



Disorders of water



Detlef Bockenhauer

Great Ormond Street
Hospital for Children

NHS Trust



European
Reference
Network

for rare or low prevalence
complex diseases

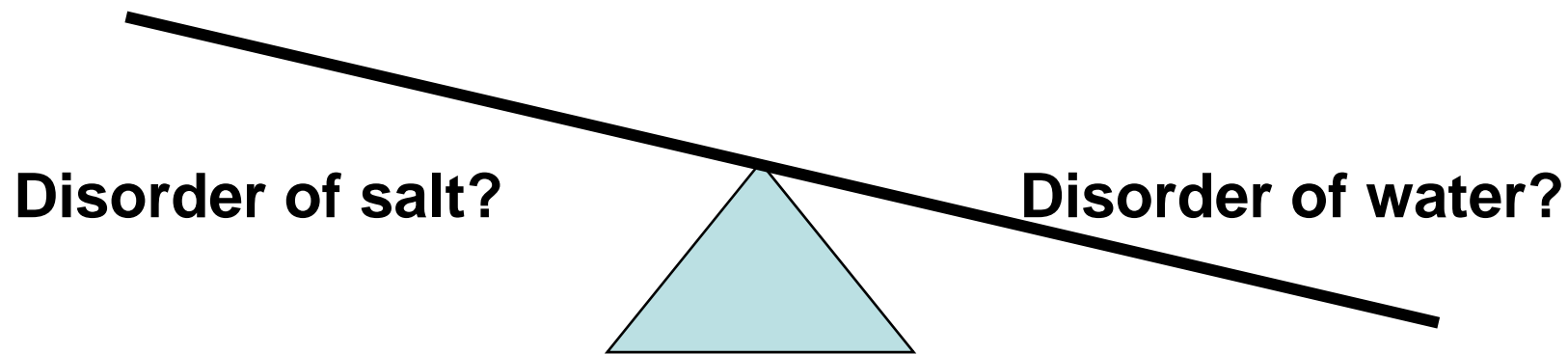
Network

Kidney Diseases (ERKNet)

How do we measure water?

How do we measure water?

- Not directly!
- Reflected best in Na concentration
- Water overload => Hyponatraemia
- Water deficiency => Hypernatraemia
- Dysnatraemia: is it salt? Or water?



True or false?

- The kidneys are to provide electrolyte homeostasis. Therefore, in hyponatraemia, the kidneys should preserve sodium (minimise renal sodium losses).

True or false?

- The urine sodium concentration can help distinguish between renal (cerebral/pulmonary) salt wasting and SIADH.

Hyponatraemia

Why is the sodium low?

- Too little salt
 - Weight should be decreased
 - Signs of dehydration/volume depletion
- Too much water
 - Weight should be stable or increased
 - Patient is eu- or hypervolaemic

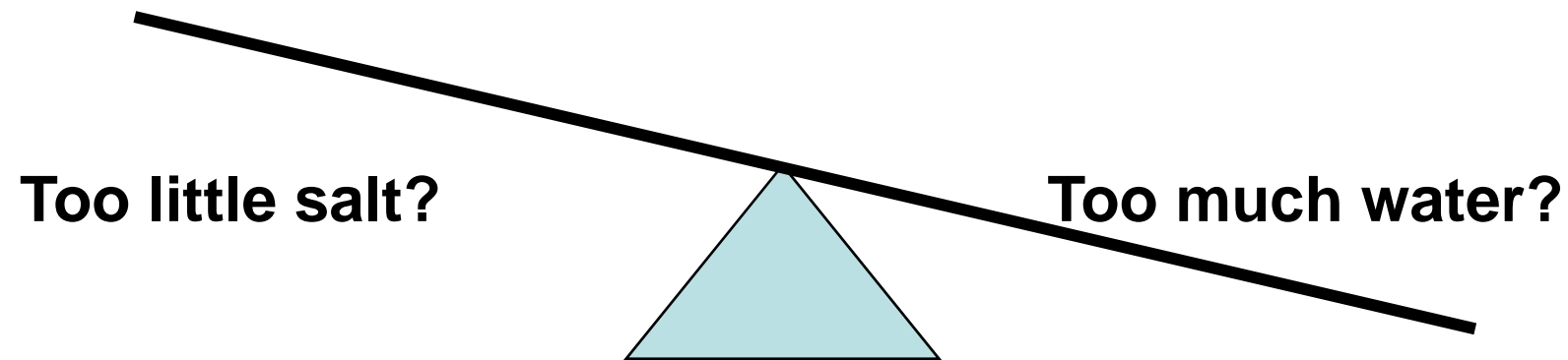
case 1

- 6-months old boy with astrocytoma
- Receives vincristine and carboplatin
- 10 days later presents for routine follow-up
- Examination: well perfused, wt: 4.7 kg (+0.2 kg), BP: 82 mmHg

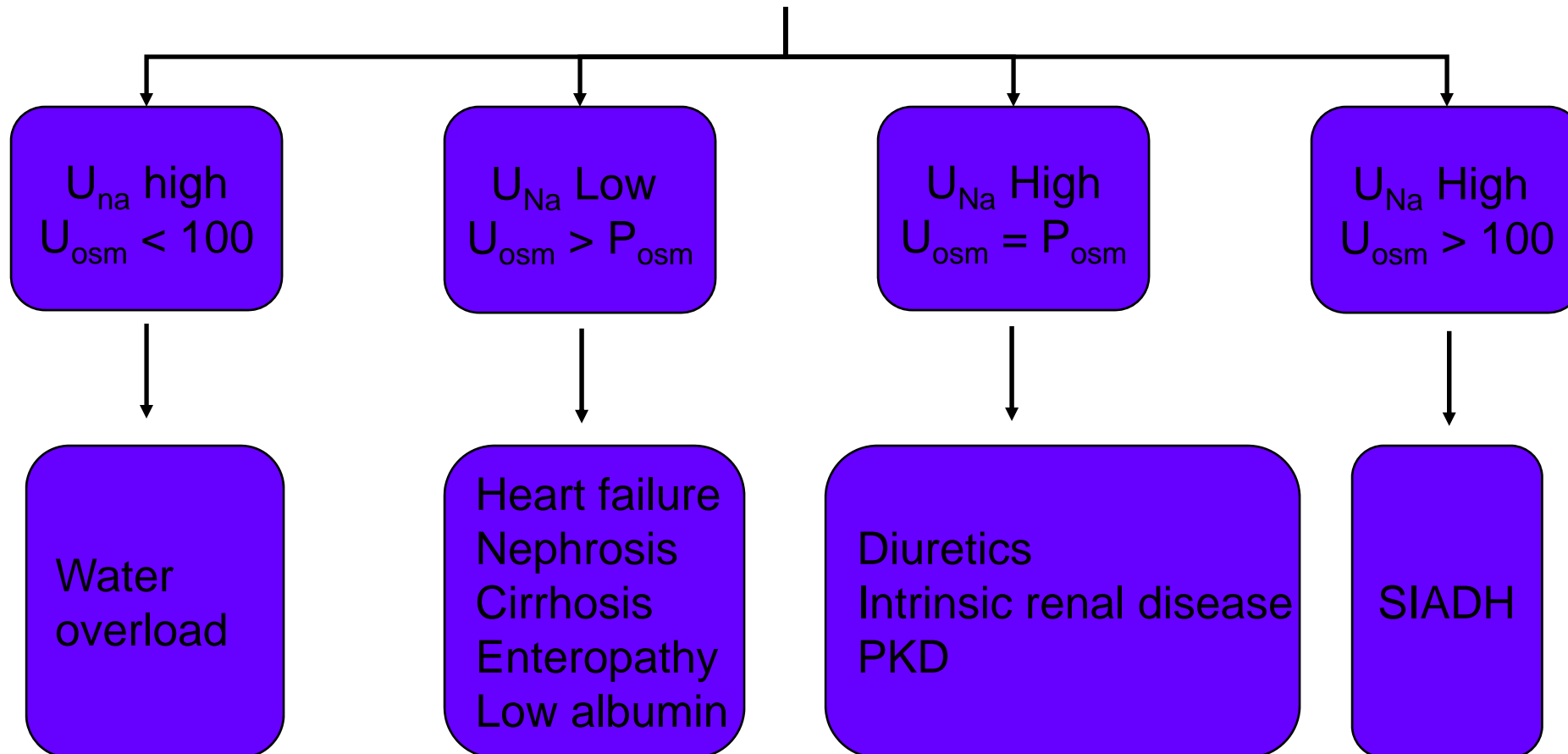
| biochemistries | plasma | urine | unit |
|----------------|--------|-------|-----------|
| Sodium | 125 | 32 | mmol/l |
| osmolality | 255 | 677 | mOsmol/kg |

Is this salt wasting? Or water excess?

- Do we need to prescribe salt?
- Or do we need to restrict/eliminate water?



Clinical euvolemic or edematous
Increased body weight
Too much water



Further course

| date | Day 4 | Day 8 | Day 11 | Day14 |
|---------------------|------------|------------|------------|------------|
| weight | 4.44 | 4.87 | 4.9 | 4.86 |
| BP | 90 | 120 | 120 | 145 |
| in | 462 | 836 | 917 | 707 |
| out | 395 | 593 | 700 | 486 |
| serum sodium | 126 | 133 | 135 | 139 |
| serum osmolality | 256 | 257 | 275 | 284 |
| urine sodium | 152 | 158 | 268 | 313 |
| urine osmolality | 657 | 569 | 610 | 744 |
| sodium in (mmol/kg) | 10 | 15 | 19 | 14 |

Further course

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| weight | 4.44 | 4.87 | 4.9 | 4.86 |
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| serum sodium | 126 | 133 | 135 | 139 |
| serum osmolality | 256 | 257 | 275 | 284 |
| urine sodium | 152 | 158 | 268 | 313 |
| urine osmolality | 657 | 569 | 610 | 744 |
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Key message

Sodium is reabsorbed to preserve intravascular volume and in response to renal perfusion

Kidney does not sense or detect serum sodium concentration

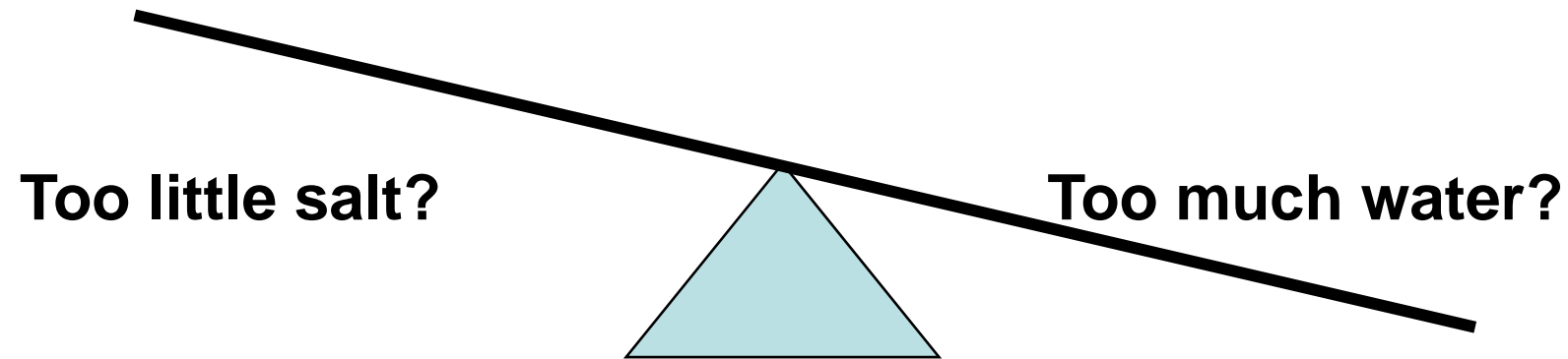
Case 2

- 3-months old infant referred for persistent hypertension
- Referred by endocrinology as BP > 100 mmHg despite treatment with 4 antihypertensive drugs (amlodipine, propranolol, furosemide, captopril)
- Ongoing salt supplementation (7.5 mmol/kg/d) for hyponatraemia since birth

History

- Initial presentation in neonatal period with hyponatraemia and hypoglycaemia
- Brain MRI – Small anterior pituitary and ectopic posterior pituitary
- Diagnosis of **panhypopituitarism**
- Commenced cortisone, thyroxine and growth hormone
- Salt supplementation with subsequent hypertension

Hyponatraemia: The first critical decision



How to decide ???

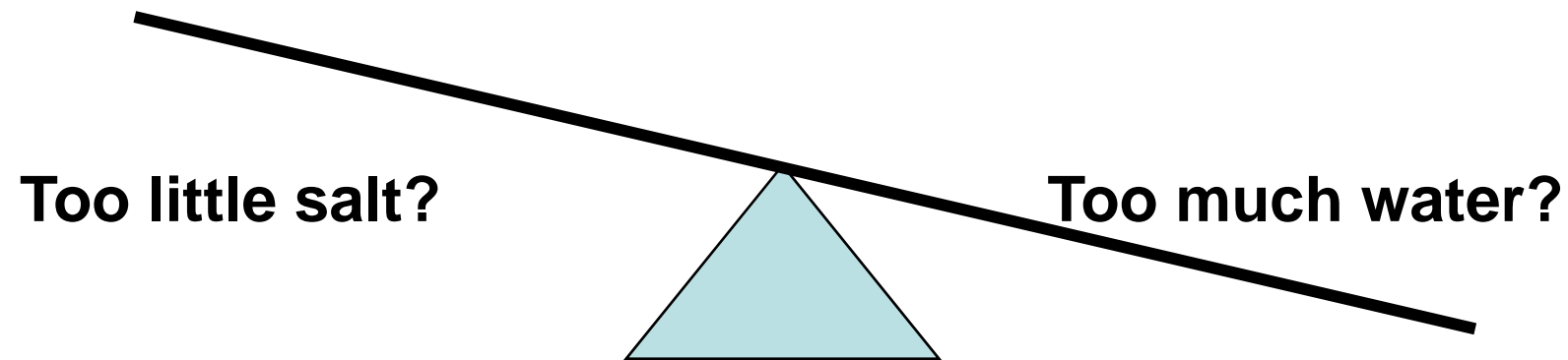
At admission (age 3 months)

- Well perfused, no oedema
- BP: 104 mmHg systolic

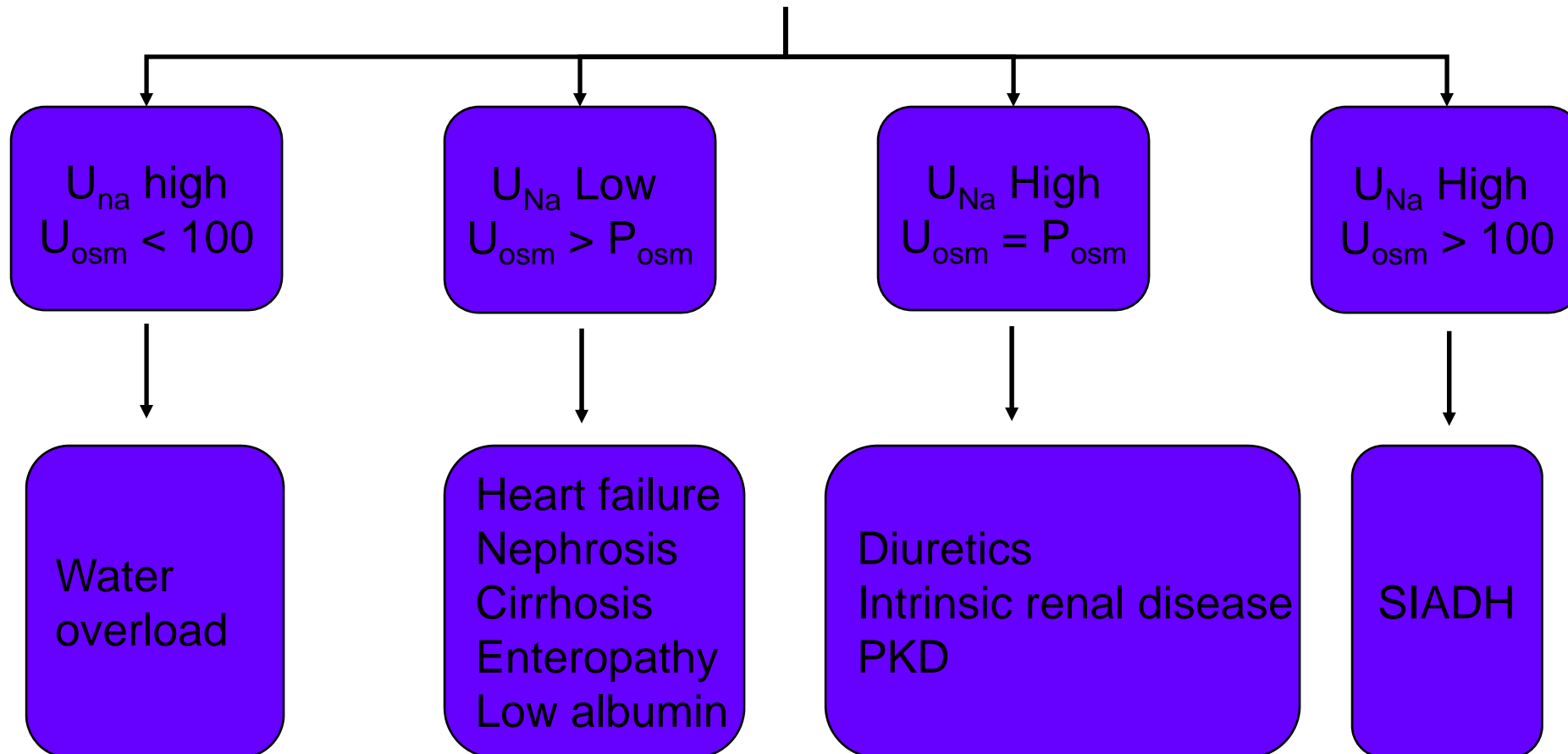
| | |
|-----------------|-----|
| | |
| Plasma | |
| Sodium (mmol/l) | 130 |
| Osmolality | 267 |
| Urine | |
| Sodium (mmol/l) | 99 |
| Osmolality | 391 |

Is this salt wasting? Or water excess?

- Do we need to prescribe salt?
- Or do we need to restrict/eliminate water?



Clinical euvolemic or edematous
Increased body weight
Too much water



Admission to renal ward

- **Step 1:** Stop Sodium supplements
- **Step 2:** Fluid restriction

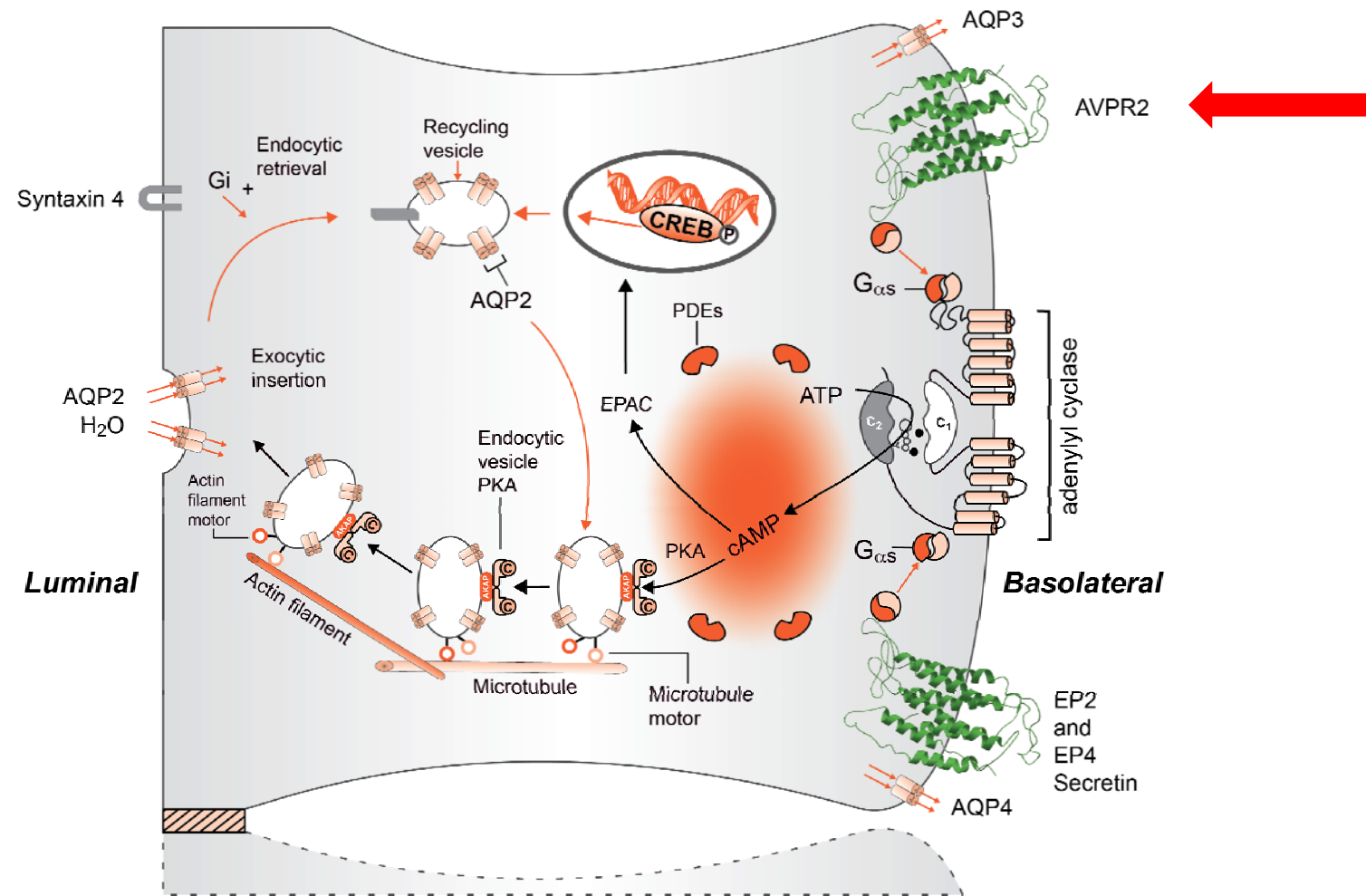
| | Admission | Day 1 |
|---------------------------------|-----------|-------|
| Age (days) | 105 | 106 |
| Fluid intake (mls/kg/d) | free | 80 |
| Sodium suppl (mmol/kg/d) | 7.5 | 0 |
| Weight (g) | 4500 | 4490 |
| Plasma | | |
| Sodium (mmol/l) | 130 | 131 |
| Osmolality (mOsm/kg) | 267 | 268 |
| Urine | | |
| Sodium (mmol/l) | 99 | 135 |
| Osmolality (mOsm/kg) | 391 | 579 |

BP normalised
All anti-hypertensives
stopped

Fluid restriction in SIADH

- Often unsuccessful, as patients also have increased thirst
- Difficult in infants, as fluid and caloric input is coupled

Tolvaptan – Vasopressin 2 antagonist



Course in hospital-2

- **Step 3: treatment with tolvaptan**

| | Admission | Day 1 | Day 2 | Day 5 | Day 17 | Day 36 |
|------------------------------------|-----------|-------|-------|-------|--------|--------|
| Age (days) | 105 | 106 | 107 | 110 | 122 | 141 |
| Tolvaptan (mg/kg) | | | 0.8 | 0.8 | Stop | 0.2 |
| Fluid intake (mls/kg/d) | free | 80 | free | free | 80 | free |
| Sodium suppl (mmol/kg/d) | 7.5 | 0 | 0 | 0 | 0 | 0 |
| Weight (g) | 4500 | 4490 | 4380 | 4278 | 4680 | 4960 |
| Plasma | | | | | | |
| Sodium (mmol/l) | 130 | 131 | 138 | 153 | 130 | 139 |
| Osmolality (mOsm/kg) | 267 | 268 | 288 | 314 | 265 | 287 |
| Urine | | | | | | |
| Sodium (mmol/l) | 99 | 135 | 9 | <5 | 75 | 8 |
| Osmolality (mOsm/kg) | 391 | 579 | 49 | 80 | 415 | 57 |

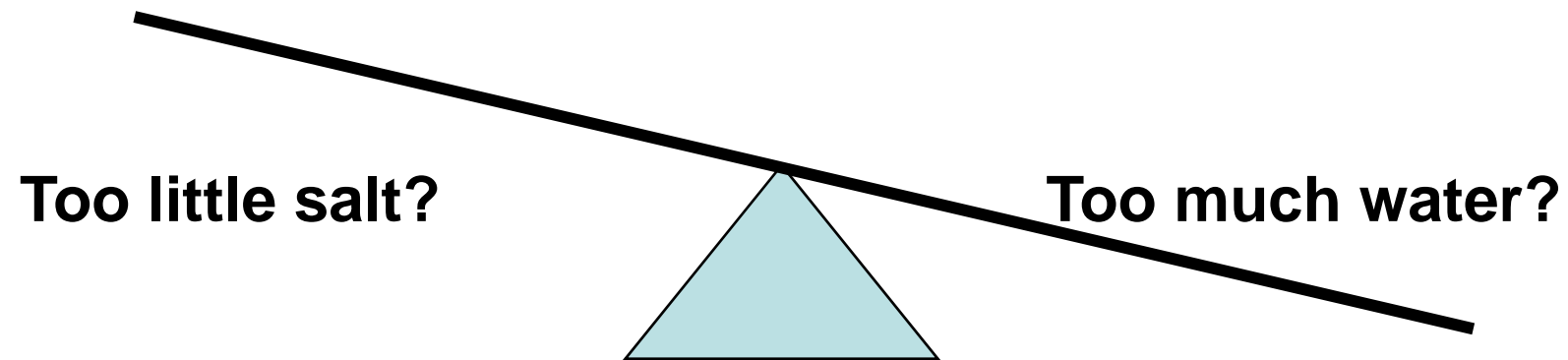
Hyponatraemia-case 3

- 11-months old girl referred for assessment of hyponatraemia, first noted incidentally during investigations for viral illness and confirmed several times subsequently
- Examination: well perfused, BP: 90 mmHg

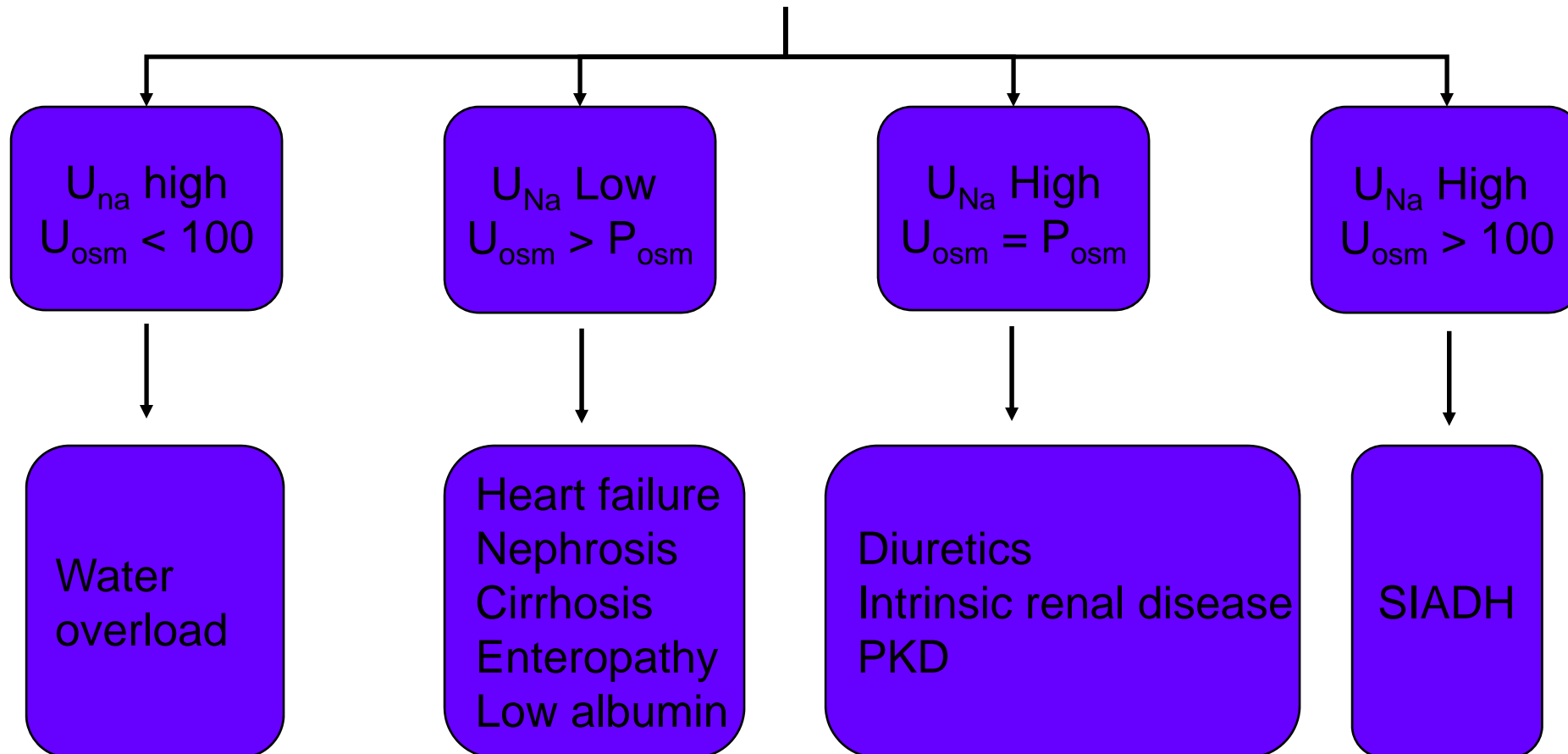
| biochemistries | plasma | urine | unit |
|----------------|--------|-------|-----------|
| Sodium | 121 | 45 | mmol/l |
| osmolality | 249 | 252 | mOsmol/kg |

Diagnosis?

- Too much water?
- Too little salt?



Clinical euvolemic or edematous
Increased body weight
Too much water

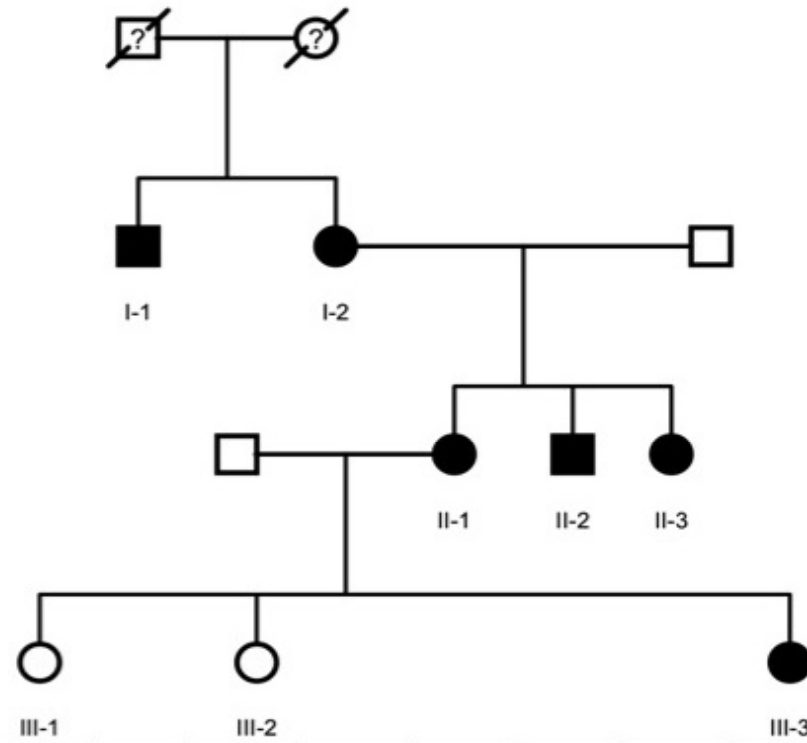


Family History

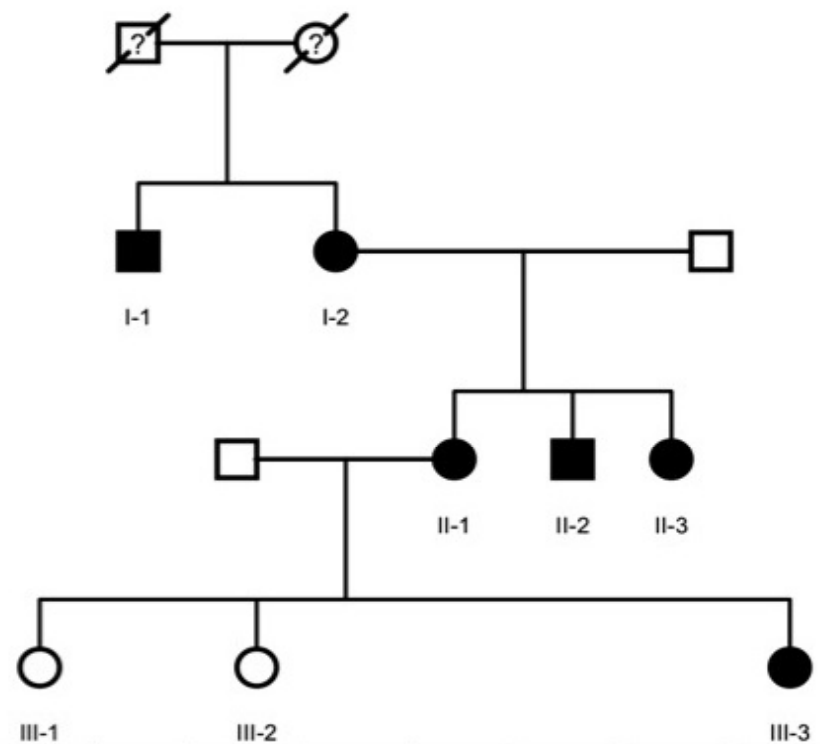
- Mother and maternal grandmother were known to have had hyponatraemia. Maternal uncle has developmental delay and recurrent hyponatraemia (often with seizures)
- Mum and grandmother “don’ t drink”

Diagnosis?

- Nephrogenic Syndrome of inappropriate antidiuresis
- X-linked inherited
- Gain-of-function in AVPR2: R137C/L
- Females usually less affected



| | III-1 | I-1 | III-2 | I-2 | II-1 | II-2 | II-3 | III-3 |
|-------------------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Age [years] | 8 | 62 | 10 | 65 | 41 | 39 | 41 | 1 |
| P-Na [mmol/l] | 146 | 126 | 145 | 141 | 134 | 120 | 136 | 134 |
| P-Osm [mosmol/kg] | 297 | ND | 295 | 300 | 274 | 252 | 284 | 281 |
| P-Creatinine [mg/dl] | 0.53 | 0.75 | 0.51 | 0.84 | 0.62 | 0.68 | 0.72 | 0.18 |
| U-Na [mmol/l] | 116 | 80 | 161 | 122 | 81 | 31 | 67 | 74 |
| U-Osm [mosmol/kg] | 1070 | 485 | 978 | 741 | 437 | 543 | 643 | 784 |
| U-AVP [log pg/min/Cosm] | 1.64 | ND | 1.39 | 0.59 | ND | 0.37 | 0.29 | 0.24 |
| Genetics | WT | R137C | WT | R137C | R137C | R137C | R137C | R137C |



| | III-1 | I-1 | III-2 | I-2 | II-1 | II-2 | II-3 | III-3 |
|-------------------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Age [years] | 8 | 62 | 10 | 65 | 41 | 39 | 41 | 1 |
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Treatment

- Intuitive by patients!
- ?Increased osmotic load during infancy (urea)

Hypernatraemia

Why is the sodium high?

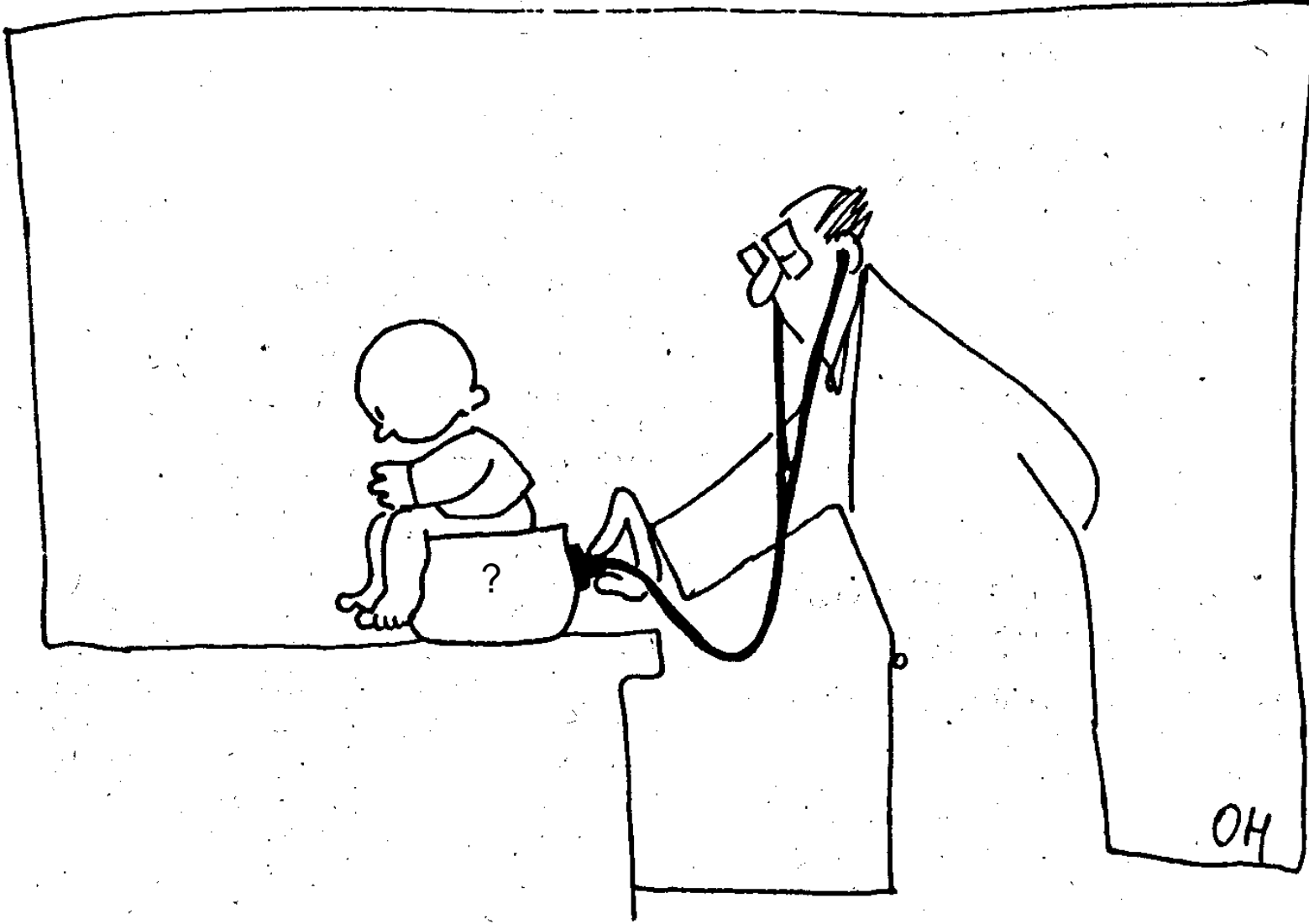
- Too little water
 - Weight should be decreased
 - Signs of dehydration/volume depletion
- Too much salt
 - Weight should be stable or increased
 - Patient is eu- or hypervolaemic

Case 1

- 18-months old boy presents with recurrent vomiting and ?mild developmental delay.
- Previously presented multiple times to GP and A&E with vomiting, thought to be reflux, but reassured due to good urine output: wets nappies 8-10 times per day
- Seen by private GI and scoped: nl
- Examination: well, wt: 9.8 kg (2nd %ile), height 80 cm (25th %ile)

Laboratory Investigations

| biochemistries | plasma | urine | unit |
|----------------|--------|-------|-----------|
| Sodium | 159 | 14 | mmol/l |
| osmolality | 328 | 78 | mOsmol/kg |



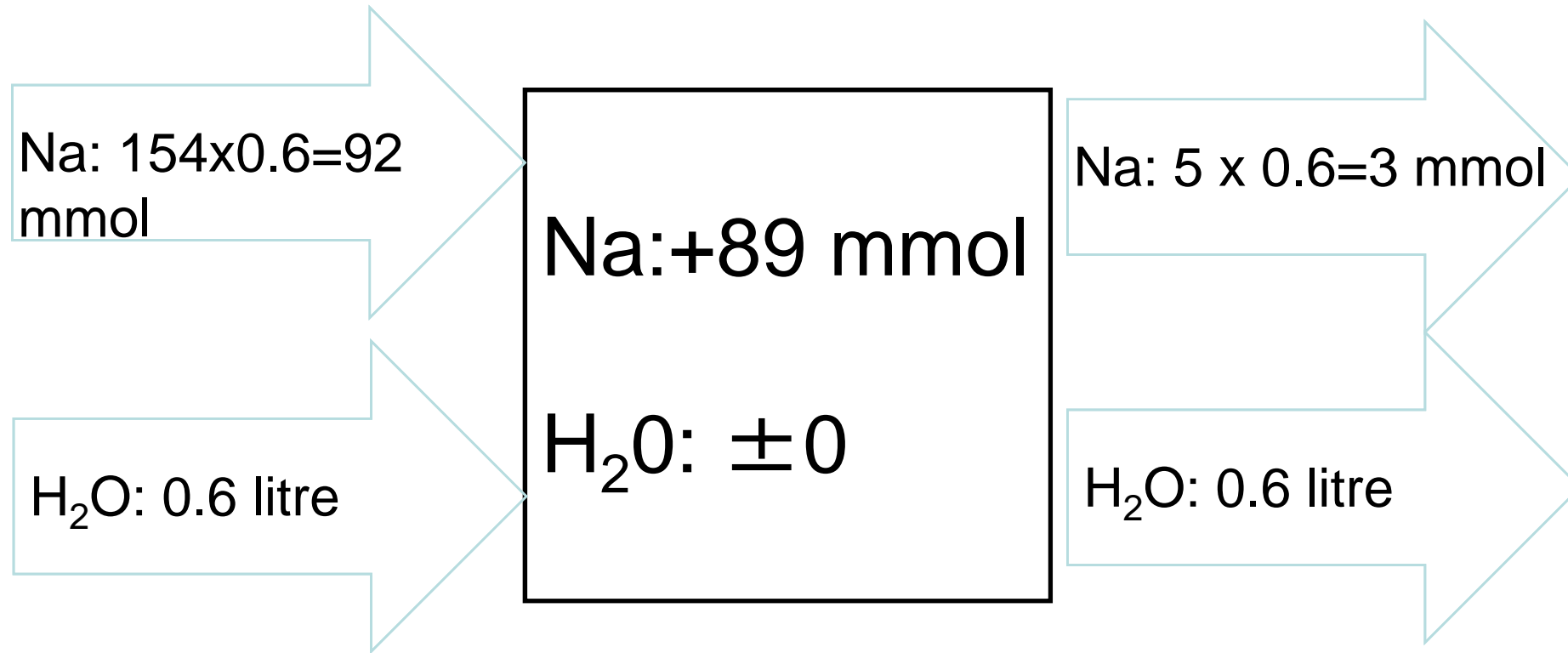
Further course

- DDAVP test: no response => Dx of NDI
- Brain MRI scheduled because of
?developmental delay
- Patient fastened prior and scan delayed:
Laboratory investigation at the time: Na
179 mmol/l
- What is the appropriate treatment?

Treatment and further course

- Received 3 bolus of 20 ml/kg of 0.9% saline
- Subsequent plasma Na: 198 mmol/l
- Patient becomes unresponsive and needs intubation and ventilation
- MRI brain c/w myelinolysis
- Once extubated, he has severe paralysis, but subsequent partial recovery: able to walk again after 2 weeks

Tonicity balance



Key messages Hyponatraemia

- Hyponatraemia is usually due to an excess in water, not a deficiency in sodium
- Kidneys do not sense or detect serum sodium
- Sodium is reabsorbed to preserve intravascular volume and in response to renal perfusion
- There is no biochemical test to distinguish salt wasting from water excess. This can only be done by clinical parameters!

Key messages Hypernatraemia

- Hypernatraemia is usually a deficiency in water, not an excess of sodium
- Beware of a dehydrated patient with "good" urine output!
- Do not give salt to a patient with NDI!
- Sometimes, we have to use our brain, instead of following protocols
- A tonicity balance can help to understand dysnatraemias

True or false?

- The kidneys are to provide electrolyte homeostasis. Therefore, in hyponatraemia, the kidneys should preserve sodium (minimise renal sodium losses).

False

True or false?

The urine sodium concentration can help distinguish between renal (cerebral/pulmonary) salt wasting and SIADH.

False