Phosphates also have **other uses**. They lower the pH of urine and have been given as adjuncts to urinary antibacterials that depend on an acid urine for their activity. Phosphates have also been used for the prophylaxis of calcium renal calculi; the phosphates reduce urinary excretion of calcium thus preventing calcium deposition. A suggested oral dose for both uses is 7.4 mmol of phosphate four times daily.

Butafosfan (1-butylamino-1-methylethylphosphinic acid) and the sodium salt of toldimfos (4-dimethylamino-*O*-tolylphosphinic acid) are used as phosphorus sources in veterinary medicine.

Bowel evacuation. A review concluded that the efficacy and tolerability of oral sodium phosphate solution was generally similar to, or significantly better than, that of polyethylene glycol-based or other colorectal cleansers in patients preparing for colorectal-related procedures.[1]

1. Curran MP, Plosker GL. Oral sodium phosphate solution: a review of its use as a colorectal cleanser. *Drugs* 2004; **64:** 1697–1714.

Hypercalcaemia. Intravenous phosphates have been used to lower plasma-calcium concentrations in hypercalcaemic emergencies (p.1668), but because of their potential to cause serious adverse effects other drugs are now preferred. Oral phosphates may be used to prevent gastrointestinal absorption of calcium in the treatment of hypercalcaemia. The dose in adults is up to 100 mmol phosphate daily adjusted according to response.

Hypophosphataemia. Phosphate salts are given in the management of hypophosphataemia when a phosphate deficiency is identified, as discussed in Uses and Administration, above. Intravenous phosphates are associated with serious adverse effects if hypophosphataemia is over-corrected, and the rise in serum-phosphorus concentration cannot be predicted from a given dose. Consequently, it has been recommended[1-4] that intravenous phosphate be used cautiously in the treatment of severe hypophosphataemia (for the standard rate and dose see Uses and Administration, above). However, some advocate a more aggressive fixed-dose regimen in critically ill patients.[5-7]

1. Vannatta JB, *et al.* Efficacy of intravenous phosphorus therapy in the severely hypophosphataemic patient. *Arch Intern Med* 1981; **141:** 885–7.
2. Anonymous. Treatment of severe hypophosphatemia. *Lancet* 1981; **ii:** 734.
3. Lloyd CW, Johnson CE. Management of hypophosphatemia. *Clin Pharm* 1988; **7:** 123–8.
4. Coyle S, *et al.* Treatment of hypophosphataemia. *Lancet* 1992; **340:** 977.
5. Perreault MM, *et al.* Efficacy and safety of intravenous phosphate replacement in critically ill patients. *Ann Pharmacother* 1997; **31:** 683–8.
6. Miller DW, Slovis CM. Hypophosphatemia in the emergency department therapeutics. *Am J Emerg Med* 2000; **18:** 457–61.
7. Charron T, *et al.* Intravenous phosphate in the intensive care unit: more aggressive repletion regimens for moderate and severe hypophosphatemia. *Intensive Care Med* 2003; **29:** 1273–8.

Osteomalacia. Vitamin D deficiency, or its abnormal metabolism, is the most usual cause of osteomalacia and rickets (p.1084); however, phosphate depletion may also contribute, and phosphate supplementation may be given as appropriate. A suggested oral dose for vitamin-D-resistant hypophosphataemic osteomalacia in adults is 65 to 100 mmol phosphate daily, and for vitamin D-resistant rickets in children is 32 to 48 mmol phosphate daily.

RICKETS OF PREMATURITY. Dietary deficiency of phosphorus is unusual, but can occur in small premature infants fed exclusively on human breast milk. The phosphate intake in these infants appears to be inadequate to meet the needs of bone mineralisation, and hypophosphataemic rickets can develop. It has been proposed that this condition, variably called metabolic bone disease of prematurity, or rickets of prematurity, could be prevented by giving phosphorus supplements to very low-birth-weight babies (less than about 1000 g) fed on breast milk alone.[1] A suggested regimen is to add 10 to 15 mg of phosphorus per 100 mL of feed (as buffered sodium phosphate) until the infant reached 2000 g. Concomitant calcium and vitamin D supplementation are also recommended.[1] A placebo-controlled study[2] in infants weighing less than 1250 g at birth confirmed that phosphate supplements (50 mg daily) could prevent the development of the bone defects of rickets of prematurity.

1. Brooke OG, Lucas A. Metabolic bone disease in preterm infants. *Arch Dis Child* 1985; **60:** 682–5.
2. Holland PC, *et al.* Prenatal deficiency of phosphate, phosphate supplementation, and rickets in very-low-birthweight infants. *Lancet* 1990; **335:** 697–701. Correction. *ibid.*; 1408–9.

Preparations

BP 2008: Dipotassium Hydrogen Phosphate Injection; Phosphates Enema; Sterile Potassium Dihydrogen Phosphate Concentrate;
Ph. Eur.: Anticoagulant Citrate-Phosphate-Glucose Solution (CPD);
USP 31: Anticoagulant Citrate Phosphate Dextrose Adenine Solution; Anticoagulant Citrate Phosphate Dextrose Solution; Potassium Phosphates Injection; Sodium Phosphates Injection; Sodium Phosphates Oral Solution; Sodium Phosphates Rectal Solution.

Proprietary Preparations (details are given in Part 3)
Arg.: Dicofan; Enemol; Fleet Enema†; Fosfacol; Fosfafarma; Fosfo-Dom; Fosfoadital; Fosfobarigraf; Gadolax; Kritel Enema; Prontonema; Silaxa; Tekfema; ***Austral.:*** Celloids PP 85; Celloids SP 96; Fleet Phospho-Soda; Fleet Ready-to-Use; Phosphate-Sandoz; Phosphoprep; ***Austria:*** Fleet Phospho-Soda; Relaxyl; ***Belg.:*** Colexklysma; Fleet Enema; Fleet Phospho-Soda; Practo-Clyss; ***Braz.:*** Fleet Enema; Phosfoenema; ***Canad.:*** Fleet Enema; Fleet Phospho-Soda; ***Chile:*** Fabulaxol; Fleet Enema; Fleet Fosfosoda; ***Denm.:*** Fleet; ***Fin.:*** K-Fosfosteril†; ***Fr.:*** Fleet Phospho-Soda; ***Ger.:*** Fleet Phospho-Soda; ***Gr.:*** Bioklysm; Enema Cooper; Fleet Enema; Fosfolax; Klysmol; ***Hong Kong:*** Fleet Enema; Fleet Phospho-Soda; Unima; ***Hung.:*** Fleet Phospho-Soda; Optacid; ***India:*** Exit; ***Indon.:*** Fleet Enema; Fleet Phosposoda; ***Irl.:*** Fleet; ***Israel:*** Fleet Enema; ***Ital.:*** Clisma Fleet; Fosfo-Soda Fleet; ***Malaysia:*** Fleet Enema; Fleet Phospho-Soda; ***Mex.:*** Deplecat†; Fleet Enema Fosf-Sodio; Fleet PS; ***Neth.:*** Fleet Gebruiksklaar Klysma; Phosphoral; ***NZ:*** Fleet Phosphate Enema; Fleet Phospho-Soda; ***Philipp.:*** Fleet Enema; Phospho-Soda; ***Pol.:*** Enema; Fleet Phospho-Soda; Phospho-Laxative; Rectanal; ***Port.:*** Fleet Enema; Fleet Phospho-Soda; ***Singapore:*** Fleet Enema†; Fleet Phospho-Soda†; ***Spain:*** Fosfoevac; Fosfosoda; ***Swed.:*** Phosphoral; ***Turk.:*** BT Enema; Fleet Enema; Fleet Fosfo Soda; ***UK:*** Fleet Phospho-Soda; Fleet Ready-to-Use; ***USA:*** Fleet Enema; Fleet Phospho-Soda; K-Phos Original; OsmoPrep; Visicol; ***Venez.:*** Fleet Enema; Fleet Fosfosoda.

Multi-ingredient: ***Arg.:*** Colonil; ***Austral.:*** Cal Alkyline; Celloid Compounds Magcal Plus; Celloid Compounds Sodical Plus; Duo Celloids PPIP; Duo Celloids PPMP; Duo Celloids SPCF; Duo Celloids SPCP; Duo Celloids SPIP; Duo Celloids SPMP; Duo Celloids SPPC; Duo Celloids SPPP; Duo Celloids SPPS; Duo Celloids SPS; Duo Celloids SPSS; Gingo A†; Ginkgo Plus Herbal Plus Formula 10†; Lifesystem Herbal Plus Formula 11 Ginkgo†; Lifesystem Herbal Plus Formula 2 Valerian†; Magnesium Plus†; ML 20†; Potasi; Travad†; Valerian Plus Herbal Plus Formula 12†; ***Austria:*** Clysmol; Prepacol; Reducto; ***Belg.:*** Lavement au Phosphate†; Prepacol; ***Braz.:*** Digestron†; ***Canad.:*** Enemol; Gent-L-Tip†; Normo Gastryl; Phosphate-Novartis; Phosphates; ***Cz.:*** Blend-a-Med†; Mopasol; Prepacol; ***Denm.:*** Phosphoral; ***Fin.:*** Phosphoral; ***Fr.:*** Bactident; Digedryl; Hepargitol; Normacol Lavement; Normogastryl†; Oxyboldine; Phosphoneuros; Phosphore Medifa; Prefagyl†; Prepacol; Tavag; ***Ger.:*** Isogutt†; Klistier; Klysma Salinisch†; Lecicarbon; Practo-Clyss; Prepacol; Reducto-spezial; ***Gr.:*** Enter-Out; Fleet Phospho-Soda; Kathargon; Mineralin; Phospho-Laxat; Phosphoclean; Trifalac; ***Hong Kong:*** PMS-Enemol†; ***Hung.:*** Nilacid; Vition; ***India:*** Cotaryl; ***Indon.:*** Fosen; Kalkurenal; ***Irl.:*** Fletchers Phosphate Enema; ***Israel:*** Calciless; Soffodex; ***Ital.:*** Clisflex; Clisma-Lax; Enemac; IperClean; Phospho-Lax; Pomag; ***Malaysia:*** Unima; ***Mex.:*** Travad†; ***Neth.:*** Colex; ***Norw.:*** Phosphoral; ***NZ:*** Phosphate-Sandoz; ***Pol.:*** Phosphor; Sal Ems Artificiale; Sal Ems Factitium; Sal Vichy Factitium; ***S.Afr.:*** Colo-Prep; Lenolax; Phosphate-Sandoz; Sabax Fosenema; ***Singapore:*** ENTsol; ***Spain:*** Alcalinos Gelos; Darmen Salt; Enema Casen; Eupeptina; Foslainco; Lebersal; ***Switz.:*** Colophos; Freka-Clyss; Lecicarbon; Practo-Clyss†; ***Thai.:*** Swiff; Uni-Ma; ***UK:*** Carbalax; Fletchers Phosphate Enema†; Phosphate-Sandoz; Salivix; ***USA:*** K-Phos MF; K-Phos Neutral; K-Phos No.2; MSP-Blu; Neutra-Phos; Neutra-Phos-K; Phos-NaK; Summers Eve Post-Menstrual; Urelle; Uretron; Urimar-T; Urimax; UriSym†; Uro Blue; Urogesic Blue; Utira; ***Venez.:*** Fisiolin; Polantac.

Potassium

Kalium; Potasio.
K = 39.0983.

Description. Potassium salts covered in this section are those principally given as a source of potassium ions, but consideration should also be given to the effect of the anion. Phosphate salts of potassium are covered under Phosphate, p.1682, and the bicarbonate and citrate salts under Bicarbonate, p.1673.

Potassium Acetate

E261; Kalii acetas; Kalio acetatas; Kaliumacetat; Kálium-acetát; Kaliumasetaatti; Octan draselný; Potasio, acetato de; Potassium, acétate de; Potasu octan.
$CH_3.CO_2K$ = 98.14.
CAS — 127-08-2.

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
Ph. Eur. 6.2 (Potassium Acetate). Deliquescent white or almost white, crystalline powder or colourless crystals. Very soluble in water; freely soluble in alcohol. A 5% solution in water has a pH of 7.5 to 9.0. Protect from moisture.
USP 31 (Potassium Acetate). Colourless, monoclinic crystals, or a white crystalline powder. It is odourless or has a faint acetous odour. Deliquesces on exposure to moist air. Soluble 1 in 0.5 of water, 1 in 0.2 of boiling water, and 1 in 3 of alcohol. pH of a 5% solution in water is between 7.5 and 8.5. Store in airtight containers.

Equivalence. Each g of potassium acetate (anhydrous) represents about 10.2 mmol of potassium. Potassium acetate (anhydrous) 2.51 g is equivalent to about 1 g of potassium.

Potassium Aspartate

Aspartate monopotassique hémihydraté; Kalii hydrogenoaspartas hemihydricus; Kalio-divandenilio aspartatas hemihidratas; Kalium-hydrogen-aspartát hemihydrát; Kaliumväteaspartathemihydrat; Kaliumvetyaspartaattihemihydraatti; Potassium Hydrogen Aspartate Hemihydrate. Potassium aminosuccinate hemihydrate.
$C_4H_6KNO_4,\ ½H_2O$ = 180.2.
CAS — 7259-25-8 (hemihydrate).

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Potassium Hydrogen Aspartate Hemihydrate). A white or almost white, powder or crystalline powder, or colourless crystals. Very soluble in water; practically insoluble in alcohol and in dichloromethane. pH of a 2.5% solution in water is between 6.0 and 7.5.

Equivalence. Each g of potassium aspartate represents about 5.5 mmol of potassium. Potassium aspartate 4.61 g is equivalent to about 1 g of potassium.

Potassium Chloride

Chlorid draselný; Cloreto de Potássio; E508; Kalii chloridum; Kalio chloridas; Kalium Chloratum; Kaliumklorid; Kálium-klorid; Kaliumkloridi; Potasio, cloruro de; Potassium, chlorure de; Potasu chlorek.
KCl = 74.55.
CAS — 7447-40-7.
ATC — A12BA01; B05XA01.
ATC Vet — QA12BA01; QB05XA01.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*
Ph. Eur. 6.2 (Potassium Chloride). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; practically insoluble in dehydrated alcohol.
USP 31 (Potassium Chloride). Colourless, elongated, prismatic, or cubical crystals, or a white, granular powder. Is odourless. Soluble 1 in 2.8 of water, and 1 in 2 of boiling water; insoluble in alcohol. Its solutions are neutral to litmus.

Equivalence. Each g of potassium chloride represents about 13.4 mmol of potassium. Potassium chloride 1.91 g is equivalent to about 1 g of potassium.

Potassium Gluconate

E577; Potasio, gluconato de. Potassium D-gluconate.
$CH_2OH.[CH(OH)]_4.CO_2K$ = 234.2.
CAS — 299-27-4 (anhydrous potassium gluconate); 35398-15-3 (potassium gluconate monohydrate).
ATC — A12BA05.
ATC Vet — QA12BA05.

Pharmacopoeias. In *Fr.*
US permits anhydrous or the monohydrate.
USP 31 (Potassium Gluconate). It is anhydrous or contains one molecule of water of hydration. A white or yellowish-white, odourless, crystalline powder or granules. Soluble 1 in 3 of water; practically insoluble in dehydrated alcohol, in chloroform, in ether, and in benzene. Its solutions are slightly alkaline to litmus. Store in airtight containers.

Equivalence. Each g of potassium gluconate (anhydrous) represents about 4.3 mmol of potassium. Each g of potassium gluconate (monohydrate) represents about 4 mmol of potassium. Potassium gluconate (anhydrous) 5.99 g and potassium gluconate (monohydrate) 6.45 g are each equivalent to about 1 g of potassium.

Potassium Sulfate

E515; Kalii sulfas; Kalio sulfatas; Kalium Sulfuricum; Kaliumsulfaatti; Kaliumsulfat; Potasio, sulfato de; Potassii Sulphas; Potassium, sulfate de; Potassium Sulphate; Síran draselný; Tartarus Vitriolatus.
K_2SO_4 = 174.3.
CAS — 7778-80-5.

Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn*.
Ph. Eur. 6.2 (Potassium Sulphate). A white or almost white, crystalline powder or colourless crystals. Soluble in water; practically insoluble in dehydrated alcohol.

Equivalence. Each g of potassium sulfate represents about 11.5 mmol of potassium. Potassium sulfate 2.23 g is equivalent to about 1 g of potassium.

Potassium Tartrate

E336; Potasio, tartrato de; Potasu winian.
$C_4H_4K_2O_6,\ ½H_2O$ = 235.3.
CAS — 921-53-9 (anhydrous potassium tartrate).

Equivalence. Each g of potassium tartrate (hemihydrate) represents about 8.5 mmol of potassium. Potassium tartrate (hemihydrate) 3.00 g is equivalent to about 1 g of potassium.

Adverse Effects

Excessive doses of potassium may lead to the development of hyperkalaemia (p.1669), especially in patients with renal impairment. Symptoms include paraesthesia of the extremities, muscle weakness, paralysis, cardiac arrhythmias, heart block, cardiac arrest, and confusion. Cardiac toxicity is of particular concern after intravenous dosage.

Pain or phlebitis may occur when given intravenously via peripheral veins, particularly at higher concentrations.

Nausea, vomiting, diarrhoea, and abdominal cramps may occur with oral potassium salts. There have been numerous reports of gastrointestinal ulceration, sometimes with haemorrhage and perforation or with the late formation of strictures, after the use of enteric-

coated tablets of potassium chloride. Ulceration has also occurred after the use of sustained-release tablets.

Treatment of Adverse Effects

The treatment of hyperkalaemia discussed on p.1669 also applies when hyperkalaemia occurs during potassium therapy. However, in mild hyperkalaemia that has developed on long-term treatment, stopping the potassium supplement and other drugs that may increase plasma-potassium concentrations, and avoidance of foods with a high potassium content may be sufficient to correct the hyperkalaemia.

In cases of acute oral overdosage of potassium supplements, the stomach should be emptied by gastric lavage in addition to the measures described on p.1669.

Precautions

Potassium salts should be given with considerable care to patients with cardiac disease or conditions predisposing to hyperkalaemia such as renal or adrenocortical insufficiency, acute dehydration, or extensive tissue destruction as occurs with severe burns. Excessive use of potassium-containing salt substitutes or potassium supplements may lead to accumulation of potassium especially in patients with renal insufficiency. Regular monitoring of clinical status, serum electrolytes, and the ECG is advisable in patients receiving potassium therapy, particularly those with cardiac or renal impairment.

Liquid or effervescent preparations are preferred to solid dosage forms for oral use; use of the former, with or after food, may reduce gastric irritation. Solid oral dosage forms of potassium salts should not be given to patients with gastrointestinal ulceration or obstruction. They should be given with care to patients in whom passage through the gastrointestinal tract may be delayed, as in pregnant patients. Treatment should be stopped if severe nausea, vomiting, or abdominal distress develops.

Potassium chloride should not be used in patients with hyperchloraemia.

Direct injection of potassium chloride concentrates without appropriate dilution may cause instant death. For the view that glucose-containing solutions should not be used for the initial intravenous administration of potassium in hypokalaemia see Administration, below.

Interactions

Potassium supplements should be used with caution, if at all, in patients receiving drugs that increase serum-potassium concentrations. These include potassium-sparing diuretics, ACE inhibitors, ciclosporin, and drugs that contain potassium such as the potassium salts of penicillin. Similarly, the concomitant use of potassium-containing salt substitutes for flavouring food should be avoided. Antimuscarinics delay gastric emptying and consequently may increase the risk of gastrointestinal adverse effects in patients receiving solid oral dosage forms of potassium.

Table 3. Some potassium salts and their potassium content.

	Potassium content per g		
Potassium salt	mg	mmol	mEq
Potassium acetate (anhydrous)	398	10.2	10.2
Potassium aspartate	217	5.5	5.5
Potassium bicarbonate	391	10.0	10.0
Potassium chloride	524	13.4	13.4
Potassium citrate (anhydrous)	383	9.8	9.8
Potassium citrate (monohydrate)	361	9.3	9.3
Potassium gluconate (anhydrous)	167	4.3	4.3
Potassium gluconate (monohydrate)	155	4.0	4.0
Potassium sulfate (anhydrous)	449	11.5	11.5
Potassium tartrate (hemihydrate)	332	8.5	8.5

Pharmacokinetics

Potassium salts other than the phosphate, sulfate, and tartrate are generally readily absorbed from the gastrointestinal tract. Potassium is excreted mainly by the kidneys; it is secreted in the distal tubules in exchange for sodium or hydrogen ions. Some potassium is excreted in the faeces and small amounts may also be excreted in sweat.

Human Requirements

Potassium is an essential body electrolyte. However, requirements are difficult to determine and have been estimated from the amount accumulated during growth and reported urinary and faecal excretion.

Over 90% of dietary potassium is absorbed from the gastrointestinal tract. Potassium is particularly abundant in vegetables, potatoes, and fruit.

UK and US recommended dietary intake. In the UK dietary reference values (DRV—see Human Requirements, p.1925)[1] have been estimated for potassium. The reference nutrient intake (RNI) for adults is 3.5 g (90 mmol) daily. In the USA, no recommended dietary allowance (RDA) has been established for potassium. However a daily intake of 1.6 to 2 g (40 to 50 mmol) is considered adequate for adults.

1. DoH. Dietary reference values for food energy and nutrients for the United Kingdom: report of the panel on dietary reference values of the committee on medical aspects of food policy. *Report on health and social subjects 41*. London: HMSO, 1991.

Uses and Administration

Potassium salts in this section are used for the prevention and treatment of potassium depletion and/or **hypokalaemia** (p.1669) and have been used in the prevention of **diuretic-induced hypokalaemia** (see Hydrochlorothiazide, Effects on Electrolyte Balance, p.1308). Doses may be expressed in terms of mmol or mEq of potassium, mass (mg) of potassium, or mass of potassium salt (for comparative purposes see Table 3, below). Treatment should be monitored by plasma-potassium estimations because of the risk of inducing hyperkalaemia, especially where there is renal impairment.

Potassium chloride is probably the most commonly used potassium salt; this is because hypochloraemic alkalosis, which is often associated with hypokalaemia, can be corrected by the chloride ions. An alkalinising salt such as potassium acetate, potassium bicarbonate, or potassium citrate may be preferable if a metabolic acidosis, such as occurs in renal tubular acidosis, accompanies the hypokalaemia (see p.1667). Other salts that are or have been used in the management of potassium deficiency include potassium ascorbate, potassium aspartate, potassium benzoate, potassium gluceptate, potassium gluconate, potassium phosphate, and potassium tartrate. Typical doses for the prevention of hypokalaemia may be up to 50 mmol daily and similar doses may be adequate in mild potassium deficiency. However, higher doses may be needed in more severe deficiency. Patients with renal impairment should receive correspondingly lower doses. *Oral* treatment is used for prophylaxis and is also suitable for treating most cases of hypokalaemia. Oral potassium salts are more irritating than the corresponding sodium salts; they should be taken with or after meals with plenty of fluid; liquid preparations are preferable.

An *intravenous* potassium salt may be required in severe acute hypokalaemia. This normally entails infusing a solution containing 20 mmol of potassium in 500 mL over 2 to 3 hours under ECG control. A recommended maximum dose is 2 to 3 mmol/kg of potassium in 24 hours. Higher concentrations have been given when an infusion pump has been used (see Administration below). Adequate urine flow must be ensured and careful monitoring of plasma-potassium and other electrolyte concentrations is essential. Potassium chloride is the salt most commonly used and solutions intended for intravenous use that are in a concentrated form (such as 1.5 or 2 mmol/mL) *must* be diluted to the appropriate concentration before use. There should be careful and thorough mixing when adding concentrated potassium chloride solutions to infusion fluids. Potassium chloride is also available as premixed infusions with sodium chloride and/or glucose containing 10 to 40 mmol/litre of potassium (but see also Administration, below). Potassium acetate is also given intravenously.

Amongst **other uses**, the sulfate, and tartrate salts of potassium have been given orally as osmotic laxatives (p.1693).

Some potassium salts are used as sodium-free condiments when sodium intake must be restricted.

Potassium chloride is sometimes used as an excipient in pharmaceutical formulations.

Administration. The standard concentration and rate of administration of potassium chloride for infusion is discussed in Uses and Administration, above. However, higher concentrations (200 or 300 mmol/litre) and faster infusion rates have been used, via an infusion pump, for cases of severe symptomatic hypokalaemia, especially with fluid overload.[1,2]

There has been controversy regarding the preferred route of administration of these higher concentrations of potassium chloride.[1] The central route avoids the problems of pain and phlebitis when potassium is given peripherally. However, it has been suggested that high concentrations of potassium given centrally may carry a greater risk of cardiac toxicity if the infusion is carried directly to the heart. Use of lidocaine has improved tolerability of peripheral administration of potassium chloride.[2]

Intravenous potassium is usually given in sodium chloride and/or glucose infusion. However, it has been pointed out that glucose can reduce serum-potassium concentrations, and that glucose-free solutions should be used for the initial intravenous administration of potassium in hypokalaemia.[3]

1. Kruse JA, Carlson RW. Rapid correction of hypokalemia using concentrated intravenous potassium chloride infusions. *Arch Intern Med* 1990; **150:** 613–17.
2. Pucino F, *et al.* Patient tolerance to intravenous potassium chloride with and without lidocaine. *Drug Intell Clin Pharm* 1988; **22:** 676–9.
3. Agarwal A, Wingo CS. Treatment of hypokalaemia. *N Engl J Med* 1999; **340:** 154–5.

Diabetic ketoacidosis. As discussed under Diabetic Emergencies on p.435, potassium replacement is given in diabetic ketoacidosis to restore total body stores of potassium and thereby prevent the hypokalaemia induced by insulin.

Hypertension. A meta-analysis[1] has reported that potassium supplementation results in reductions of both systolic and diastolic blood pressure. The size of the effect in hypertensive patients was sufficiently great to suggest a possible role in the treatment of hypertension (p.1171); effects in normotensive subjects were less marked but consistent with a role for potassium supplementation in preventing hypertension. Most studies have used potassium chloride, but an effect has also been demonstrated with the aspartate[2] and the citrate.[3]

1. Whelton PK, *et al.* Effects of oral potassium on blood pressure: meta-analysis of randomized controlled clinical trials. *JAMA* 1997; **277:** 1624–32.
2. Franzoni F, *et al.* Antihypertensive effect of oral potassium aspartate supplementation in mild to moderate arterial hypertension. *Biomed Pharmacother* 2005; **59:** 25–9.
3. He FJ, *et al.* Effect of short-term supplementation of potassium chloride and potassium citrate on blood pressure in hypertensives. *Hypertension* 2005; **45:** 571–4.

Myocardial infarction. A glucose, insulin, and potassium infusion has been investigated in acute myocardial infarction (see p.452).

Termination of pregnancy. Solutions of potassium chloride are used to reduce fetal numbers in multifetal pregnancies[1-3] or for severe fetal malformation by abolishing the fetal cardiac activity. The solution is injected into the thorax of the fetus without affecting the others which are allowed to continue to term. Alternatively, potassium chloride may be injected into the umbilical vein when access to the fetal heart is difficult. A retrospective comparison[4] found both techniques to be effective. Significantly smaller doses were required for the umbilical route, possibly because a sustained dose is delivered directly to the fetal heart and myocardium, compared with intraventricular injection.

1. Wapner RJ, *et al.* Selective reduction of multifetal pregnancies. *Lancet* 1990; **335:** 90–3.
2. Berkowitz RL, *et al.* The current status of multifetal pregnancy reduction. *Am J Obstet Gynecol* 1996; **174:** 1265–72.
3. De Catte L, Foulon W. Obstetric outcome after fetal reduction to singleton pregnancies. *Prenat Diagn* 2002; **22:** 206–10.
4. Bhide A, *et al.* Comparison of feticide carried out by cordocentesis versus cardiac puncture. *Ultrasound Obstet Gynecol* 2002; **20:** 230–2.

Preparations

BP 2008: Bumetanide and Prolonged-release Potassium Tablets; Effervescent Potassium Chloride Tablets; Potassium Chloride and Glucose Intravenous Infusion; Potassium Chloride and Sodium Chloride Intravenous Infusion; Potassium Chloride Oral Solution; Potassium Chloride, Sodium Chloride and Glucose Intravenous Infusion; Prolonged-release Potassium Chloride Tablets; Sterile Potassium Chloride Concentrate;
USP 31: Half-strength Lactated Ringer's and Dextrose Injection; Lactated Ringer's and Dextrose Injection; Lactated Ringer's Injection; Potassium Ace-

tate Injection; Potassium Bicarbonate and Potassium Chloride Effervescent Tablets for Oral Solution; Potassium Bicarbonate and Potassium Chloride for Effervescent Oral Solution; Potassium Chloride Extended-release Capsules; Potassium Chloride Extended-release Tablets; Potassium Chloride for Injection Concentrate; Potassium Chloride for Oral Solution; Potassium Chloride in Dextrose and Sodium Chloride Injection; Potassium Chloride in Dextrose Injection; Potassium Chloride in Lactated Ringer's and Dextrose Injection; Potassium Chloride in Sodium Chloride Injection; Potassium Chloride Oral Solution; Potassium Chloride, Potassium Bicarbonate, and Potassium Citrate Effervescent Tablets for Oral Solution; Potassium Gluconate and Potassium Chloride for Oral Solution; Potassium Gluconate and Potassium Chloride Oral Solution; Potassium Gluconate and Potassium Citrate Oral Solution; Potassium Gluconate Elixir; Potassium Gluconate Tablets; Potassium Gluconate, Potassium Citrate, and Ammonium Chloride Oral Solution; Trikates Oral Solution.

Proprietary Preparations (details are given in Part 3)
Arg.: Co-Salt; Control K; Gluco-K; Kaon; Orakit; QBE Elixir†; ***Austral.:*** Celloids PC 73; Celloids PS 29; Chlorvescent; Duro-K; KSR†; Slow-K; Span-K; ***Austria:*** KCl-retard; Micro-Kalium; ***Belg.:*** Chloropotassuril; Kali-Steropˆ†; Kalium Durettes†; Steropotassium; Ultra-K; ***Braz.:*** Clotassio; Decorfen; ***Canad.:*** Apo-K; K-10; K-Dur; K-Lor†; K-Lyte/Cl; Kaon†; Micro-K; Potassium-Rougier†; Proflavanol C; Roychlor†; Slow-K; ***Chile:*** Kaion Retard; Sal Dietetica; Slow-K; Yonka; ***Cz.:*** Kaldyum; Kalnormin; Spofalyt-Kalium†; ***Denm.:*** Kaleorid; ***Fin.:*** Durekal; Kalinorm; Kalisol; Kalisteril†; ***Fr.:*** Diffu-K; Kaleorid; Nati-K; ***Ger.:*** Kalinor-retard P; Kalium-Duriles†; Kalium†; KCl-retard; Rekawan; ***Gr.:*** Sopa-K; ***Hong Kong:*** Addi-K†; Apo-K; Kalium†; KSR; Slow-K; Span-K; ***Hung.:*** Kaldyum; Kalium Durules; Kalium-R; ***India:*** Diucontin-K; Keylyte; Potklor; ***Irl.:*** Kay-Cee-L; Slow-K; ***Israel:*** Slow-K; ***Ital.:*** K-Flebo; Kadalex; Lento-Kalium; ***Malaysia:*** Apo-K; Beacon K; KSR†; Slow-K; ***Mex.:*** Ceposil; Clor-K-Zaf; Corpotasin GK; Corpotasin LP; K-Dur; Kaliolite; Kaselé†; Kelefusin; Potasoral; ***Neth.:*** Kalium Durettes†; Slow-K; ***Norw.:*** Kaleorid; ***NZ:*** Chlorvescent; K-SR†; Slow-K; Span-K; ***Philipp.:*** Ion-O-Trate; Kalium; ***Pol.:*** Kaldyum; Kalimat; Kalipoz; ***S.Afr.:*** Micro-K; Plenish-K; Sandoz K; Slow-K; Swiss-Kal SR†; ***Singapore:*** Addi-K†; Apo-K; KSR†; ***Spain:*** AP Inyect Cloruro Potasico; Boi K; Boi K Aspartico; Boi K Gluconato; Potasion; Potasion Solucion; ***Swed.:*** Kaleorid†; Kalitabs; Kalium Duretter†; Kalium Retard; ***Switz.:*** Kaliglutol; Plus Kalium retard; ***Thai.:*** Addi-K; Enpott; Kaliject; Potassride; ***Turk.:*** Kadaleks; ***UK:*** Kay-Cee-L; Slow-K; ***USA:*** Cena-K; Gen-K; K + 10; K + 8†; K-Dur; K-G Elixir; K-Lease†; K-Lor; K-Lyte/Cl; K-Norm†; K-Tab; Kaon; Kaon-Cl; Kay Ciel; Klor-Con; Klorvess; Klotrix; Micro-K; Potasalan; Rum-K†; Slow-K†; Ten-K; ***Venez.:*** Kaon†; Konat†.

Multi-ingredient: ***Arg.:*** Dialitica II; Potasio C; Water Pill c Potasio†; ***Austral.:*** Aspartatol; Cardioplegia A; Cardioplegia Concentrate; Digestaid; Duo Celloids PCCP; Duo Celloids PCIP; Duo Celloids PCMP; Duo Celloids PSMP; Duo Celloids PSPC; Duo Celloids SPPC; Duo Celloids SPPS; Duo Celloids SSPC; Extralife Uri-Care; Iron Compound†; K-Mag†; Kali Mag†; Mag-Oro; Potasi; Silicic Complex†; ***Austria:*** Centramin; Corozell; Elozell; Elozell spezial; Gladixol; Maycardin K; Trommcardin; ***Braz.:*** Albicon; Furosemide Composto; Hidrion; ***Canad.:*** Uracyst Test Kit; ***Chile:*** Sal Lite; Sal Liviana En Sodio; ***Cz.:*** Acidigen†; Avinl H†; Cardilan; Solutio Thomas cum Procaino; Tromcardin; ***Denm.:*** Burinex med kaliumklorid; Centyl med Kaliumklorid; ***Fin.:*** Miral; ***Fr.:*** Decramp; Rhinodoron; ***Ger.:*** Ardeycordal N†; Bascardial†; Cardio-Kreislauf-Longoral; Chinosol; Cordesin; Galacordin; Kalium-Magnesium†; Magium K; Movicard; Rhinodoron; Septacord; Tromcardin; Trophicard; ***Gr.:*** Cardioplegia; ***Hong Kong:*** Cardioplegia; ***Hung.:*** Acidigen†; Aspacardin†; Panangin; Tromcardin; ***India:*** Cotaryl; ***Indon.:*** Cardioplegia; Totilac; ***Irl.:*** Burinex K†; Centyl K; Diumide-K Continus; Low Centyl K; ***Israel:*** Lyteers; ***Ital.:*** Briovitase; Polase; Pomag; Potassion; Potassium MG†; ***Malaysia:*** Burinex K†; Cardioplegia; Pot-Citra; ***Mex.:*** Corpotasin CL; Forcremol; Kaposalt; ***Norw.:*** Burinex K; Centyl med Kaliumklorid; ***Philipp.:*** Diumide-K; ***Pol.:*** Aspargin; Magne-Balans Plus; Magnokal; Sal Ems Artificiale; Sal Ems Factitium; ***Port.:*** Miostenil; Polase; Safrux; ***Rus.:*** Panangin (Панангин); Triresid K (Трирезид К); ***S.Afr.:*** Burinex K; Kloref; Lenurex-K; Urirex-K; ***Singapore:*** Burinex K; Cardioplegia; ***Spain:*** Acetuber; Glucopotasico; Leberetic; Potasico; Salcedol; Suero Potassico Bieffe ME†; ***Swed.:*** Centyl K; Salures-K; ***Thai.:*** Cardioplegia; ***Turk.:*** Kadeks; Sensodyne-F; ***UK:*** Burinex K†; Centyl K; Kloref; Lasikal; Neo-NaClex-K; Sando-K; Sensodyne-F; ***USA:*** Chlor-3; K-Lyte/Cl; Klorvess; Slo-Salt-K†; Temp Tab; Tri-K; Twin-K†.

Sodium

Natrium; Sód; Sodio.
Na = 22.98976928.

Description. Sodium chloride is the principal sodium salt used as a source of sodium ions. Sodium salts used chiefly as sources of bicarbonate ions, such as the acetate, bicarbonate, citrate, and lactate, are covered under Bicarbonate, p.1673. Phosphate salts of sodium are covered under Phosphate, p.1682.

Sodium Chloride

Chlorid sodný; Chlorure de Sodium; Cloreto de Sódio; Natrii chloridum; Natrio chloridas; Natriumklorid; Nátrium-klorid; Natriumkloridi; Salt; Sodio, cloruro de; Sodium, chlorure de; Sodu chlorek; Sodyum Klorür.

NaCl = 58.44.
CAS — 7647-14-5.
ATC — A12CA01; B05CB01; B05XA03.
ATC Vet — QA12CA01; QB05CB01; QB05XA03.

NOTE. An aqueous solution of sodium chloride 0.9% is often known as physiological saline.
SALINE is a code approved by the BP 2008 for use on single unit doses of eye drops containing sodium chloride 0.9% where the individual container may be too small to bear all the appropriate labelling information. HECL is a similar code approved for hyetellose and sodium chloride eye drops.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*
Ph. Eur. 6.2 (Sodium Chloride). A white or almost white, crystalline powder or colourless crystals or white or almost white pearls. Freely soluble in water; practically insoluble in dehydrated alcohol.
USP 31 (Sodium Chloride). Colourless cubic crystals or white crystalline powder. Soluble 1 in 2.8 of water, 1 in 2.7 of boiling water, and 1 in 10 of glycerol; slightly soluble in alcohol.

Equivalence. Each g of sodium chloride represents about 17.1 mmol of sodium and of chloride. Sodium chloride 2.54 g is equivalent to about 1 g of sodium.

Storage. Solutions of some sodium salts, including sodium chloride, when stored, may cause separation of solid particles from glass containers and solutions containing such particles must not be used.

Adverse Effects

Adverse effects of sodium salts are attributable to electrolyte imbalances from excess sodium; there may also be effects due to the specific anion.

Retention of excess sodium in the body usually occurs when there is defective renal sodium excretion. This leads to the accumulation of extracellular fluid to maintain normal plasma osmolality, which may result in pulmonary and peripheral oedema and their consequent effects.

Hypernatraemia (a rise in plasma osmolality) is usually associated with inadequate water intake, or excessive water losses (see p.1670). It rarely occurs after therapeutic doses of sodium chloride, but has occurred with the use of hypertonic saline for induction of emesis or for gastric lavage and after errors in the formulation of infant feeds. Hypernatraemia may also occur after inappropriate intravenous use of hypertonic saline.

The most serious effect of hypernatraemia is dehydration of the brain which causes somnolence and confusion progressing to convulsions, coma, respiratory failure, and death. Other symptoms include thirst, reduced salivation and lachrymation, fever, sweating, tachycardia, hypertension or hypotension, headache, dizziness, restlessness, irritability, weakness, and muscular twitching and rigidity.

Gastrointestinal effects associated with acute oral ingestion of hypertonic solutions or excessive amounts of sodium chloride include nausea, vomiting, diarrhoea, and abdominal cramps.

Excessive use of chloride salts may cause a loss of bicarbonate with an acidifying effect.

Intra-amniotic injection of hypertonic solutions of sodium chloride, which has been used for termination of pregnancy, has been associated with serious adverse effects including disseminated intravascular coagulation, renal necrosis, cervical and uterine lesions, haemorrhage, pulmonary embolism, pneumonia, and death.

◊ General references.

1. Moder KG, Hurley DL. Fatal hypernatremia from exogenous salt intake: report of a case and review of the literature. *Mayo Clin Proc* 1990; **65:** 1587–94. Correction. *ibid.* 1991; **66:** 439.
2. Martos Sánchez I, *et al.* Hipernatremia grave por administración accidental de sal común. *An Esp Pediatr* 2000; **53:** 495–8.
3. Adeleye O, *et al.* Hypernatremia in the elderly. *J Natl Med Assoc* 2002; **94:** 701–5.
4. Coulthard MG, Haycock GB. Distinguishing between salt poisoning and hypernatraemic dehydration in children. *BMJ* 2003; **326:** 157–60. Correction. *ibid.*; 497.

Treatment of Adverse Effects

In patients with mild sodium excess, drinking water and restricting sodium intake is sufficient. However, in the event of recent acute oral overdose of sodium chloride, gastric lavage should be carried out along with general symptomatic and supportive treatment. Serum-sodium concentrations should be measured, and if severe hypernatraemia is present this should be treated (see p.1670).

Precautions

Sodium salts should be used with caution in patients with hypertension, heart failure, peripheral or pulmonary oedema, renal impairment, pre-eclampsia, or other conditions associated with sodium retention.

When sodium supplements are given orally, adequate water intake should be maintained. Sustained-release tablets should not be given to patients with gastrointestinal disorders associated with strictures or diverticula because of the risk of obstruction.

Sodium chloride solutions should *not* be used to induce emesis; this practice is dangerous and deaths from resulting hypernatraemia have been reported.

Pharmacokinetics

Sodium chloride is well absorbed from the gastrointestinal tract. Excess sodium is mainly excreted by the kidney, and small amounts are lost in the faeces and sweat.

Human Requirements

The body contains about 4 mol (92 g) of sodium of which about one-third is found in the skeleton and about half is present in the extracellular fluid.

The body can adapt to a wide range of intakes by adjustment of renal excretion through physical and hormonal factors. Loss through the skin is significant only if excessive sweating occurs. Sodium requirements may be increased with exercise or exposure to high ambient temperatures in the short term, until the body adjusts.

Sodium is widely available in foods and is also added as salt during processing, cooking, and at the table. Dietary deficiency of sodium is therefore extremely rare and more concern has been expressed that current intakes are excessive. Restriction of sodium intake, by limiting the amount of culinary salt consumed, may be a useful aid in the management of some patients with hypertension (p.1171).

UK and US recommended dietary intake. In the UK dietary reference values (DRV—see Human Requirements, p.1925)[1] have been published for sodium. The reference nutrient intake (RNI) for adults is 1.6 g of sodium (70 mmol) daily, which is about 4 g of sodium chloride. In the USA, it has been recommended that daily intakes of sodium be limited to 2.4 g (6 g of sodium chloride) or less.[2] Dietary intake is often in excess of these recommendations, and may be a factor in essential hypertension,[3] and osteoporosis.[4]

1. DoH. Dietary reference values for food energy and nutrients for the United Kingdom: report of the panel on dietary reference values of the committee on medical aspects of food policy. *Report on health and social subjects 41*. London: HMSO, 1991.
2. Subcommittee on the tenth edition of the RDAs, Food and Nutrition Board, Commission on Life Sciences, National Research Council. *Recommended dietary allowances*. 10th ed. Washington, DC: National Academy Press, 1989. Also available at: http://www.nap.edu/openbook.php?isbn=0309046335 (accessed 21/07/08)
3. Midgley JP, *et al.* Effect of reduced dietary sodium on blood pressure: a meta-analysis of randomized controlled trials. *JAMA* 1996; **275:** 1590–7.
4. Devine A, *et al.* A longitudinal study of the effect of sodium and calcium intakes on regional bone density in postmenopausal women. *Am J Clin Nutr* 1995; **62:** 740–5.

Uses and Administration

Sodium chloride is used in the management of deficiencies of sodium and chloride ions in salt-losing conditions (see Hyponatraemia, p.1670). Sodium chloride solutions are used as a source of sodium chloride and water for hydration.

A 0.9% solution in water is iso-osmotic, and thus in most cases isotonic with serum and lachrymal secretions. Doses may be expressed in terms of mEq or mmol of sodium, mass (mg) of sodium, or mass of sodium salt. For comparative purposes, see Table 4, below.

A typical oral replacement dose of sodium chloride in **chronic salt-losing conditions** is about 2.4 to 4.8 g (about 40 to 80 mmol of sodium) daily as a modified-release preparation, accompanied by a suitable fluid intake; doses of up to 12 g daily may be necessary in

Table 4. Some sodium salts and their sodium content.

	Sodium content per g		
Sodium salt	mg	mmol	mEq
Sodium acetate (anhydrous)	280	12.2	12.2
Sodium acetate (trihydrate)	169	7.3	7.3
Sodium acid citrate	175	7.6	7.6
Sodium bicarbonate	274	11.9	11.9
Sodium chloride	394	17.1	17.1
Sodium citrate (anhydrous)	267	11.6	11.6
Sodium citrate (dihydrate)	235	10.2	10.2
Sodium lactate	205	8.9	8.9