given by intravenous infusion but must be administered slowly to avoid causing hyperkalaemia and associated cardiac toxicity; plasma-potassium concentrations should be closely monitored and ECG monitoring may be required. The choice of salt for oral potassium replacement depends on co-existing acid–base and electrolyte disturbances. Potassium chloride is generally the drug of choice for the treatment of hypokalaemia in patients with metabolic alkalosis with hypochloraemia, whereas a salt such as the bicarbonate may be preferred in patients with hyperchloraemic acidosis as in some renal tubular acidoses. Hypokalaemia secondary to hypomagnesaemia requires magnesium replacement therapy.

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***BARTTER'S SYNDROME.*** Bartter's syndrome is a set of closely related disorders thought to result from inherited defects in ion transport in various sections of the renal tubule.[1,2] Patients exhibit hyperplasia of the juxtaglomerular cells, hypokalaemia and metabolic alkalosis, and excess aldosterone, prostaglandin, and renin production. Symptoms are primarily those of the hypokalaemia, including muscle weakness; polyuria and enuresis, and growth retardation in children, can occur. In contrast to other hyperreninaemic states, patients do not have hypertension or oedema.

**Treatment** rarely completely corrects hypokalaemia. Potassium supplementation may be given, while a cyclo-oxygenase inhibitor such as indometacin, or an ACE inhibitor such as captopril, can produce benefit.[2] Spironolactone and propranolol have also been tried and magnesium salts may be given if there is hypomagnesaemia.[2]


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***DIURETIC-INDUCED HYPOKALAEMIA.*** Reduced potassium concentrations may result from the use of potassium-losing diuretics, particularly thiazides and loop diuretics. Clinically significant hypokalaemia is unlikely at the doses used in hypertension and the routine use of potassium supplements is no longer recommended. However, the concomitant use of a potassium-sparing diuretic such as amiloride or, less usually, a potassium supplement, may be necessary in patients at risk of hypokalaemia (see also Hydrochlorothiazide, Effects on Electrolyte Balance, p.1308).

***HYPOKALAEMIC PERIODIC PARALYSIS.*** Hypokalaemic periodic paralysis is an inherited disorder in which episodes of hypokalaemia with muscle weakness or paralysis appear to be associated with a shift in potassium from the extracellular to the intracellular fluid. Acute attacks are treated with potassium, given orally or intravenously. Prophylaxis with acetazolamide has been found to reduce the frequency and severity of attacks.[1,2]


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## Sodium Homoeostasis

Sodium is the principal cation in the extracellular fluid and is responsible for the maintenance of the extracellular fluid volume and osmolality. In addition, sodium is also involved in nerve conduction, muscle contraction, acid–base balance, and cell nutrient uptake. A usual plasma concentration of sodium would be expected to be within 135 to 145 mmol/litre.

Sodium homoeostasis is complex and closely associated with fluid balance. The osmolality and volume of the extracellular fluid are tightly regulated. Small changes in osmolality (plasma-sodium concentrations) are corrected by alteration of extracellular volume. This balance of plasma osmolality is achieved by the secretion or suppression of antidiuretic hormone (ADH; vasopressin), which primarily controls water excretion by the kidney. A tendency towards hyponatraemia suppresses ADH secretion and promotes renal loss of water; an increase in ADH secretion increases water reabsorption by the renal distal tubules. Changes in extracellular volume will also affect ADH release independently of osmolality. In addition, changes in extracellular volume result in modulation of the renal excretion of sodium.

Total body sodium content is regulated by renal sodium excretion, which can vary widely depending on dietary intake. Various mechanisms are involved in controlling renal sodium excretion including the renin-angiotensin system, glomerular filtration rate, and natriuretic factors. A reduction in extracellular fluid volume leads to the production of angiotensin II which stimulates the secretion of aldosterone. Aldosterone promotes the reabsorption of sodium ions by the distal tubules. There may be significant effects on sodium homoeostasis if adrenal insufficiency or mineralocorticoid excess disturb this mechanism.

**Hypernatraemia.** Hypernatraemia is an abnormal rise in the plasma-sodium concentration with a simultaneous rise in plasma osmolality. It is generally associated with volume depletion when water intake is less than water losses through renal or extrarenal routes. The causes include impaired thirst, as in coma or essential hypernatraemia, osmotic diuresis (solute diuresis), as in diabetic ketoacidosis (see Diabetic Emergencies, p.435) or after drugs such as mannitol, and excessive water losses, either from the kidney, as in diabetes insipidus (p.2179), or extrarenally, for example because of excessive sweating or diarrhoea.

Hypernatraemia can also occur after excessive oral sodium intake (but this is uncommon) and after inappropriate use of intravenous sodium chloride.

The clinical manifestations of hypernatraemia are caused by the effect of increased plasma osmolality on the brain and include somnolence, confusion, respiratory paralysis, and coma. CNS symptoms are more severe when hypernatraemia develops rapidly. If there is volume depletion, other symptoms such as hypotension, tachycardia, and symptoms of circulatory insufficiency may occur as well. A high volume of dilute urine is seen in patients with abnormal renal water conservation, whereas a low volume of concentrated urine is expected in patients with impaired thirst or excessive extrarenal water loss.

**Treatment** of hypernatraemia usually requires water replacement, and drinking water may be sufficient for some patients. In more severe conditions, glucose 5% may be given by slow intravenous infusion. Alternatively, some recommend the use of sodium chloride 0.9% if volume depletion is severe. Care is required, as too rapid correction can induce cerebral oedema, particularly in chronic conditions.

If the total body sodium is too high, loop diuretics may be used to increase sodium excretion, with fluid losses being replaced by an infusion of glucose 5% and potassium chloride. It has also been suggested that dialysis may be necessary if there is significant renal impairment, if the patient is moribund, or if the serum-sodium concentration is greater than 200 mmol/litre.

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**Hyponatraemia.** Hyponatraemia, an abnormal fall in the plasma-sodium concentration, usually with a simultaneous fall in the plasma osmolality, is not uncommon, and may occur in diseases as diverse as heart failure, cirrhosis, adrenocortical insufficiency, hyperglycaemia, and AIDS.

The kidney is able to conserve sodium, and sodium depletion due to low salt intake is rare. Sodium depletion may occur if there are abnormal losses, either from the gut as a consequence of repeated diarrhoea and/or vomiting or from the kidney, for example, due to various renal disorders or the overuse of diuretics (see under Hydrochlorothiazide, Effects on Electrolyte Balance, p.1308).

The most common cause of hyponatraemia is dilution. This may result from excessive fluid intake, for example the ingestion of large volumes of water in patients with primary polydipsia (psychogenic polydipsia). More often, however, it is a result of reduced water excretion, as in renal impairment or the syndrome of inappropriate secretion of antidiuretic hormone (SIADH—p.2182). Postoperative hyponatraemia is a frequent complication which can be exacerbated by the inappropriate intravenous use of hypotonic,[1] or even isotonic,[2] fluids.

Hyponatraemia due to sodium depletion in the presence of volume contraction may cause orthostatic hypotension and circulatory insufficiency. Dilutional hyponatraemia can be asymptomatic but headache, confusion, nausea, vomiting, somnolence, and weakness may occur. If severe, cerebral oedema may lead to respiratory arrest, convulsions, and coma. CNS symptoms are more common when the condition is acute.

**Therapy** is guided by the rate of development and degree of hyponatraemia, accompanying symptoms, and the state of water balance, and should also take into account the underlying cause. Mild asymptomatic hyponatraemia does not usually require specific therapy. Chronic mild to moderate sodium depletion, such as occurs in salt-losing bowel or renal disease, may be treated with oral sodium chloride supplements while ensuring adequate fluid intake.

When there is substantial volume depletion, volume replacement is necessary and intravenous sodium chloride 0.9% is often used.[3-5]

Chronic dilutional hyponatraemia, which is often asymptomatic, can generally be managed by correcting the underlying disease; water restriction may also be necessary and drugs that interfere with the action of ADH such as demeclocycline or lithium carbonate may be useful in SIADH.[3-6] Furosemide plus oral sodium chloride supplements have also been used.[7]

Acute symptomatic hyponatraemia (water intoxication) is generally associated with plasma-sodium concentrations below 120 mmol/litre and requires more aggressive therapy. This involves giving hypertonic or isotonic sodium chloride intravenously, often with a loop diuretic such as furosemide, especially if fluid overload is likely to be a problem.[4,6,7] The aim is to render the patient asymptomatic, with a plasma-sodium concentration of 120 to 130 mmol/litre; the plasma-sodium concentration should not be corrected to normal values nor should hypernatraemia be allowed to develop.[1,6,7] Plasma-sodium concentrations and the total body-water volume should be monitored throughout.

A rare neurological syndrome known as central pontine myelinolysis (osmotic demyelination) has been associated with the over-rapid correction of symptomatic hyponatraemia, particularly if the condition is well established. However, there is no consensus about the optimal administration of intravenous sodium chloride, and a number of regimens have been suggested. Generally, it has been recommended that the rate of correction of plasma-sodium should be 0.5 to 1 mmol/litre per hour, and not exceeding 2 mmol/litre per hour; maximum corrections have included 8 mmol/litre per 24 hours,[7] 12 mmol/litre per 24 hours or 18 mmol/litre over the first 48 hours,[6] and 20 mmol/litre in the first 48 hours.[1] Some[1,5] have given more specific recommendations depending on the severity of symptoms, suggesting that patients with severe symptoms, such as seizures, respiratory arrest, or neurogenic pulmonary oedema, require rapid correction in the first few hours, aiming for an initial increase in plasma-sodium of 2 to 4 mmol/litre, followed by a continuous infusion.

More recently, the vasopressin receptor antagonist conivaptan has become available for the management of euvolaemic and hypervolaemic hyponatraemia. It must be given intravenously, and other vasopressin receptor antagonists that are orally active are under investigation.[5,6]


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# Dialysis Solutions

Soluciones para diálisis.

**Pharmacopoeias.** In *Eur.* (see p.vii), which includes separate monographs for solutions for haemodialysis, haemofiltration and haemodiafiltration, and peritoneal dialysis.