APPROACH TO HYPERNATREMIA

Dr. S. Thangavelu MD DCH DNB MRCP
Pediatric Consultant and Director of Pediatrics
Mehta Multispeciality Hospitals, Chennai
Former AP, Madras Medical College
Scope of the talk

• Salt water physiology
• Causes, Clinical findings, laboratory work up
• Seven step algorithm for Management.
• Case scenario
Suspect and anticipate hypernatremia

• In any child with history of fluid loss or neurological manifestations, anticipate and chase the serum sodium result early within 1 or 2 hours

• It is not a diagnosis. It is a lab finding caused by diverse etiology.

• Definition: Serum Na > 145 mmols/L or mEq/L. Some literatures keep > 150

• It always implies that there is intracellular dehydration.
Salt and water homeostasis
Two thirds of the Earth is made up of water.

TBW (60% of BW) in different compartments:
- ICF: intracellular space
- ECF: Extracellular space
- ISF: Interstitial space
- PV: Plasma volume

- ICF: 40%
- ECF (ISF and PV): 20%
- ISF: 13%
- PV: 7%
Fluid compartments are divided by two membranes

FLUID MOVEMENT:

1. **Cell membrane**: (ICF – ECF)
   Only water can pass through and not permeable to electrolytes.
   Water passes from lower tonicity side to higher. In hyperNa, ICF to ECF

2. **Capillary membrane** (IVFS – ISF)
   Oncotic and hydrostatic pressure decides the movement of water
   • Permeable to all electrolytes
<table>
<thead>
<tr>
<th></th>
<th>ECF</th>
<th>ICF</th>
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<tbody>
<tr>
<td><strong>Na</strong></td>
<td>135-145 mmol/L</td>
<td>Na 10-20 mmols/L</td>
</tr>
<tr>
<td><strong>K</strong></td>
<td>3.5 -4.5 mmols/L</td>
<td>K 120 -150 mmol/L</td>
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Osmolality is equal, (290) ICF and ECF solutes are markedly different

Oceans meet at gulf of Alaska and still maintains their own colours
DEFENCE AGAINST DYSNATREMIA

• Against developing hyponatremia:
  • ADH secretion stops and kidney excrete free water.
  • Pathological situation: SIADH.

• Against developing hypernatremia:
  a) ADH is secreted to produce concentrated urine
  b) Powerful thirst.
  • Pathological situation: when DI child kept NIL oral or becomes unconscious – thirst is knocked off and restricted access to water.
Osmotic regulation of ADH release and thirst

DEFENCE AGAINST HYPERNATREMIA

Osmotic threshold for thirst begins is about 5 to 10 mOsm/kg higher than the threshold for ADH release.

1. NORMAL ECF WATER - 140 mEq/1000 mL

2. DIARRHEA, HYPOTONIC FLUID LOSS

3. WATER SHIFT FROM HIGHER TO LOWER OSM

ICF to ECF shift

SERUM NA IS 170 mEq/L. WHAT DOES IT MEAN?

Basically hypernatremia does not imply more sodium in the body, but occurs due to water loss. It means there is more sodium relative to water content in the body fluid. This pictures explain this concept.
Causes, clinical features and role of lab
<table>
<thead>
<tr>
<th>HYPOTONIC FLUID OR ELECTROLYTE FREE WATER LOSS</th>
<th>SALT EXCESS OR GAIN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. GI loss: Diarrhea</strong></td>
<td>1. Improperly mixed formula/ORS</td>
</tr>
<tr>
<td></td>
<td>2. Excess NaHCO3 / hypertonic saline</td>
</tr>
<tr>
<td></td>
<td>3. Salt poisoning</td>
</tr>
<tr>
<td></td>
<td> child abuse, Munchausen syndrome by proxy</td>
</tr>
<tr>
<td></td>
<td> salt with milk instead of sugar</td>
</tr>
<tr>
<td></td>
<td> pica</td>
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<tr>
<td></td>
<td>4. Ingestion of seawater</td>
</tr>
<tr>
<td></td>
<td>5. Hyperaldosteronism</td>
</tr>
<tr>
<td><strong>2. Renal loss: Osmotic diuresis</strong></td>
<td></td>
</tr>
<tr>
<td>(Mannitol, DM)</td>
<td></td>
</tr>
<tr>
<td><em>Diabetes Insipidus</em></td>
<td></td>
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<tr>
<td>CKD (Obst uropathy)</td>
<td></td>
</tr>
<tr>
<td>Polyuric phase of ATN</td>
<td></td>
</tr>
<tr>
<td><strong>3. Cutaneous loss: Excessive sweating or</strong></td>
<td></td>
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<tr>
<td>burns</td>
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</tbody>
</table>

There is always a component of reduced intake of not replacing physiological water losses.
In 1962, fourteen infants in a hospital were salt poisoned by drinking formula accidentally made with salt instead of sugar. Five infants died before the error was recognized. Autopsy showed hemorrhagic encephalopathy.

Implicated milk formula contained between 739 to 1170 mmol/L of sodium. The case fatality rate was 6 of 14 exposed.
How hypernatremia affects brain?

Effects of (A) isotonic, (B) hypertonic (C) hypotonic ECF on cell (brain) volume.

In hyponatremia, brain swells up.

In hypernatremia, brain shrinks.

From food to physiology.
Clinical features in hypernatremia

1. Dehydration and shock: Not obvious as ECF water content is near normal. Subtle findings – thirst and “doughy” skin, tachycardia, wt loss.

2. CNS symptoms: Convulsions, irritability, high-pitched cry and. Some alert infants are very thirsty.
   - Brain hemorrhage: Brain shrinks, results in tearing of bridging blood vessels - subarachnoid, subdural, parenchymal bleed.
   - Thrombosis: Stroke, dural sinus thrombosis, peripheral thrombosis, and renal vein thrombosis - possibly due to hypercoagulability.

Does he feel thirsty? No – Suspect thirst disorders
What is the urine frequency? Voiding urine despite dehydration or polyuria - clue for DI/DM; Oliguria – Non renal loss.
<table>
<thead>
<tr>
<th></th>
<th>Hypovolemic hypernatremia (Hypernatremic dehydration)</th>
<th>Hypervolemic hypernatremia (Salt excess)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History</strong></td>
<td>Diarrhea, (voiding urine despite dehydration), polyuria</td>
<td>Suspicious. Salt instead of sugar, wrong preparation - ORS or formula</td>
</tr>
<tr>
<td><strong>Body Wt change</strong></td>
<td>Wt loss 5-10%</td>
<td>Wt gain upto 5%</td>
</tr>
<tr>
<td><strong>Hydration</strong></td>
<td>Signs not obvious. Orthostatic BP changes, tachycardia,</td>
<td>Normal/peripheral edema/pulmonary edema</td>
</tr>
<tr>
<td><strong>Urinary sodium</strong></td>
<td>&lt; 10 mEq</td>
<td>&gt; 20 mEq</td>
</tr>
<tr>
<td><strong>FENa</strong></td>
<td>&lt; 1 % in a dehydrated child</td>
<td>values &gt;2% in salt poisoning</td>
</tr>
<tr>
<td><strong>USG abd, chest, CXR</strong></td>
<td>IVC size – for volume status. Collapsing</td>
<td>IVC in USG: Distended and non collapsible. Lung – B lines. CXR-Pulm edema, pleural fluid..</td>
</tr>
</tbody>
</table>
Lab investigations

• CBC: high HCT favours dehydration
• CXR: Can identify volume overload-plulmonary congestion, pleural fluid
• USG Lungs: presence of B lines. IVC filling will indicate the volume status
• Urine Sodium: < 10 favours dehydration> 20 – Salt excess
• FENA: < 1.0 – hypovolemia > 2.0 Salt excess and hypervolemia
• Blood sugar, urea, creatine, other electrolytes, calcium and magnesium. High serum chloride – Salt excess
• Serum and urine osmolarity
• Serum AVP level and response to AVP
• Neuroimaging: For cause in DI and CNS complications
• ABG: Edema, hypertension, hypokalemia, hypernatremia and metabolic alkalosis - hyperaldosteronism
Management of hypernatremia
Seven steps
**SEVEN STEPS ALGORITHM (HYPOVOLEMIC) HYPERNATREMIA**

**STEP 1:** Stabilization of ABC and seizure control.

**STEP 2:** Estimate the volume status. (HYPOVOLEMIC) or (ISO to HYPERVOLEMIC).

**STEP 3:** *(Treatment In hypovolemic hypernatremia)*

a) Emergent fluid bolus isotonic NS 20 mL/kg over 30-60 min. RL not the right choice

b) Deficit calculation 1. Formula based 2. Simple strategy based

**STEP 4:** Look for specific diagnosis like DI requiring any specific therapy

a) UO > 4 mL kg/hr. Serum osmolarity > 300; Urine osmolarity < 300

b) Check plasma AVP level. - start vasopressin. Decide - Cranial or Nephrogenic
(Hypovolemic) Hypernatremia – algorithm

**STEP 5:** After starting deficit correction, Monitor vital signs and the trend

a) Ensure rate of fall of Na - 0.5 mEq/hr
b) Any time shock appears another bolus of NS 10 mL/kg
c) If volume overload heart failure, or AKI – dialysis
d) Any time seizure – Presume as rapid fall of Na, give 3% saline 2-5 mL/kg over 15-30 min (alternative DD – CNS bleed or thrombosis or hypocalcemia)
e) Check CBG – Don’t use insulin but adjust dextrose content D5 to D2.5.
(Hypovolemic) Hypernatremia – algorithm

**STEP 6:** *If child worsens, watch for complications* which may alter the prognosis. AKI, cerebral hemorrhage, cerebral thrombosis, underlying sepsis

**STEP 7:** *If child improves, plan the transition.* Regaining consciousness, Na level declining. Ready for oral. Allow ad lib breast feeds in infants, water by NGT or oral. Recheck serum Na. Switch to less intense management
Management of Hypovolemic hypernatremia
Deficit correction in hypovolemic hypernatremia. Two choices. Intense formula driven vs Practical titration

1. FORMULAS DRIVEN
   • Many complicated formula
   • Deficit calculation
   • And add maintenance to deficit

2. SIMPLE PRACTICAL STRATEGY
   • After initial bolus, deficit correction is started. 1) What rate 2) what fluid
     1. Volume or rate of flow? 1.25-1.5 times maintenance
     2. Type of fluid? 1/5 NS or ¼ or ½ NS.

Rate of decrease depends on EFW delivery
Deficit calculation. BW 10 kg. Serum Na - 175 mEq

**Formula 1:** Free water deficit in mL = Current TBW x ([current plasma Na/140] - 1)

- BW – 10 kg. (10 x 0.6 = 6) x ([175/145]) – 1 = 1.21 - 1.0 = 0.21. This is 6x 0.21 = 1.26 L = 1260 mL

**Formula 2:** Free water deficit in mL = (4 mL/kg) x (BW in kg) x (desired change in plasma Na)

- 10 kg; 4 x 10 x (175-145 = 30) = 1200 mL

**Formula 3:** Water deficit = BW x 0.6 {1 – (145/Current Na)}

= 6 x {1 - 0.83 = 0.17} = 0.6 L or 1020 mL

- Time taken to correct (175-145) = 30 mEq/0.5 = 60 hrs
- Hourly deficit replacement -1200/60 = 20 mL/hr
- Add Maintenance fluid 40 + 20 = 60 mL/hr (1 ½ times maintenance)
Formula 4. Adrogue Madias formula- BW 10 kg. Serum Na 175

1) Choose the IVF of choice – NS, \( \frac{1}{2} \) NS, \( \frac{1}{4} \) NS or 1/5 NS

2) Calculate amount of drop in Na if one Litre is given? E.g \( \frac{1}{2} \) NS (77 mEq/L)

\[
\text{Change in serum Na}^{+} = \frac{\text{infusate Na}^{+} - \text{serum Na}^{+}}{\text{total body water} + 1}
\]

- When one Liter \( \frac{1}{2} \) NS is given = (77-175/6+1) = 14.0 mmol drop in Na
- (175 -145 = 30 mmol/l correction needs 30/14.0 = 2.0 L of \( \frac{1}{2} \) NS
- Rate of administration = 2.0 L /60 hrs = 33 ml/hour of \( \frac{1}{2} \) NS

- **Total rate of fluid (including free water deficit + maintenance)**
  - Free water deficit correction = 33 ml/hour 0.45 saline.
  - Maintenance = 40 ml/hour.
  - **Total 40 +33 =73 mL/hr (1.75 times maintain)**. Type of fluid: \( \frac{1}{2} \) NS
### Time taken for correction based on initial serum Na

<table>
<thead>
<tr>
<th>Serum Na (mEq/L)</th>
<th>Time taken (hrs)</th>
</tr>
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<tbody>
<tr>
<td>140–157</td>
<td>24</td>
</tr>
<tr>
<td>158–170</td>
<td>48</td>
</tr>
<tr>
<td>171–183</td>
<td>72</td>
</tr>
<tr>
<td>184–196</td>
<td>84</td>
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</table>

Per hour – 0.5 mEq/hour  
Per day – 8-10 mEq/day
What is common in all these calculations

• They are complex, takes time, potential for miscalculation and human errors with its clinical implications

• But they reasonably arrive at similar results.

• 1.25 to 1.75 times the maintenance, ½ NS to ¼ NS to 1/5 NS;

• This would provide adequate replacement of maintenance needs and would provide free water.

• CAN WE HAVE SOMETHING SIMPLER?

• Yes simple strategy starts from the answers concluded from the formula
Our life is frittered away by detail... simplify, simplify.

- Henry David Thoreau
Do Emergency measures

**HYPERNATREMIA > 145 - ASSESS VOLUME STATUS**

<table>
<thead>
<tr>
<th>Monitoring</th>
<th>Clinical and laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Support A, B, C</td>
</tr>
<tr>
<td></td>
<td>• Correction of shock – NS bolus</td>
</tr>
<tr>
<td></td>
<td>• Control of seizures</td>
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**STEP 3 – SIMPLE EMPIRICAL STRATEGY**

10-20 mL NS over 30-60 min

Initial fluid: **Type of fluid -Na con:** ¼ to ½ NS in D5

**Rate:** 1.25 to 1.5 times maintenance

↓

Reassess clinical status & serum Na 4-6 hourly

*Expected fall of Na 0.5 mmol/L per hour*

Adjust the IVF rate and con of sodium based on serum Na. Wt of the baby 10 kg e.g initial Na -170. After 6 hrs.....

<table>
<thead>
<tr>
<th>Rapid fall &gt; 0.5 mEq/hr (160)</th>
<th>Optimum fall 0.5 mEq/hr (167)</th>
<th>Slow fall &lt;0.5 mEq/hr (169)</th>
</tr>
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<tbody>
<tr>
<td>• Increase salt. Decrease water</td>
<td>• Continue the same fluid at same rate</td>
<td>• Decrease salt. Increase water</td>
</tr>
<tr>
<td>• Increase Na con ¼ NS to ½ NS</td>
<td></td>
<td>• Decrease Na con ½NS to 1/4 NS</td>
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<tr>
<td>or</td>
<td></td>
<td>or</td>
</tr>
<tr>
<td>• Decrease the rate of IVF</td>
<td></td>
<td>•Increase the rate of IVF</td>
</tr>
<tr>
<td>1.5 times to 1.25 times. (60 to 50 mL/hr)</td>
<td></td>
<td>1.25 times to 1.5 times (50 to 60 mL/hr)</td>
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Adjust the IVF rate and con of sodium based on serum Na. Wt of the baby 10 kg e.g initial Na -170. After 6 hrs ......

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- Increase salt.
- Increase Na con
- ¼ NS to ½ NS

- Continue the same fluid at same rate

- Decrease salt.
- Decrease Na con
- ½NS to 1/4 NS
(Hypovolemic) Hypernatremia – algorithm

**STEP 5: Monitor vital signs and the trend**

a) Ensure rate of fall of Na - 0.5 mEq/hr

b) Any time shock appears another bolus of NS 10 mL/kg

c) If volume overload heart failure, or AKI – dialysis

d) Any time seizure – Presume as rapid fall of Na, give 3% saline 2-5 mL/kg over 15-30 min (alternative DD – CNS bleed or thrombosis or hypocalcemia)

e) Check CBG – Don’t use insulin but adjust dextrose content D5 to D2.5.
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**STEP 6:** Watch for complications which may alter the prognosis. AKI, cerebral hemorrhage, cerebral thrombosis, underlying sepsis

**STEP 7:** Transition. Regaining consciousness, Na level declining. Ready for oral. Allow ad lib breast feeds in infants, water by NGT or oral. Recheck serum Na. Switch to less intense management
Management of Hypervolemic hypernatremia
(Iso/hypervolemic) Hypernatremia – algorithm

**STEP 1:** Stabilization of ABC and seizure control.

**STEP 2:** Estimate the volume status. HYPERVOLEMIC - No fluid loss, weight gain, voiding urine normally, edema, pulmonary edema and respiratory distress. Check ORS/formula preparation for errors. Confirm by lab: Urine Na > 20 mEq FENa > 2. Impaired renal function

**STEP 3:** IV Frusemide as infusion (0.1-0.2 mg/kg/hr) to reduce fluid overload. Meticulously measure UO. Replace UO with ¼ or 1/5 GNS. Serum potassium, should be monitored and should be replaced as needed

**STEP 4:** Stop 3% Saline or NAHCO3

**STEP 5:** Consider RRT, if UO low, or creatinine high or very high serum Na > 180 or multiple electrolyte deficiency or fluid overload and CCF
MANAGEMENT STEPS (hypervolemia pathway)

Acute hypernatremia (< 24 hrs)
- Mostly iatrogenic. Rapid correction preferred (because idiogenic osmoles have not had time to accumulate).

Chronic hypernatremia (>48 h)
- Here dangers of hypernatremia > dangers of overly rapid correction.
- One has to balance the risk of disease vs treatment related risks.
When the child is recovering - transition

• Level of consciousness recovered. Demands oral feeds, No tachypnea, shock improved.

• Time to change the strategy:
  • Gradually taper IVF, increase oral/NGT feeds as plain water or breast milk in infants adlib.
  • Meticulously account the intake and output
  • Recheck the electrolytes, RFT and change the plan
Some concepts
Few points need clarification at the end

• What are idiogenic osmols?
• Clarity of events happening due to water shift across cell membrane during adaptation and rapid correction..
Osmotic equilibrium and disequilibrium.

ACUTE: Fluid shift out, brain cell shrink

Water shifts out. Brain shrinks, symptomatic
Osmotic equilibrium and disequilibrium. ADAPTATION: Idiogenic osmoles created, cell size restored

To restore cell volume, brain cell creates Idiogenic osm in 24-48 hrs
Osmotic equilibrium and disequilibrium
RAPID CORRECTION: Fluid shift into the brain cells

Water shifts out. Brain shrinks, symptomatic

To restore cell volume, brain cell creates Idiogenic osm in 24-48 hrs

Water shifts, in reverse direction & cell size increases-cerebral edema
Some case scenario
CASE REPORT 1: Kupiec TC, Goldenring JM, Vishnu Raj. A Non-Fatal Case of Sodium Toxicity. Journal of Analytical Toxicology, Vol. 28, September 2004 (PICA, ROCK SALT INGESTION)

• Six-year-old boy was taken to the hospital California following a seizures, serum sodium - 234 mEq/L and serum chloride -205 mEq/L. Clinical tests ruled out all pathological causes.

• A search of the boy's house led to the discovery of rock salt in the cabinet and a container of table salt. It was estimated that the child had ingested approximately four tablespoons of rock salt, leading to the acute salt toxicity.
• A 6-month-old Bangladeshi girl with acute watery diarrhea, lethargy and hypernatremia (208mmol/L serum sodium). As child was table and conscious, treated exclusively with ORS thro NGT.

<table>
<thead>
<tr>
<th></th>
<th>Day of admission</th>
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<tbody>
<tr>
<td></td>
<td>Day 1</td>
</tr>
<tr>
<td>Weight (g)</td>
<td>5900</td>
</tr>
<tr>
<td>G-ORS³ (ml/hr)</td>
<td>14.5</td>
</tr>
<tr>
<td>Serum sodium (mmol/L)</td>
<td>208.2</td>
</tr>
<tr>
<td>Serum potassium (mmol/L)</td>
<td>3.95</td>
</tr>
<tr>
<td>Serum chloride (mmol/L)</td>
<td>166.2</td>
</tr>
<tr>
<td>Serum bicarbonate (mmol/L)</td>
<td>26.4</td>
</tr>
</tbody>
</table>

• An 8-week-old infant with profuse diarrhea, with Salmonella sepsis and was treated in PICU
• Lab: Na - 166 mEq/L, [Cl] = 142 mEq/L, and glucose = 713 mg/dL.
• WHEN problem resolved, shifted to level 2 and mother was allowed to stay. There was recurrence of severe hypernatremia (214 mEq/L).
• Surveillance of the mother revealed that she manipulated the indwelling nasogastric tube; confronted, she admitted to salt administration. A gastric aspirate during the crisis demonstrated an extremely high sodium - 1416 mEq/L, consistent with salt intoxication and Munchausen syndrome by proxy
**Seven steps (Hypovolemic) Hypernatremia – algorithm**

(Hypotonic fluid in 1.5 times maintenance)

**STEP 1:** Stabilization of ABC and seizure control.

**STEP 2:** Estimate the volume status. *(HYPOVOLEMIC)* or *(ISO to HYPEROVOLEMIC)*.

**STEP 3:** (Treatment In hypovolemic hypernatremia)

a) Emergent fluid bolus isotonic NS 20 mL/kg over 30-60 min. Deficit calculation 1. formula based 2. Simple strategy based

**STEP 4:** Look for specific diagnosis like DI & specific therapy

a) UO > 4 mLkg/hr. Serum osmolarity > 300; Urine osmolarity < 300

b) Check plasma AVP level. - Trial of vasopressin.
(Hypovolemic) Hypernatremia – algorithm

**STEP 5: Monitor the trend**

a) Any time shock appears (CHECK LACTATE) - another bolus of NS 10 mL/kg

b) If volume overload heart failure, pulmonary edema or AKI – dialysis

d) Any time seizure – give 3% saline 2-5 mL/kg over 15-30 min

e) Check CBG – Don’t use insulin but adjust dextrose content D5 to D2.5.

**STEP 6: Watch for complications** which may alter the prognosis. AKI, cerebral hemorrhage, cerebral thrombosis, underlying sepsis

**STEP 7: Transition.** Regaining consciousness, Na level declining. Ready for oral. Allow ad lib breast feeds in infants, water by NGT or oral. Recheck serum Na. Switch to less intense management.
(Iso/hypervolemic) Hypernatremia – algorithm

(Hypotonic fluid in restricted volume)

**STEP 1:** Stabilization of ABC and seizure control.

**STEP 2:** Estimate the volume status. HYPERVOLEMIC -

**STEP 3:** IV Frusemide as infusion (0.1-0.2 mg/kg/hr) to reduce fluid overload. Meticulously measure UO. Replace UO with ¼ or 1/5 GNS.

**STEP 4:** Stop 3% Saline or NAHCO3

**STEP 5:** Consider RRT, if UO low, or creatinine high or very high serum Na> 180 or multiple electrolyte deficiency or fluid overload and CCF
Carry home message

• Hypernatremia is commonly due to “water problem,” and not a problem of sodium homeostasis.
• It can only develop as a result of either a loss of free water or a gain of sodium or a combination of both.
• Sodium disturbances predominantly affect brain cells
• In hypovolemia- bolus of NS over 30-60 min is essential
• In Both hypo and hypervolemic hypernatremia, hypotonic fluid is used, for deficit correction. But 1.5 times maintenance in the former and restricted volume in hypervolemic hypernatremia.
• Meticulous calculation of fluid intake - output and specific therapy form the key for success
“The stability of the internal environment [the milieu intérieur] is essential for the free and independent life.”

Claude Bernard (1813 –1878)
French physiologist