PRESENTING PROBLEMS IN DISORDERS OF SODIUM BALANCE

SODIUM DEPLETION (USUALLY ASSOCIATED WITH HYPOVOLAEMIA)

CAUSES OF SODIUM AND WATER DEPLETION

1. Inadequate intake e.g. Environmental deprivation, inadequate therapeutic replacement
2. Gastrointestinal sodium loss e.g. Vomiting, diarrhoea, nasogastric suction, external fistula
3. Skin sodium loss e.g. Excessive sweating, burns
4. Renal sodium loss e.g. Diuretic therapy, mineralocorticoid deficiency, tubulointerstitial disease (sometimes)
5. Internal sequestration e.g. Bowel obstruction, peritonitis, pancreatitis, crush injury
6. Whole blood loss.

Diagnosis of hypovolaemia is based on clinical evaluation, seeking the characteristic symptoms and signs such as Thirst, Dizziness on standing, Weakness and Low JVP, Postural hypotension, Tachycardia, Dry mouth, Reduced skin turgor, Reduced urine output, Weight loss, Confusion and stupor, in the context of a relevant precipitating illness.

Laboratory investigation

1. Plasma urea concentration rises, while the plasma creatinine may be relatively well preserved early in hypovolaemic states, reflecting maintenance of near-normal GFR, the plasma urea will rise as urinary flow rate is reduced as a consequence of activation of sodium- and water-retaining mechanisms in the nephron.
2. Plasma uric acid may also rise, reflecting activation of compensatory proximal tubular reabsorption.
3. Urine osmolality increases as urine concentrating mechanisms are activated.
4. Urine sodium concentration falls as a result of activation of sodium-retaining mechanisms. Under these circumstances, sodium excretion may fall to less than 0.1% of the filtered sodium load.

Management

Management of sodium and water depletion has two main components:

1. Treatment of the cause where possible, to stop ongoing salt and water losses
2. Replacement of salt and water deficits, and provision of ongoing maintenance requirements, usually through the intravenous route when depletion is severe.

BASIC DAILY WATER AND ELECTROLYTE REQUIREMENTS:

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<table>
<thead>
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<tbody>
<tr>
<td>Water</td>
<td>35-45 ml/kg</td>
<td>2.5-3.0 l/day</td>
</tr>
<tr>
<td>Sodium</td>
<td>1.5-2 mmol/kg</td>
<td>100-140 mmol/day</td>
</tr>
<tr>
<td>Potassium</td>
<td>1.0-1.5 mmol/kg</td>
<td>70-100 mmol/day</td>
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</tbody>
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COMPOSITION OF SOME ISOTONIC INTRAVENOUS FLUIDS (1 LITRE):

<table>
<thead>
<tr>
<th>Fluid</th>
<th>D-glucose</th>
<th>Calories</th>
<th>Na+</th>
<th>Cl-</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>5% dextrose</td>
<td>50 g</td>
<td>200</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Normal saline</td>
<td>0</td>
<td>0</td>
<td>154</td>
<td>154</td>
<td>0</td>
</tr>
</tbody>
</table>
In the absence of normal oral intake (as in a fasting or post-operative patient in hospital), maintenance quantities of fluid, sodium and potassium should be provided. If any deficits or continuing pathological losses are identified, additional fluid and electrolytes will be required.

In prolonged periods of fasting (greater than a few days), attention needs also to be given to providing sufficient caloric and nutritional intake to prevent catabolism of body energy stores.

**SODIUM EXCESS (USUALLY ASSOCIATED WITH HYPERVOLAEMIA)**

**Aetiology and clinical assessment**

In the presence of normal function of the heart and kidneys, an excessive intake of salt and water is compensated for by increased excretion and so is unlikely to lead to clinically obvious features of hypervolaemia. However, diseases affecting the kidney, heart or liver frequently set in train a sequence of events leading to the clinical features of hypervolaemia.

**CAUSES OF SODIUM AND WATER EXCESS**

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Examples</th>
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<tbody>
<tr>
<td>1. Impaired renal function</td>
<td>Primary renal disease</td>
</tr>
<tr>
<td>2. Primary hyperaldosteronism</td>
<td>Conn's syndrome</td>
</tr>
<tr>
<td>3. Secondary hyperaldosteronism</td>
<td>Congestive cardiac failure, Cirrhotic liver disease, Nephrotic syndrome, Other hypoalbuminaemic states like Protein-losing enteropathy, Malnutrition, Idiopathic/cyclical oedema, Renal artery stenosis*</td>
</tr>
</tbody>
</table>

Peripheral oedema is the most common physical sign associated with these conditions. The volume expansion seen in the three most common systemic disorders associated with sodium and fluid overload (cardiac failure, cirrhosis and nephrotic syndrome) is largely due to secondary responses to the circulatory insufficiency associated with the primary disorder. These concepts are illustrated in the following Figure.
Management

The management of ECF volume overload involves a number of components:

1. specific treatment (where available) directed at the cause, e.g. ACE inhibitors in heart failure, corticosteroids in minimal change nephropathy
2. restriction of dietary sodium to more nearly match the diminished excretory capacity, e.g. 50-80 mmol/day
3. treatment with diuretic drugs.

DIURETIC THERAPY

Diuretics are important in the treatment of conditions of ECF expansion due to salt and water retention. They act by inhibiting sodium reabsorption at various locations along the nephron.

In proximal tubule carbonic anhydrase inhibitor (acetazolamide) inhibit the intracellular production of H⁺ ion thereby reducing sodium reabsorption which is exchanged with H⁺ ion in the proximal tubule by the apical membrane sodium–hydrogen exchanger.

In the thick ascending limb of loop of Henle, loop diuretics (e.g. furosemide) inhibit sodium reabsorption by blocking the action of apical membrane Na,K,2Cl cotransporter.

In the early distal convoluted tubule, thiazide diuretics inhibit sodium reabsorption by blocking the sodium chloride cotransporter in the apical membrane.

In the late distal/cortical collecting duct system the potassium sparing diuretics, amiloride and triametrine block sodium reabsorption from the apical sodium channel in the principal cells, while spironolactone and eplerenone block mineralocorticoid aldosterone receptor.
Adverse effect:

1. Renal side effect: hypovolemia, hyponatremia, hypokalemia, metabolic alkalosis, hyperuricemia, hypomagnesemia, hypercalciuria (loop), hypocalciuria (thiazide).
3. Miscellaneous side effect: hypersensitivity reaction, erectile dysfunction, acute pancreatitis, cholecystitis (thiazides).

**DISORDERS OF WATER BALANCE**

Daily water intake can vary over a wide range, from 500 ml to several litres a day. While a certain amount of water is lost through the stool, sweat and the respiratory tract, the kidneys are chiefly responsible for adjusting water excretion to maintain constancy of body water content and body fluid osmolality (normal range 280–300 mmol/kg).

**FUNCTIONAL ANATOMY AND PHYSIOLOGY OF RENAL WATER HANDLING**

While regulation of total ECF volume is largely achieved through the kidneys' control of sodium excretion, there must also be mechanisms to allow for the excretion of a 'pure' water load when free water intake is high, and for the avid retention of water by the kidneys when access to water is restricted. These functions are largely achieved by the properties of the loop of Henle and the collecting ducts.

*In summary for adequate dilution of the urine, there must be:*

1. Adequate solute delivery to the loop of Henle and early distal tubule
2. Normal function of the loop of Henle and early distal tubule
3. No ADH in the circulation.

If any of these processes are faulty, water retention and hyponatraemia may result.

*Conversely, to achieve concentration of the urine there must be:*

1. Adequate solute delivery to the loop of Henle
2. Normal function of the loop of Henle
3. ADH release into the circulation
4. ADH action on the collecting ducts.

Failure of any of these steps may be expected to result in inappropriate water loss, with resultant hypernatremia.

**PRESENTING PROBLEMS IN DISORDERS OF WATER BALANCE**

Disturbances in body water metabolism, in the absence of changes in sodium balance, manifest principally as abnormalities of plasma sodium concentration, and hence of plasma osmolality. The main consequence of changes in plasma osmolality, especially when rapid, is altered cerebral function. This is because when extracellular osmolality...
HYPONATRAEMIA

Aetiology and clinical assessment

Hyponatraemia (plasma Na < 135 mmol/l) is a common electrolyte abnormality, often detected asymptptomatically, but it may also be associated with profound disturbances of cerebral function, manifesting as anorexia, nausea, vomiting, confusion, lethargy, seizures and coma. The degree of cerebral symptomatology depends more on the rate of development of the electrolyte abnormality than on its severity. This is because when the plasma osmolality falls rapidly, water flows into cerebral cells which become swollen and ischaemic. However, when hyponatraemia develops more gradually, cerebral neurons have time to respond by reducing the intracellular osmolality, through reduction in cell potassium and by reduced synthesis of intracellular organic osmolytes.

Hyponatraemia with hypovolaemia: Patients in this category have clinical features of hypovolaemia as described earlier in hypovolaemia.

Hyponatraemia with euvoelaemia: Patients in the second group ('dilutional hyponatraemia') have no major disturbance of body sodium content, and are clinically euvoelaemic. Excess body water may be the result of abnormally high intake, either orally (primary polydipsia) or as a result of medically infused fluids (as intravenous dextrose solutions, or by absorption of sodium-free bladder irrigation fluid after prostatectomy), and (SIADH).

Syndrom of inappropriate ADH secretion (SIADH): In this condition an endogenous source of ADH promotes renal water retention in the absence of an appropriate physiological stimulus. The clinical diagnosis requires the patient to be euvoelaemic, with no evidence of organ system disease potentially associated with hyponatraemia (heart, liver, kidney).

Causes of (SIADH): 1. tumours, e.g. lung or colon cancer. 2. CNS disorder: stroke, trauma, infection, psychosis. 3. pulmonary disorder: pneumonia, tuberculosis, COPD. 4. DRUGS: carbamazepine, haloperidol, amitriptyline, fluxitine, cytotoxic, chlorpropamide, morphine. 5. Idiopathic.

Diagnosis of (SIADH): 1. low plasma Na, osmolality; low-normal plasma urea, creatinine and uric acid. 2. urinary sodium and osmolality are higher than that of the plasma. 3. exclusion of other causes of hyponatremia. 4. Appropriate clinical context.

Treatment 1. fluid restriction. 2. removal of precipitating stimulus. 3. demeclocyclin. 4. oral urea. 5. oral vasopressin receptor antagonist (vaptans).

Hyponatraemia with hypervolaemia: where excess water retention is associated with sodium retention and volume expansion, as in heart failure and other oedematous disorders.

CAUSES OF HYPONATRAEMIA

Examples
DR. LAITH ALDABBAGH LEC. 2  PRESENTING PROBLEMS IN DISORDERS OF SODIUM BALANCE

**Hypovolaemic** (sodium deficit with a relatively smaller water deficit)
- Renal Na losses
- Diuretic therapy (especially thiazides)
- Adrenocortical failure
- Gastrointestinal Na losses
- Vomiting
- Diarrhoea

**Euvolaemic** (water retention alone)
- Primary polydipsia
- Excessive electrolyte-free water infusion
- SIADH
- Hypothyroidism

**Hypervolaemic** (sodium retention with relatively greater water retention)
- Congestive cardiac failure
- Cirrhosis
- Nephrotic syndrome
- Chronic renal failure (during free water intake)

**Investigations**:
Plasma and urine electrolytes and osmolality are usually the only tests required to classify the hyponatraemia.

**Management**:
- The treatment for hyponatraemia is critically dependent on the rate of development and severity, and on the underlying cause. In general, if hyponatraemia has developed rapidly (over hours to days), morbidity will be high due to cerebral oedema, and it is generally safe to correct the plasma sodium relatively rapidly. This can include infusion of hypertonic (3%) sodium chloride solutions, especially when the patient is obtunded or convulsing.
- On the other hand, rapid correction of hyponatraemia which has developed slowly (over weeks to months) can itself be hazardous to the brain. This is because cerebral cells adapt to slowly developing hypo-osmolality by reducing the intracellular osmolality, thus maintaining normal cell volume. Under these conditions, an abrupt increase in extracellular osmolality can lead to water shifting out of the cerebral neurons, abruptly reducing their volume and risking detachment from their myelin sheaths. The resulting 'myelinolysis' can produce permanent structural and functional damage to midbrain structures, and is generally fatal. The rate of correction of the plasma Na concentration in chronic asymptomatic hyponatraemia should not exceed 10 mmol/l/day, and an even slower rate would generally be safer.
- Specific treatment measures should be related to the underlying cause.

**HYPERNATRAEMIA**

**Aetiology and clinical assessment**
Hyponatraemia (plasma Na > 150 mmol/l) reflects an inadequacy of the kidney in concentrating the urine in the face of relatively restricted water intake. This can be due to failure to generate an adequate medullary concentration gradient (low GFR states, loop diuretic therapy), but more commonly it is due to failure of the ADH system, either because no ADH is released from the pituitary (central or 'cranial' diabetes insipidus). It is important to note the risk of iatrogenic induction of hypernatraemia, and to reiterate that whatever the underlying cause, sustained or severe hypernatraemia must reflect an impaired thirst mechanism or responsiveness to thirst, which would otherwise lead to sufficient water being ingested to prevent this disorder progressing.

**CAUSES OF HYPERNATRAEMIA**
1. Hypovolaemic (sodium deficit with a relatively greater water deficit) due to Renal Na losses (especially osmotic diuretic, or loop diuretic during water restriction), GIT losses, skin losses and excessive sweating.
2. Euvolaemic (water deficit alone) due to DI.
3. Hypervolaemic (sodium retention with relatively less water retention) due to enteral or parenteral feeding, CRF.

MANAGEMENT

Treatment of hypernatremia depends on both the rate of development and the underlying cause. If the condition develop rapidly, it needs rapid correction with IV isotonic 5% dextrose or hypotonic 0.45% saline otherwise it needs slow correction to avoid the risk of cerebral oedema.