MANAGEMENT OF HYPERNATRAEMIA

Hypernatraemia (HrN) is a serum sodium concentration (s[Na])>146mmol/L. Hyponatraemia develops in very young or very old patients; those with altered mental state and dependent elderly are at particularly high risk[1-8].

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>HrN is due to deficiency of body water in relation to existing Na stores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms and Signs</td>
<td>Primarily neurologic. Thirst; Neurologic symptoms vary – lethargy, confusion, fits and coma in acute cases. Hypernatraemia is chronic (i.e. ≥48hrs) in almost all patients.</td>
</tr>
<tr>
<td>Prominent when the increase in s[Na] occurs rapidly or is large</td>
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<tr>
<td>Clinical assessment:</td>
<td>For dehydration (dry mucus membranes, reduced skin turgor); and volume status, hypovolaemia (postural BP and tachycardia)</td>
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<tr>
<td>Investigations</td>
<td>Paired Serum/Urine (spot sample) for U&amp;E, osmolality. Serum glucose</td>
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</tbody>
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### Management of Hypernatraemia, flow chart[^1-8]

<table>
<thead>
<tr>
<th>Extracellular Volume (ECV)</th>
<th>Hypovolaemia (Un-replaced water loss) the commonest cause of HrN</th>
<th>Euvolaemia (Un-replaced water loss)</th>
<th>Oedema</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td>Relative depletion of water to salt</td>
<td>Depletion of water, normal total body [Na]</td>
<td>Relative increase of salt to water</td>
</tr>
<tr>
<td><strong>Expected results</strong></td>
<td>uOsm* (&gt;600) (\geq) sOsm u[Na] &lt; 20</td>
<td>uOsm* (&lt;300) (&lt;) sOsm (\geq) u[Na] &gt; 100</td>
<td></td>
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<tr>
<td><strong>Causes:</strong></td>
<td>Inability to drink; failure of thirst – (rare) hypothalamic lesions</td>
<td>Renal ‘free’ water losses e.g. Diabetes Insipidus (DI)</td>
<td>Excess salt administration</td>
</tr>
<tr>
<td></td>
<td>Renal ‘free’ water losses: Osmotic diuresis, e.g. hyperglycaemia</td>
<td>1. Nephrogenic – lithium is the commonest cause 2. Pituitary (ADH administration will differentiate between central and nephrogenic DI)</td>
<td></td>
</tr>
<tr>
<td><strong>Rate of onset:</strong></td>
<td>Acute (&lt;) 48hrs</td>
<td>Euvolaemia: Conn’s S Cushing’s S (Rare)</td>
<td></td>
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<td></td>
<td>Chronic (\geq) 48hrs</td>
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</tbody>
</table>

**Immediate treatment**

- Only hypotonic fluids are appropriate[^4]
- Prompt determination and treatment of the underlying cause
- Restore euvolaemia in hypovolaemic patients[^4][5]
- Fluid replacement: enterally where possible, the safest route

**Asymptomatic:**

- Oral fluids Monitor s[Na] daily
- a. 0.9% NS for stabilisation (1L in 2hrs).
- b. Correct HrN with hypotonic fluids:
  - Monitor s[Na] 4–6 hourly.
  - s[Na] must not fall by \(-10\) mmol/l in 24hrs

**Normovolaemic + Symptomatic:**

- Correct HrN with hypotonic fluids: using fluids estimation equations, see text below

**Further management:**

- If the cause is not apparent at this stage, DI should be considered and patient referred to endocrine team

**Abbreviations:** uOsm = urine osmolality; sOsm = serum osmolality; GI = gastrointestinal; UOP = urine output; DI = diabetes insipidus; NS = normal saline;
*HrN: normally induces (maximally) concentrated urine, uOsm > 600; or “inappropriately” dilute urine if uOsm < 300 in DI.

[^1]: [Management of Hypernatraemia](#)
[^2]: [Excess salt administration](#)
[^4]: [Immediate treatment](#)
[^5]: [Asymptomatic](#)
Management of Hypernatraemia

Treatment of Hypernatraemia (continuation)\(^{[1-8]}\):

1. Prompt determination and treatment of the underlying cause: control GI losses, fever/sepsis, hyperglycaemia, hypercalcaemia, etc.

2. Fluid therapy to correct hypernatraemia:
   a. First, restore euvoelma in hypovolaemic patients\(^{[4,5]}\).
   b. The type of fluid depends on whether there is overall fluid depletion or sodium excess.
   c. The rate of hypernatremia correction relies on its duration:
      - Rapid if acute
      - Slow over 2–3 days if chronic at a maximum reduction of 10mmol/24hrs – rapid correction is potentially dangerous
   d. Add the 24-hour obligatory fluid losses and any further ongoing incidental fluid losses.

3. Everything else: anticonvulsants for patients with seizures, involve ICU team.

Only hypotonic fluids are appropriate. In pure water loss (e.g. DI) use water or 5% D. In hypotonic sodium loss (e.g. GI) use 0.18% or 0.45% sodium chloride in mild to moderate ECV reduction states respectively.

Indications for urgent admission to hospital are:
- \(s[Na]\) >155mmol/L
- \(s[Na]\) 146–155mmol/L with neurological disturbance or an inability to drink adequately

Indications requiring urgent treatment of HrN using hypotonic fluids (e.g. 5%D, 1/5 or ½ NS)\(^{[3]}\):
- Hyperosmolar Hyperglycaemic State (HHS), HyperOsmolar Non-Ketotic (HONK): stabilise with 0.9%NS if severely haemotically compromised followed by hypotonic fluids.
- DI (central or nephrogenic) if \(s[Na]\) >170: needs urgent correction with IV 5% dextrose
- Exogenous sodium ingestion or infusion can result in marked HrN \(s[Na]\) >190: infusion of IV 5% dextrose combined with a diuretic administration to remove excess sodium.
A. **Chronic Hypernatraemia (or unknown duration)**, almost all patients: The Total Water Deficit (TWD) should be corrected over 2–3 days. A fraction (~50%) of the TWD is replaced in the first day as per the equation below. It is replaced [preferably by oral/enteral water; IV 5% D if severe or oral/enteral not possible] to avoid the risk of rapid lowering of $s[Na]$ and the grave Osmotic Demyelination Syndrome (ODS). Equations for estimating fluid replacement to correct hypernatraemia are given below.

\[
\text{The response to correction should be guided by monitoring the clinical status and } s[Na] \text{ levels.}
\]

Re-measure $s[Na]$ after 4-6hrs and adjust infusion rate if the correction is either too fast or too slow. Monitor $s[Na]$ levels every 4–6hrs in patients with ongoing fluid losses and ‘Replace’.

\[
\text{The goal is to slowly lower } s[Na] \text{ by a maximum of 10mmol/l in a 24hr period (0.4mmol/h). Overly rapid correction of chronic Hypernatraemia may lead to cerebral oedema.}
\]

B. **Acute Hypernatremia ($\leq 48$)** is rare$^{[5-8]}$:

Treatment: The goal is to rapidly reduce $sNa^+$ to normal in <24hrs using the equations for estimating fluid replacement to correct hypernatraemia given below.

\[
\text{The entire TWD is replaced [by iv 5% Dextrose] within 24hrs; (hourly infusion rate = TWD/24hr)}
\]

- Monitor $s[Na]$ and blood glucose every 1–2hrs until $s[Na]$ is $\leq 145$mmol/l.
- Once $s[Na]$ has reached 145mmol/l, the rate of infusion is reduced and continued until normal level (140mmol/l) is restored.
- DI: give desmopressin – with consultant approval
- Rapid infusion of 5% D may induce hyperglycaemia (and osmotic diuresis); worsen hypertonicity:
  - Slow infusion
  - Use the 2.5% D; use insulin if persistent
Untreated acute hypernatremia can lead to permanent neurologic injury from:
- ODS
- Cerebral haemorrhage – brain shrinkage can cause vascular rupture and IC haemorrhage

**NB. Fluid Resuscitation/Replacement:** many patients with hypernatraemia have concurrent ECF volume depletion (i.e. hypovolaemia) and/or hypokalaemia. **Resuscitate;** monitor fluids input and output and **Replace** any further ongoing water and electrolytes losses.

**Estimating fluid replacement to correct hypernatraemia:**

Using formula 1 and its derivative 2[^4]:
1. Change in \( s[Na] \) (mmol/L) = \( \frac{(\text{infusate } [Na] - s[Na])}{TBW + 1} \)
   Estimates the effect of 1 litre of any infusate on \( s[Na] \)
2. Change in \( s[Na] \) (mmol/L) = \( \frac{(\text{infusate } [Na] + \text{infusate } [K] - s[Na])}{TBW + 1} \)
   Estimates the effect of 1 litre of any infusate containing Na and K on \( s[Na] \)

The numerator in formula 1 is a simplification of the expression \( (\text{infusate } [Na] - s[Na]) \times 1 \) litre, with the value yielded by the equation in mmol/L[^4]. The estimated TBW (in litres) is calculated as a fraction of body weight. The fraction is 0.6 and 0.5 in young men and women, respectively and 0.5 and 0.45 in elderly men and women, respectively[^4].

Formula 1 (and its derivative formula 2) estimates the change in the \( s[Na] \) caused by the retention of 1 litre of any infusate. The required volume of infusate and hence the infusion rate, is determined by dividing the change in the \( s[Na] \) targeted for a given treatment period by the value obtained from formula 1. The more hypotonic the infusate the less volume required[^4].

Formula 1 (and its derivative formula 2) permits a quantitative and flexible approach to the prescription of fluids that can easily accommodate different infusates and treatment periods[^4].
The conventional formula, given in the practical exercise below, provides an adequate estimate of the water deficit if hypernatremia is caused by pure water loss, but is not useful when sodium and potassium, in addition to water, must be prescribed\(^4\).

**CONCLUSION**

Prevention of hypernatraemia is very important. Ensure adequate intake in ill patients, pre-emptive management of possible causes, e.g. DM, Hypercalcaemia, DI, etc. Strict fluid balance charts and daily weighing, actioned appropriately.

**PRACTICAL EXERCISE**

A 72-year-old male, a known case of bipolar disorder on Lithium for eight years, has a long-term urinary catheter, admitted with general malaise, confusion and impaired oral intake for few days. A diagnosis of severe urosepsis was made. Weight was 70kg, dry mucus membranes, febrile and tachycardic, normal BP, no postural drop. His attentive daughter was prompting him to eat and drink. She measured the fluid input/output for the last 24 hours prior to admission at 2.1/4.5L respectively.

\[ s[Na] = 166\text{mmol/litre} \, (L), \, s[K] = 4.3\text{mmol/L}, \, \text{and} \, s[Cr] = 115\mu\text{mol/L}, \, u[Na] < 10\text{mmol/L}. \]

Q1: What caused hypernatraemia?
   a. Fever
   b. Lithium
   c. Confusion
   d. All of the above
   e. None of the above

A1: This is a case of pre-renal acute kidney injury and chronic hypernatremia secondary mainly to pure water loss. Hypernatremia is caused by the unreplaced free water loss secondary to fever and Lithium-induced nephrogenic diabetes insipidus, statement (d). He was unwell and confused, hence unable to compensate for the large urinary water loss, for few days prior to admission. Thus, the hypernatraemia correction should be over 2–3 days.

Q2: How would you replace the fluids?

A2: The required fluid volume for replacement is estimated using Formula 1, or conventional equation.
a. **Estimating fluid replacement using Formula 1**: the desired water replacement in the first 24 hours to reduce $s[Na]$ by $\sim 10$mmol/L using 5% dextrose is:

$1L$ of 5% dextrose will reduce $s[Na]$ by $-4.6$mmol/l, obtained from the equation (formula 1): $0 \times \frac{166}{35} + 1$. Therefore, the volume required to reduce $s[Na]$ by $10$mmol/l $= \frac{10}{4.6} = 2.2L$, **Plus** $1.5L$ to compensate for 24 hour obligatory water losses $= total$ of $3.7L$, given over 24 hours at $154ml/hour$.

Close monitoring of $s[Na]$ and for hyperglycaemia. Introduce insulin if hyperglycaemia develops. Hyperglycaemia is deleterious; it will induce osmotic diuresis and worsen hypertonicity.

b. **Estimating fluid replacement using the Conventional equation:**

Estimating total water deficit (eTWD) equation to reduce $s[Na]$ to $140 = \%LBW \times \left(\frac{s[Na]}{140} - 1\right)$

(The eTWD equations provide a simplified guide to initial therapy)

%LBW (lean body weight) = Total body water (TBW): % = Young men: 0.6; Young women: 0.5; Elderly men: 0.5; Elderly women: 0.45. This formula gives an estimation of the volume of *additional* fluid required to correct $s[Na]$ to $140$mmol/L.

*Aim to replace 50% of this, eTWD, in 24hrs with water or IV 5% Dextrose.*

The desired water replacement volume in the first 24 hours (to reduce sNa by 10mmol/L) $= eTWD \times 10mmol/l \div (sNa - 140)$; divide by 24hrs for hourly infusion rate.

**Calculations:**

$eTWD = 0.5 \times LBW \times \left(\frac{s[Na]}{140} - 1\right) = 6.5L$

The desired water replacement in the first 24 hours to reduce $s[Na]$ by $\sim 10$mmol/L $= (eTWD \times 10) / (sNa - 140) = 2.5L$, **Plus** $1.5L$ to compensate for the 24 hour obligatory water losses. Total $= 4L$, given over 24 hours at $166ml/hour$.

The volumes obtained from these equations are indicative: the correction needs good clinical acumen and close monitoring.
REFERENCES


