16. American College of Obstetricians and Gynecologists Committee on Practice Bulletins. Management of preterm labor (ACOG Practice Bulletin number 43, May 2003). *Obstet Gynecol* 2003; **101:** 1039–47.
17. Di Renzo GC, Roura LC. European Association of Perinatal Medicine-Study Group on Preterm Birth. Guidelines for the management of spontaneous preterm labor. *J Perinat Med* 2006; **34:** 359–66. Also available at: http://www.reference-global.com/doi/pdfplus/10.1515/JPM.2006.073 (accessed 02/07/08)
18. Grimes DA, Nanda K. Magnesium sulfate tocolysis: time to quit. *Obstet Gynecol* 2006; **108:** 986–9.
19. Simhan HN, Caritis SN. Prevention of preterm delivery. *N Engl J Med* 2007; **357:** 477–87.

Pulmonary hypertension of the newborn. Preliminary studies have suggested that intravenous magnesium sulfate may be effective in treating persistent pulmonary hypertension of the newborn, as mentioned on p.1179.

Respiratory disorders. Magnesium sulfate, given intravenously over 20 minutes in doses of 1.2 g to patients with acute exacerbations of chronic obstructive pulmonary disease (p.1112) who had received inhaled salbutamol, appeared to have moderate efficacy.[1]

Infusion of magnesium has been reported to be of benefit in some patients with acute asthma (p.1108), but results have been conflicting;[2-5] meta-analyses of these and other studies concluded that its routine use was not justified, but that it may benefit some patients with severe exacerbations.[6,7] A meta-analysis of 5 studies in children concluded that intravenous magnesium sulfate is likely to be an effective adjunct to standard therapy in the symptomatic treatment of moderate to severe acute childhood asthma.[8] Inhalation of magnesium has also been investigated, either alone or with salbutamol; another meta-analysis considered that it improved pulmonary function, particularly in combination with a beta$_2$ agonist, with the best results seen in more severe cases.[9]

1. Skorodin MS, *et al.* Magnesium sulfate in exacerbations of chronic obstructive pulmonary disease. *Arch Intern Med* 1995; **155:** 496–500.
2. Skobeloff EM, *et al.* Intravenous magnesium sulfate for the treatment of acute asthma in the emergency department. *JAMA* 1989; **262:** 1210–13.
3. Green SM, Rothrack SG. Intravenous magnesium for acute asthma: failure to decrease emergency treatment duration or need for hospitalization. *Ann Emerg Med* 1992; **21:** 260–5.
4. Ciarallo L, *et al.* Intravenous magnesium therapy for moderate to severe pediatric asthma: results of a randomized, placebo-controlled trial. *J Pediatr* 1996; **129:** 809–14.
5. Silverman RA, *et al.* IV magnesium sulfate in the treatment of acute severe asthma: a multicenter randomized controlled trial. *Chest* 2002; **122:** 489–97.
6. Rowe BH, *et al.* Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2000 (accessed 21/06/05).
7. Alter HJ, *et al.* Intravenous magnesium as an adjuvant in acute bronchospasm: a meta-analysis. *Ann Emerg Med* 2000; **36:** 191–7.
8. Cheuk DKL, *et al.* A meta-analysis on intravenous magnesium sulphate for treating acute asthma. *Arch Dis Child* 2005; **90:** 74–7.
9. Blitz M, *et al.* Inhaled magnesium sulfate in the treatment of acute asthma. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2005 (accessed 18/12/07).

Stroke. Intravenous magnesium sulfate has been investigated for a neuroprotective effect in stroke (p.1185), but results have been largely disappointing.[1]

1. Intravenous Magnesium Efficacy in Stroke (IMAGES) Study Investigators. Magnesium for acute stroke (Intravenous Magnesium efficacy in Stroke trial): randomised controlled trial. *Lancet* 2004; **363:** 439–45.

Tetanus. Magnesium sulfate has been found to minimise autonomic disturbance in ventilated patients and control spasms in non-ventilated patients when used in the treatment of tetanus (p.1901).

References.

1. Attygalle D, Rodrigo N. Magnesium as first line therapy in the management of tetanus: a prospective study of 40 patients. *Anaesthesia* 2002; **57:** 811–17.
2. William S. Use of magnesium to treat tetanus. *Br J Anaesth* 2002; **88:** 152–3.

Preparations

BP 2008: Magnesium Chloride Injection; Magnesium Sulphate Injection; Magnesium Sulphate Mixture; Magnesium Sulphate Paste;
USP 31: Magnesium Gluconate Tablets; Magnesium Sulfate in Dextrose Injection; Magnesium Sulfate Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Biomag; Magnebe; Magnesoide†; ***Austral.:*** Celloids MP 65; Mag 50†; Magmin; ***Austria:*** Cormagnesin; Emgecard; FX Passage; Magium; Magnesium Diasporal; Magnesulf; Magvital; Mg 5-Longoral; Solumag; Ultra-Mag; ***Belg.:*** Magnespasmyl; Ultra-Mg; ***Braz.:*** Mag-Tab; Magnolat†; Magnoston; Pidomag; Sal Amargo Purificado; ***Canad.:*** Maglucate; Magnolex; Magnorol; Proflavanol C; Slow-Mag†; ***Chile:*** Mag-Tab; ***Cz.:*** Coradol†; Cormagnesin†; Magnerot; Magnesium Diasporal†; Mg 5-Granulat†; Mg 5-Longoral†; ***Fr.:*** Efimag†; Ionimag†; Mag 2; Magnespasmyl; Magnogene; Megamag; Solumag†; Spasmag; Top-Mag; Vivamag†; ***Ger.:*** Basti-Mag; Cormagnesin; FX Passage; Magium; Magnaspart; Magnerot; Magnerot A; magnerot Classic; Magnesiocard; Magnesium Diasporal; Magnesium Verla; Magnesium Verla N; Magnesorot; metamagnesol†; Mg 5-Granulat†; Mg 5-Longoral; Mg 5-Sulfat; Mgnor; Nourymag†; Power Orot; Retterspitz Darmreinigungspulver ST; ***Gr.:*** Mag 2; Solumag; Trofocard; ***Hung.:*** Astat†; Cormagnesin; Magnerot; Magnesiocard; ***India:*** Mag; ***Irl.:*** Magnesium Verla; ***Ital.:*** Actimag†; Mag 2; MG 50; Olimag†; Solumag; ***Mex.:*** Conducat†; Ifupeptol Magnesiado; Magnefusin†; ***Pol.:*** Asmag; Biomag; Laktomag; Laktomag B ; Magnefar; Slow-Mag; ***Port.:*** Cormagnesin; Magnesiocard; Magnesona; Magnespasmil; Magnoral; Metabol-Mg; ***Rus.:*** Cormagnesin (Кормагнезин); Magnerot (Магнерот); ***S.Afr.:*** Be-Lax; Magnesit; SB Laxative Mixture; Slow-Mag; ***Spain:*** Actimag; Magnesioboi; Sulmetin†; ***Switz.:*** Mag 2; Mag-Min; Magnegon; Magnesiocard; Magnesium Biomed; Magnesium Vital; Magnesium-Sandoz; Magnespasmyl†; Magnogene; Mg 5-Granoral; Mg 5-Longoral; Mg 5-Oraleff; Mg 5-Sulfat; Solmag†; ***UK:*** Kest; ***USA:*** Almora†; Chloromag: Mag-G; Mag-SR; Mag-Tab; Magtrate; Slow-Mag.

Multi-ingredient: ***Arg.:*** Anartrit; Antikatarata†; Drenocol†; Magnesia Phosphorica I Oligoplex; Magnesio Incaico; Mylanta Extra; Nervigenol Magnesio†; Noacid Diates; Sigmafem; Sigmaflex; Total Magnesiano con Ginseng; Veraldid; ***Austral.:*** Aspartatol; Bio Magnesium; Bioglan Bioage Peripheral; Caprilate; Cardioplegia A; Cardioplegia Concentrate; Celloid Compounds Magcal Plus; Chelated Cal-Mag; Citri Slim+Trim; Duo Celloids CPMP; Duo Celloids PCMP; Duo Celloids PPMP; Duo Celloids PSMP; Duo Celloids SPMP; Duo Celloids SSMP; Extralife Migrai-Care; Extralife Sleep-Care; K-Mag†; Kali Mag†; Machlor; Mag-Oro; Magnesium Plus†; Magnoplasm; ML 20†; Pro-Shape†; Salvital; Zinvit; Zinvit C; Zinvit G; ***Austria:*** Cascara-Salax; Centramin; Corozell; Elozell; Elozell spezial; Gladixol; Illings Bozner Maycur-Tee†; Mag Kottas May-Cur-Tee; Maycardin K; Trommcardin; Trommgallol; ***Braz.:*** Alcafelol†; Sal de Andrews; ***Canad.:*** Osmopak-Plus; ***Chile:*** Cholinogo; ***Cz.:*** Acne Lotio†; Cardilan; Magne-B ; Solutio Thomas cum Procaino; Tromcardin; ***Fin.:*** Wicnelact; ***Fr.:*** Biopause; Cataridol†; Cemaflavone; Chloro-Magnesion†; Cristopal†; Decramp; Delbiase†; Ionyl; Kaologeais; Karayal; Magne-B ; Osmogel; Phosphoneuros; Prefagyl†; Revitalose; Spasmag; Supro; Thalgo Tonic; Tryptonat; Uvimag B ; ***Ger.:*** Ardeycordal N†; Bascardial†; Biomagnesin; Cardio-Kreislauf-Longoral; Cardioplegin N†; Cordesin; Galacordin; Geo-magnit†; Kalium-Magnesium†; Lacoerdin Mg Plus†; Magium K; Magnerot N; Magnesium compositum†; Movicard; rohasal†; Scordal†; Septacord; Tromcardin; Trophicard; ***Gr.:*** Cardioplegia; Magnesium Sandoz; ***Hong Kong:*** Cardioplegia; Osteocare; ***Hung.:*** Aspacardin†; Magne-B ; Osteocare; Panangin; Tromcardin; Vition; ***India:*** Calcinol; Cotaryl; ***Indon.:*** Cardioplegia; Osteocare; ***Irl.:*** Andrews; Bio-Calcium + D ; ***Ital.:*** Briovitase; Calmason; Fertomcidina-U; Fisioreve; Hiperogyn; Polase; Reocol†; Sedofit; Vagostabil; ***Malaysia:*** Adult Citrex Cal-Mag-D3; Cardioplegia; Junior Citrex Cal-Mag-D3; ***Mex.:*** Chofabol; Cidetox; Dicentril; Gavicid†; Hepedren; Peptocholʼ†; Ulgel; ***Philipp.:*** Osteocare; ***Pol.:*** Aspargin; Bemag; Filomag B ; Maglek B ; Magne-B ; Magne-Balans Plus; Magnefar B ; Magnezytki; Magnokal; Magsolvit B ; Magvit B ; Osteogel; Slow-Mag B ; Wamag; ***Port.:*** Actilam; Miostenil; Polase; ***Rus.:*** Magne B6 (Магне В6); Panangin (Панангин); ***S.Afr.:*** Phytopause BSF; Ultimag; ***Singapore:*** Cardioplegia; Vita Calmag Zn†; ***Spain:*** Darmen Salt; Depurativo Richelet; Eupeptina; Lebersal; Magnesium Pyre; Magnogene; Salmagne; Sugarbil; Sulmetin Papaver; Sulmetin Papaverina†; ***Switz.:*** Acne Lotion; Activital Forte; Kawaform†; Klyx Magnum; Magnesium Complexe; Siesta-1; Vigoran†; ***Thai.:*** Calcioday-D†; Cardioplegia; ***Turk.:*** Osteocare; ***UK:*** Andrews; Pegna; ***USA:*** Chlor-3; Mag-Cal Mega; Mag-SR plus Calcium; Magonate; ***Venez.:*** Calcinor D; Fugras; Kalsis.

Phosphate

Fosfato.

Description. Phosphate is an anion given as various potassium or sodium salts.

Incompatibility. Phosphates are incompatible with calcium salts; the mixing of calcium and phosphate salts can lead to the formation of insoluble calcium-phosphate precipitates. Incompatibility has also been reported with magnesium salts.

Monobasic Potassium Phosphate

Dihydrogenfosforečnan draselný; E340; Kalii dihydrogenophosphas; Kalio-divandenilio fosfatas; Kálium-dihidrogén-foszfát; Kaliumdivätefosfat; Kaliumdivetyfosfaatti; Monopotassium Phosphate; Phosphate monopotassique; Potasio, dihidrogenofosfato de; Potassium Acid Phosphate; Potassium Biphosphate; Potassium Dihydrogen Phosphate; Potasu diwodorofosforan. Potassium dihydrogen orthophosphate.

KH_2PO_4 = 136.1.
CAS — 7778-77-0.

Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF.*
Ph. Eur. 6.2 (Potassium Dihydrogen Phosphate). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; practically insoluble in alcohol. A 5% solution in water has a pH of 4.2 to 4.5.
USNF 26 (Monobasic Potassium Phosphate). Colourless crystals or a white granular or crystalline powder. Is odourless. Freely soluble in water; practically insoluble in alcohol. pH of a 1% solution in water is about 4.5. Store in airtight containers.

Equivalence. Each g of monobasic potassium phosphate represents about 7.3 mmol of potassium and of phosphate.

Dibasic Potassium Phosphate

Dikalii phosphas; Dikalio fosfatas; Dikaliumfosfaatti; Dikaliumfosfat; Dikálium-hidrogén-foszfát; Dipotasio, hidrogenofosfato de; Dipotassium Hydrogen Phosphate; Dipotassium Phosphate; Dipotasu wodorofosforan; E340; Hydrogenofosforečnan draselný; Kalii Hydrogenophosphas; Phosphate dipotassique; Potassium Phosphate. Dipotassium hydrogen orthophosphate.

K_2HPO_4 = 174.2.
CAS — 7758-11-4.

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
Ph. Eur. 6.2 (Dipotassium Phosphate; Dipotassium Hydrogen Phosphate BP 2008). A very hygroscopic, white or almost white powder or colourless crystals. Very soluble in water; very slightly soluble in alcohol. Store in airtight containers.
USP 31 (Dibasic Potassium Phosphate). Colourless or white, somewhat hygroscopic, granular powder. Freely soluble in water; very slightly soluble in alcohol. pH of a 5% solution in water is between 8.5 and 9.6.

Equivalence. Each g of dibasic potassium phosphate represents about 11.5 mmol of potassium and 5.7 mmol of phosphate.

Monobasic Sodium Phosphate

Dihydrogenfosforečnan sodný; E339; Monobazik Sodyum Fosfat; Natrii dihydrogenophosphas; Natrio-divandenilio fosfatas; Natrium Phosphoricum Monobasicum; Nátrium-dihidrogén-foszfát; Natriumdivätefosfat; Natriumdivetyfosfaatti; Phosphate monosodique; Sodio, dihidrogenofosfato de; Sodium Acid Phosphate; Sodium Biphosphate; Sodium Dihydrogen Phosphate; Sodu diwodorofosforan; Sodyum Dihidrojen Fosfat. Sodium dihydrogen orthophosphate.

$NaH_2PO_4.xH_2O$.
CAS — 7558-80-7 (anhydrous monobasic sodium phosphate); 10049-21-5 (monobasic sodium phosphate monohydrate); 13472-35-0 (monobasic sodium phosphate dihydrate).
ATC — A06AD17; A06AG01.
ATC Vet — QA06AD17; QA06AG01.

Pharmacopoeias. In *Eur.* (see p.vii) (with $2H_2O$); in *Chin.* (with $1H_2O$). *Br.* also includes monographs for the anhydrous and monohydrate forms. *US* permits the anhydrous, monohydrate, and dihydrate forms.
Ph. Eur. 6.2 (Sodium Dihydrogen Phosphate Dihydrate; Natrii Dihydrogenophosphas Dihydricus). A white or almost white powder or colourless crystals. Very soluble in water; very slightly soluble in alcohol. A 5% solution in water has a pH of 4.2 to 4.5.
The BP 2008 gives Sodium Acid Phosphate as an approved synonym.
BP 2008 (Anhydrous Sodium Dihydrogen Phosphate). A white, slightly deliquescent, crystals or granules. Very soluble in water; very slightly soluble in alcohol. A 5% solution in water has a pH of 4.2 to 4.5.
BP 2008 (Sodium Dihydrogen Phosphate Monohydrate). A white powder or colourless crystals. Very soluble in water; very slightly soluble in alcohol. A 5% solution in water has a pH of 4.2 to 4.5.
USP 31 (Monobasic Sodium Phosphate). It contains one or two molecules of water of hydration, or is anhydrous. Colourless crystals or white crystalline powder. Is odourless and is slightly deliquescent. Freely soluble in water; practically insoluble in alcohol. Its solutions are acid to litmus and effervesce with sodium carbonate. pH of a 5% solution in water of the monohydrate form is between 4.1 and 4.5.

Equivalence. Each g of monobasic sodium phosphate (anhydrous) represents about 8.3 mmol of sodium and of phosphate. Each g of monobasic sodium phosphate (monohydrate) represents about 7.2 mmol of sodium and of phosphate. Each g of monobasic sodium phosphate (dihydrate) represents about 6.4 mmol of sodium and of phosphate.

Dibasic Sodium Phosphate

Dibazik Sodyum Hidrojen Fosfat; Dinatrii phosphas; Dinatrio fosfatas; Dinatriumfosfaatti; Dinatriumfosfat; Dinátrium-hidrogén-foszfát; Disodio, hidrogenofosfato de; Disodium Hydrogen Phosphate; Disodium Phosphate; Disodu fosforan; Disodu wodorofosforan; Disodyum Hidrojen Fosfat; E339; Hydrogenofosforečnan sodný; Natrii Hydrogenophosphas; Natrii Phosphas; Natrii Phosphatis; Natriumfosfaatti; Natriumfosfat; Phosphate disodique; Sodium Phosphate. Disodium hydrogen orthophosphate.

$Na_2HPO_4.xH_2O$.
CAS — 7558-79-4 (anhydrous dibasic sodium phosphate); 10028-24-7 (dibasic sodium phosphate dihydrate); 7782-85-6 (dibasic sodium phosphate heptahydrate); 10039-32-4 (dibasic sodium phosphate dodecahydrate).
ATC — A06AD17; A06AG01; B05XA09.
ATC Vet — QA06AD17; QA06AG01; QB05XA09.

Pharmacopoeias. In *Eur.* (see p.vii), *Jpn,* and *US.* The pharmacopoeias may specify one or more states of hydration; monographs and specifications can be found for the anhydrous form (Na_2HPO_4 = 142.0), the dihydrate ($Na_2HPO_4.2H_2O$ = 178.0), the heptahydrate ($Na_2HPO_4.7H_2O$ = 268.1), and the dodecahydrate ($Na_2HPO_4.12H_2O$ = 358.1), although not necessarily all will be found in any one pharmacopoeia.
Ph. Eur. 6.2 (Disodium Phosphate, Anhydrous; Dinatrii Phosphas Anhydricus; Anhydrous Disodium Hydrogen Phosphate BP 2008). A white or almost white, hygroscopic powder. Soluble in water; practically insoluble in alcohol. A 5% solution in water is slightly alkaline. Store in airtight containers.
Ph. Eur. 6.2 (Disodium Phosphate Dihydrate; Dinatrii Phosphas Dihydricus; Disodium Hydrogen Phosphate Dihydrate BP 2008). A white or almost white powder or colourless crystals. Soluble in water; practically insoluble in alcohol. A 5% solution in water is slightly alkaline.
The BP 2008 gives Sodium Phosphate Dihydrate as an approved synonym.
Ph. Eur. 6.2 (Disodium Phosphate Dodecahydrate; Dinatrii Phosphas Dodecahydricus; Disodium Hydrogen Phosphate Dodecahydrate BP 2008). Colourless, transparent, very efflorescent crystals. Very soluble in water; practically insoluble in alcohol. A 10% solution in water is slightly alkaline.

USP 31 (Dibasic Sodium Phosphate). It is dried, or contains one, two, seven, or twelve molecules of water of hydration.
The dried substance is a white powder that readily absorbs moisture. It is soluble 1 in 8 of water; insoluble in alcohol.
The heptahydrate is a colourless or white, granular or caked salt that effloresces in warm, dry air. It is freely soluble in water; very slightly soluble in alcohol. Its solutions are alkaline to phenolphthalein, a 0.1M solution having a pH of about 9.
Store all forms in airtight containers.

Equivalence. Each g of dibasic sodium phosphate (anhydrous) represents about 14.1 mmol of sodium and 7.0 mmol of phosphate. Each g of dibasic sodium phosphate (dihydrate) represents about 11.2 mmol of sodium and 5.6 mmol of phosphate. Each g of dibasic sodium phosphate (heptahydrate) represents about 7.5 mmol of sodium and 3.7 mmol of phosphate. Each g of dibasic sodium phosphate (dodecahydrate) represents about 5.6 mmol of sodium and 2.8 mmol of phosphate.

Tribasic Sodium Phosphate

E339; Sodio, fosfato de; Trisodium Orthophosphate; Trisodium Phosphate.

Na_3PO_4 = 163.9.
CAS — 7601-54-9.
ATC — A06AD17; A06AG01.
ATC Vet — QA06AD17; QA06AG01.

Pharmacopoeias. In *USNF*.
USNF 26 (Tribasic Sodium Phosphate). It is anhydrous or contains 1 to 12 molecules of water of hydration. White, odourless crystals or granules, or a crystalline powder. Freely soluble in water; insoluble in alcohol. pH of a 1% solution in water is between 11.5 and 12.0. Store in airtight containers.

Equivalence. Each g of tribasic sodium phosphate (anhydrous) represents about 18.3 mmol of sodium and 6.1 mmol of phosphate.

Adverse Effects and Treatment

Excessive doses of intravenous phosphate cause hyperphosphataemia, particularly in patients with renal failure. Hyperphosphataemia leads in turn to hypocalcaemia, which may be severe, and to ectopic calcification, particularly in patients with initial hypercalcaemia. Tissue calcification may cause hypotension and organ damage and result in acute renal failure. Hyperphosphataemia, hypocalcaemia, and tissue calcification are rare after oral or rectal doses (but see Effects on Electrolytes, and Effects on the Kidneys, below).

Adverse effects of oral phosphates may include nausea, vomiting, diarrhoea, and abdominal pain. When they are being used for indications other than their laxative effects, diarrhoea may necessitate a reduction in dosage. Sodium phosphates given rectally for bowel evacuation may cause local irritation.

Phosphates are given as the potassium or sodium salts or both, and may thus be associated with hyperkalaemia, and hypernatraemia and dehydration. Sodium phosphate may cause hypokalaemia.

Treatment of adverse effects involves withdrawal of phosphate, general supportive measures, and correction of serum-electrolyte concentrations, especially calcium. Measures to remove excess phosphate such as oral phosphate binders and haemodialysis may be required (see also Hyperphosphataemia, p.1669).

Effects on electrolytes. Although less common than after intravenous therapy, hyperphosphataemia, accompanied by hypocalcaemia or other severe electrolyte disturbances and resulting in tetany[1,2] and even death,[2] has been reported after the use of phosphate enemas. Similar effects have also been reported with the use of oral phosphate laxatives,[3-7] and in the USA, the FDA has issued warnings of the risk of electrolyte disturbances after the use of high oral doses of sodium phosphate, particularly in vulnerable patients.[8] Infants or children,[2,9,10] the elderly,[4,11] and those with renal impairment,[1,4,11] or congestive heart failure[4] have often had these adverse effects. Licensed product information for one oral sodium phosphate bowel cleanser (*Visicol; Salix, USA*) states that there have been reports of generalised tonic-clonic seizures and/or loss of consciousness in patients with no history of seizures; these cases were associated with electrolyte abnormalities, and low serum osmolality.

Hyperphosphataemia may precipitate nephrocalcinosis, causing an acute phosphate nephropathy, see Effects on the Kidneys, below.

1. Haskell LP. Hypocalcaemic tetany induced by hypertonic-phosphate enema. *Lancet* 1985; **ii:** 1433.
2. Martin RR, *et al.* Fatal poisoning from sodium phosphate enema: case report and experimental study. *JAMA* 1987; **257:** 2190–2.
3. Peixoto Filho AJ, Lassman MN. Severe hyperphosphatemia induced by a phosphate-containing oral laxative. *Ann Pharmacother* 1996; **30:** 141–3.
4. Adverse Drug Reactions Advisory Committee (ADRAC). Electrolyte disturbances with oral phosphate bowel preparations. *Aust Adverse Drug React Bull* 1997; **16:** 2. Also available at: http://www.tga.gov.au/adr/aadrb/aadr9702.htm (accessed 04/08/08)
5. Ullah N, *et al.* Fatal hyperphosphatemia from a phosphosoda bowel preparation. *J Clin Gastroenterol* 2002; **34:** 457–8.
6. Woo YM, *et al.* A life threatening complication after ingestion of sodium phosphate bowel preparation. *BMJ* 2006; **333:** 589–90.
7. Domico MB, *et al.* Severe hyperphosphatemia and hypocalcemic tetany after oral laxative administration in a 3-month-old infant. *Pediatrics* 2006; **118:** e1580–e1583. Also available at: http://pediatrics.aappublications.org/cgi/reprint/118/5/e1580 (accessed 13/12/06)
8. FDA. Safety of Sodium Phosphates Oral Solution (issued 17th September, 2001). Available at: http://www.fda.gov/cder/drug/safety/sodiumphospate.htm (accessed 18/05/04)
9. McCabe M, *et al.* Phosphate enemas in childhood: cause for concern. *BMJ* 1991; **302:** 1074.
10. Harrington L, Schuh S. Complications of Fleet enema administration and suggested guidelines for use in the pediatric emergency department. *Pediatr Emerg Care* 1997; **13:** 225–6.
11. Boivin MA, Kahn SR. Symptomatic hypocalcemia from oral sodium phosphate: a report of two cases. *Am J Gastroenterol* 1998; **93:** 2577–9.

Effects on the kidneys. Acute renal failure and nephrocalcinosis have been reported after the use of oral phosphate-based cathartics for bowel cleansing.[1,2] Although relatively rare with oral preparations, this acute phosphate nephropathy is a serious adverse effect; most patients were left with chronic renal insufficiency, and some developed end-stage renal disease. Potential contributing factors include inadequate hydration, increased age, a history of hypertension and arteriosclerosis, and concurrent use of ACE inhibitors, angiotensin receptor antagonists, diuretics, or NSAIDs.[2] The FDA has issued warnings[3] about the use of oral sodium phosphate products, especially in patients with impaired renal function, dehydration, or uncorrected electrolyte abnormalities, or in those taking drugs likely to contribute to the risk of nephropathy. The patient should be advised to take the correct dose of oral sodium phosphate, to drink sufficient liquid during bowel cleansing, and to avoid other phosphate-containing laxatives. Patients at increased risk should have their electrolytes and renal function monitored.

Nephrocalcinosis has also been reported in children with hypophosphataemic rickets treated with calcitriol and phosphate supplements; this was found to be associated with the phosphate dose.[4]

1. Desmeules S, *et al.* Acute phosphate nephropathy and renal failure. *N Engl J Med* 2003; **349:** 1006–7.
2. Markowitz GS, *et al.* Acute phosphate nephropathy following oral sodium phosphate bowel purgative: an underrecognized cause of chronic renal failure. *J Am Soc Nephrol* 2005; **16:** 3389–96.
3. FDA. Oral sodium phosphate products for bowel cleansing (issued May 2006). Available at: http://www.fda.gov/cder/drug/InfoSheets/HCP/OSP_solutionHCP.pdf (accessed 11/12/06)
4. Verge CF, *et al.* Effects of therapy in X-linked hypophosphatemic rickets. *N Engl J Med* 1991; **325:** 1843–8.

Local toxicity. Rectal gangrene has been associated with the use of phosphate enemas in elderly patients and was believed to be due to a direct necrotising effect of the phosphate on the rectum.[1]

1. Sweeney JL, *et al.* Rectal gangrene: a complication of phosphate enema. *Med J Aust* 1986; **144:** 374–5.

Precautions

Phosphates should not generally be given to patients with severe renal impairment. They should be avoided in patients who may have low serum-calcium concentrations, as these may decrease further, and in patients with infected phosphate renal calculi. Potassium phosphates should be avoided in patients with hyperkalaemia and sodium phosphates should generally be avoided in patients with congestive heart failure, hypertension, and oedema. Serum electrolytes and renal function should be monitored during therapy, particularly if phosphates are given parenterally.

Oral or rectal sodium phosphate preparations for bowel evacuation should not be used in patients with gastrointestinal obstruction, inflammatory bowel disease, and conditions where there is likely to be increased colonic absorption. They should be used cautiously in elderly and debilitated patients, and in those with pre-existing electrolyte disturbances (see Effects on Electrolytes, above).

Interactions

Oral phosphate supplements should not be used with aluminium, calcium, or magnesium salts as these will bind phosphate and reduce its absorption. Vitamin D increases the gastrointestinal absorption of phosphates and therefore increases the potential for hyperphosphataemia.

Hyperphosphataemia, hypocalcaemia, and hypernatraemia are more likely to occur with phosphate enemas or oral laxatives if these are given to patients receiving diuretics or other drugs that may affect serum electrolytes. The risk of ectopic calcification may be increased by concurrent use of calcium supplements or calcium-containing antacids.

The risk of hyperkalaemia is increased if potassium phosphates are given with drugs that can increase serum-potassium concentrations.

Pharmacokinetics

About two-thirds of ingested phosphate is absorbed from the gastrointestinal tract. Excess phosphate is mainly excreted in the urine, the remainder being excreted in the faeces.

◊ References.

1. Larson JE, *et al.* Laxative phosphate poisoning: pharmacokinetics of serum phosphorus. *Hum Toxicol* 1986; **5:** 45–9.

Human Requirements

Phosphorus requirements are usually regarded as equal to those of calcium.

Most foods contain adequate amounts of phosphate, particularly meat and dairy products, hence deficiency is virtually unknown except in certain disease states, in patients receiving total parenteral nutrition, or in those who have received phosphate-binding drugs for prolonged periods; for further details see under Hypophosphataemia, p.1669.

UK and US recommended dietary intake. In the UK dietary reference values (DRV—see Human Requirements, p.1925)[1] and in the USA dietary reference intakes including recommended dietary allowances (RDA)[2] have been published for phosphorus. In the UK the reference nutrient intake (RNI) for adults is about 550 mg (17.5 mmol) daily; no additional amount is recommended for pregnancy although an additional amount of about 440 mg (14.3 mmol) daily is advised during lactation. In the USA the RDA is 1250 mg daily for those aged 9 to 18 years and 700 mg daily in adults; no increase in RDA is recommended during pregnancy and lactation. A tolerable upper intake level of 4 g daily has been set in adults aged up to 70 years; in those older than 70 a maximum of 3 g daily is recommended.[2]

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. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board. *Dietary Reference Intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride*. Washington, DC: National Academy Press, 1999. Also available at: http://www.nap.edu/openbook.php?isbn=0309063507 (accessed 21/07/08)

Uses and Administration

Phosphates are used in the management of **hypophosphataemia** caused by phosphate deficiency or hypophosphataemic states (p.1669). Doses of up to 100 mmol of phosphate daily may be given orally. The intravenous route is seldom necessary, but a dose of up to 9 mmol of phosphate as monobasic potassium phosphate may be given over 12 hours and repeated every 12 hours as necessary for severe hypophosphataemia. Alternatively, 0.2 to 0.5 mmol/kg phosphate, up to a maximum of 50 mmol, may be given over 6 to 12 hours (see also below). Plasma-electrolyte concentrations, especially phosphate and calcium, and renal function should be carefully monitored. Reduced doses may be necessary in patients with renal impairment. Phosphate supplements are used in total parenteral nutrition regimens; typical daily requirements are 20 to 30 mmol of phosphate.

Phosphates act as mild osmotic **laxatives** (p.1693) when given orally as dilute solutions or by the rectal route. Phosphate enemas or concentrated oral solutions are used for bowel cleansing before surgery or endoscopy procedures. Preparations typically combine monobasic and dibasic sodium phosphates but the composition and dosage do vary slightly. Phosphate enemas act within 2 to 5 minutes, whereas the oral solutions act within 30 minutes to 6 hours.