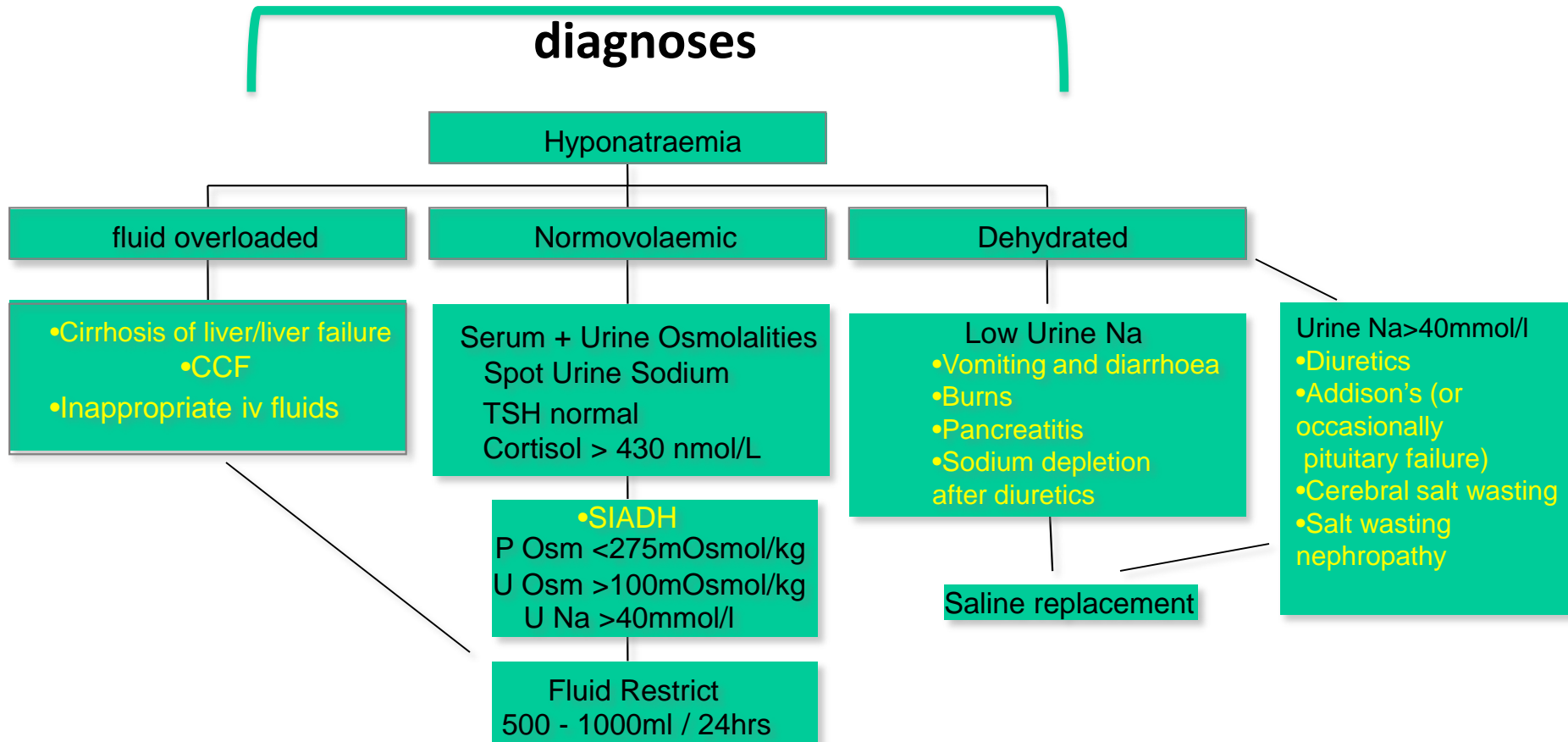
Na	113 mmol/L
K	3.9 mmol/L
Urea	2.9 mmol/L
Creat	52 umol/L

## Case 2

Na	113 mmol/L
K	3.9 mmol/L
Urea	2.9 mmol/L
Creat	52 $\mu$ mol/L
Plasma osmolality	251 mOsmol/kg
Urine osmolality	510 mOsmol/kg
Urine sodium	124 mmol/L
TSH	2.5 mU/L
Cortisol	510 nmol/L

# Assessment and management of chronic hyponatraemia

## Combinations of diagnoses



1. Ellison DH, et al. *N Engl J Med.* 2007;356:2064-2072..

2. Verbalis JG, et al. *Am J Med.* 2007;120(11A):S1-S21.



# Case 2

Na 113 mmol/L

K 3.9 mmol/L

Urea 2.9 mmol/L

Creat 52  $\mu$ mol/L

**Euvolaemic  
= SIADH**

Plasma osmolality 251 mOsmol/kg

Urine osmolality 510 mOsmol/kg

Urine sodium 124 mmol/L

TSH 2.5 mU/L

Cortisol 510 nmol/L

# Treatment of Chronic Euvolaemic Hyponatremia (SIADH)

- **First line therapy:**

Fluid restriction is generally first-line therapy – not always well tolerated or imposed

- **Second line therapy:**

Demeclocycline

Vaptans

Furosemide and oral NaCl

[Urea (0.25-0.5g/kg per day)]

- **Treat underlying cause and stop precipitating drugs**

# Case 2

Fluid restriction 750ml/day:

	Na
Day1	106
Day 2	108
Day 3	107
Day 4	109
Day 5	111
Day 6	108

**Is the diagnosis correct?**

**Other therapy?**

# Predictors of the likely failure of fluid restriction

- High urine osmolality ( $>500$  mOsm/kg  $H_2O$ )
- Sum of the urine  $Na^+$  and  $K^+$  concentrations exceeds serum  $Na^+$  concentration
- 24-hour urine volume  $<1500$  mL/day
- Increase in serum  $Na^+$  concentration  $<2$  mmol/L/d in 24-48 hours on a fluid restriction of 1 L/d

# Predictors of the likely failure of fluid restriction

- High urine osmolality ( $>500$  mOsm/kg  $H_2O$ ) 510 mOsm/kg
- Sum of the urine  $Na^+$  and  $K^+$  concentrations exceeds serum  $Na^+$  concentration Serum  $Na^+$  113, Urine  $Na^+$  124 mmol/L
- 24-hour urine volume  $<1500$  mL/day
- Increase in serum  $Na^+$  concentration  $<2$  mmol/L/d in 24-48 hours on a fluid restriction of 1 L/d

# Case 2 contd

- Fluid restriction 750ml/day

Taking 750ml water + 4 cups of tea + fruit Juice

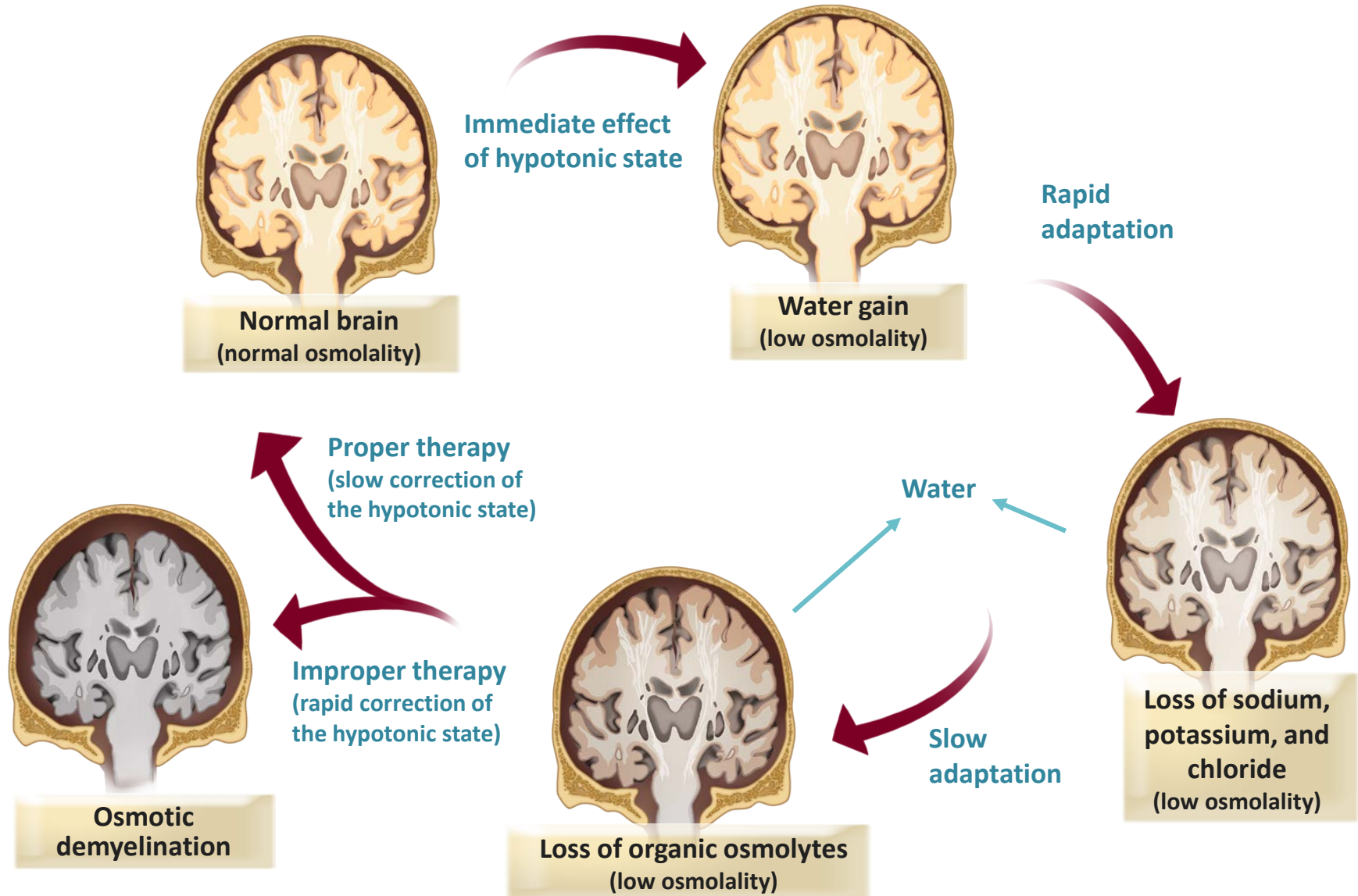
- Reinforced fluid restriction

- 5 days later

Na	134	U Osmo	475
K	4.1	U Na	16
Ur	4.5		
Cr	54		

Cause - carcinoma of the lung

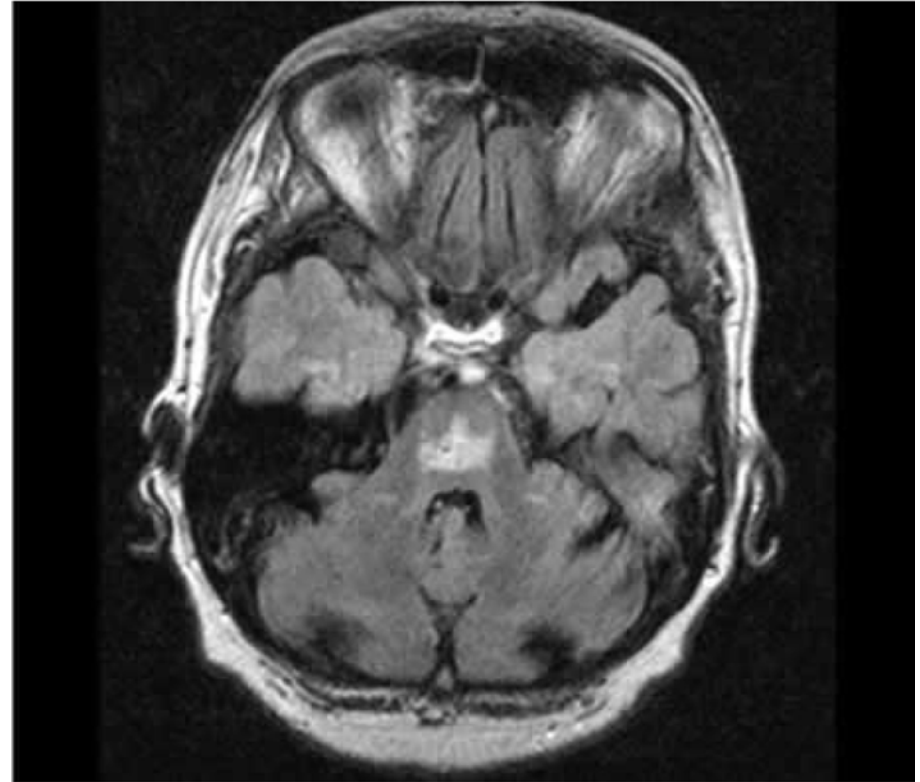
# The brain undergoes volume adaptation in response to gradual-onset hyponatraemia



Adroge HJ, Madias NE, *NEJM*. 2000; 342: 21: 1581-1589.

# Osmotic demyelination syndrome

- White areas in the middle of the pons
- Massive demyelination of descending axons
- May take up to 2 weeks to manifest





# Risk Factors for Osmotic Demyelination Syndrome (ODS)

- Serum Na<sup>+</sup> <105mmol/L
- Hypokalaemia
- Chronic excess alcohol
- Malnutrition
- Advanced Liver disease
- >18mmol/L Na<sup>+</sup> increase in 48 hour

## LIMITS (not targets) for NA<sup>+</sup> rise

- High risk <8mmol/l in any 24 hour period
- Normal <10-12mmol/l in any 24 hour period

# Re-lowering serum Na<sup>+</sup>

- Desmopressin s/c to prevent further water losses eg 2-4 µg every 8 hours (as necessary)
- Replace water orally or as 5% dextrose (IV 3 mL/kg/h)

**Recheck serum Na<sup>+</sup> hourly and continue therapy infusion until serum Na<sup>+</sup> is reduced to goal**

# Case 3

- 67 yr old lady
- Found on Floor
- Mucous membrane - dry
- Diminished skin turgor
- DHx
  - Simvastatin 40 mg OD
  - Bisoprolol 2.5 mg OD
  - Bendroflumethazide 2.5 mg OD

# Case 3 investigations

Na	106	mmol/l
K	2.2	mmol/l
U	5.2	mmol/l
Cr	97	micromol/l
C Ca	2.2	mmol/l

S Osmo	228	mOsmol/kg
U Osmo	307	mOsmol/kg
Urine sodium	<6	mmol/L

CXR - rotated, over-penetrated

# Treatment of Chronic Hypovolaemic Hyponatremia

- Stabilise blood pressure with fluid resuscitation as required
- $K^+$  supplementation is also often required - this may lead to a more rapid increase in  $Na^+$
- In diuretic induced hypovolaemic hyponatraemia
  - Stopping thiazides and correction of volume deficits can lead to a rapid rise in  $Na^+$  due to a **rapid spontaneous water diuresis with overcorrection**
  - Monitor serum sodium (6-8 hourly)

# Case 3 continued

- Thiazide stopped
- Careful Saline replacement
- Serum sodium normalised after 6 days

# Case 4

- 68 female
- Metastatic gastric cancer – needing chemotherapy
- Rx
  - Thyroxine 50
  - simvastatin 40mg
- Serum Na<sup>+</sup> 122 mmol/L
- Urine sodium 128 mmol/L
- All biochemistry consistent with SIADH

# Vasopressin 2 Receptor antagonist - Tolvaptan commissioning NHSE 27.09.17

All need to be fulfilled:

1. Mild / moderate hyponatraemia (serum sodium 125-135mmol/L)
2. Patient fulfils diagnostic criteria for SIADH
3. Oncologist confirms that chemotherapy delayed due to hyponatraemia secondary to SIADH
4. Tolvaptan has been authorised by the locally designated endocrinologist
5. Used for a limited period (maximum of 10 days)

<https://www.england.nhs.uk/publication/clinical-commissioning-policy-tolvaptan-for-hyponatraemia-secondary-to-the-syndrome-of-inappropriate-antidiuretic-hormone-siadh-in-patients-requiring-cancer-chemotherapy/>



# Conclusions

- Hyponatraemia is very common in clinical practice
- Type of morbidity depends on whether onset and duration of hyponatraemia is acute or chronic
- Treatment depends on whether acute or chronic/ symptomatic and volume status
- If you treat hyponatraemia you have to monitor the progress closely and react