

deficiency, such as certain types of osteomalacia and rickets (p.1084). Oral doses of 1 to 3 g of calcium daily are used in osteomalacia.

Oral calcium supplements can also be used as an adjunct in the management of osteoporosis (p.1084) and corticosteroid-induced osteoporosis (see Effects on Bones and Joints, under Corticosteroids, p.1491).

Cramps. Calcium salts are one of a number of interventions that have been tried in the management of cramps (see Muscle Spasm, p.1887). However, evidence for these interventions is mostly lacking and a small systematic review concluded that oral calcium was not of benefit for leg cramps during pregnancy.¹

- Young GL, Jewell D. Interventions for leg cramps in pregnancy. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2002 (accessed 21/06/05).

Diagnosis of insulinoma. Calcium stimulates the release of insulin from insulinomas. Intra-arterial calcium gluconate, followed by hepatic venous sampling, has been found to be accurate and sensitive in the diagnosis and localisation of insulinomas,^{1,4} even when other investigations have been negative.^{5,6}

- Dopman JL, et al. Localization of insulinomas to regions of the pancreas by intra-arterial stimulation with calcium. *Ann Intern Med* 1995; **123**: 269–73.
- Lo CY, et al. Value of intra-arterial calcium stimulated venous sampling for regionalization of pancreatic insulinomas. *Surgery* 2000; **128**: 903–9.
- Brändle M, et al. Assessment of selective arterial calcium stimulation and hepatic venous sampling to localize insulin-secreting tumours. *Clin Endocrinol (Oxf)* 2001; **55**: 357–62.
- Grant CS. Insulinoma. *Best Pract Res Clin Gastroenterol* 2005; **19**: 783–98.
- O’Shea D, et al. Localization of insulinomas by selective intraarterial calcium injection. *J Clin Endocrinol Metab* 1996; **81**: 1623–7.
- Pereira PL, et al. Insulinoma and islet cell hyperplasia: value of the calcium intraarterial stimulation test when findings of other preoperative studies are negative. *Radiology* 1998; **206**: 703–9.

Fluoride toxicity. Inorganic fluoride is corrosive to skin and mucous membranes and acute intoxication disrupts many physiological systems; severe burns and profound hypocalcaemia may ensue. Absorption of the fluoride can be prevented by conversion to an insoluble form such as calcium fluoride and thus irrigation of skin (or gastric lavage as appropriate) with lime water, milk, or a 1% solution of calcium gluconate is recommended. Immediate treatment should also consist of 10 mL of calcium gluconate 10% intravenously, repeated after one hour; 30 mL should be given if tetany is present. In the short term affected skin and tissue should be injected with a 10% solution of calcium gluconate at a dose of 0.5 mL/cm² and burnt skin treated with a calcium gluconate 2.5% gel.¹

See also under Hydrofluoric Acid, p.2322.

- McIvor ME. Acute fluoride toxicity: pathophysiology and management. *Drug Safety* 1990; **5**: 79–85.

Hypertension. Meta-analysis suggests that calcium supplementation results in a small reduction in systolic and diastolic blood pressure.¹ Although the effect was too small to support the use of calcium supplementation for preventing or treating hypertension (p.1171), it is possible that calcium supplementation might have beneficial effects on blood pressure in those with an inadequate intake. In a controlled trial, calcium with vitamin D supplementation reduced systolic blood pressure more effectively than calcium alone.²

- Griffith LE, et al. The influence of dietary and nondietary calcium supplementation on blood pressure: an updated metaanalysis of randomized controlled trials. *Am J Hypertens* 1999; **12**: 84–92.
- Peifer M, et al. Effects of a short-term vitamin D and calcium supplementation on blood pressure and parathyroid hormone levels in elderly women. *J Clin Endocrinol Metab* 2001; **86**: 1633–7.

PREGNANCY. Despite an earlier meta-analysis¹ which concluded that calcium supplementation during pregnancy reduced systolic and diastolic blood pressure and the incidence of pre-eclampsia and hypertension, results from a double-blind, placebo-controlled trial in a total of 4589 women indicated that calcium supplementation during normal pregnancy did not prevent pre-eclampsia, pregnancy-associated hypertension without pre-eclampsia, or a number of other related disorders.² A subsequent review³ found that calcium supplementation was beneficial, but it was noted that there was wide variation in results between different studies; most of the effect was in studies including women identified as being at high risk for pre-eclampsia, and results from studies including lower-risk women found that calcium had no effect. The high-risk studies were carried out in areas with a low dietary calcium intake, suggesting that benefit might be greatest in such populations. However, a further study⁴ in 8325 women living in areas with a low calcium intake but not specifically at high risk found that calcium supplementation had no significant effect on the incidence of pre-eclampsia, although it did reduce the risk of severe pre-eclamptic complications. An updated meta-analysis,⁵ which included this study, concluded that calcium supplementation during pregnancy was safe and that it did reduce the incidence of pre-eclampsia and serious complications, particularly in high-risk women.

For discussions of hypertension in pregnancy and eclampsia and pre-eclampsia, see p.1171 and p.470, respectively.

- Bucher HC, et al. Effect of calcium supplementation on pregnancy-induced hypertension and preeclampsia: a meta-analysis of randomized controlled trials. *JAMA* 1996; **275**: 1113–17. Correction. *ibid*; **276**: 1388.
- Levine RJ, et al. Trial of calcium to prevent preeclampsia. *N Engl J Med* 1997; **337**: 69–76.
- DerSimonian R, Levine RJ. Resolving discrepancies between a meta-analysis and a subsequent large controlled trial. *JAMA* 1999; **282**: 664–70.
- Villar J, et al. World Health Organization Calcium Supplementation for the Prevention of Preeclampsia Trial Group. World Health Organization randomized trial of calcium supplementation among low calcium intake pregnant women. *Am J Obstet Gynecol* 2006; **194**: 639–49.
- Hofmeyr GJ, et al. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2006 (accessed 17/01/08).

Malignant neoplasms. There is some evidence that calcium supplementation may modestly reduce the risk^{1–3} of colorectal cancer and its recurrence.^{4–6} This protective effect appears to be more pronounced for advanced colorectal lesions,⁷ and when serum concentrations of vitamin D are in the higher range.⁸

- Wu K, et al. Calcium intake and risk of colon cancer in women and men. *J Natl Cancer Inst* 2002; **94**: 437–46.
- McCullough ML, et al. Calcium, vitamin D, dairy products, and risk of colorectal cancer in the Cancer Prevention Study II Nutrition Cohort (United States). *Cancer Causes Control* 2003; **14**: 1–12.
- Cho E, et al. Dairy foods, calcium, and colorectal cancer: a pooled analysis of 10 cohort studies. *J Natl Cancer Inst* 2004; **96**: 1015–22. Correction. *ibid*; **1724**.
- Baron JA, et al. Calcium supplements for the prevention of colorectal adenomas. *N Engl J Med* 1999; **340**: 101–7.
- Bonithon-Kopp C, et al. Calcium and fibre supplementation in prevention of colorectal adenoma recurrence: a randomised intervention trial. *Lancet* 2000; **356**: 1300–6.
- Martínez ME, et al. Calcium, vitamin D, and risk of adenoma recurrence (United States). *Cancer Causes Control* 2002; **13**: 213–20.
- Wallace K, et al. Effect of calcium supplementation on the risk of large bowel polyps. *J Natl Cancer Inst* 2004; **96**: 921–5.
- Grau MV, et al. Vitamin D, calcium supplementation, and colorectal adenomas: results of a randomized trial. *J Natl Cancer Inst* 2003; **95**: 1765–71.

Premenstrual syndrome. Calcium supplementation was effective in relieving the luteal phase symptoms of premenstrual syndrome (p.2099) in 1 study.¹ A review of this and other studies suggested that calcium supplementation at a dose of 1.2 to 1.6 g daily should be considered in patients with premenstrual syndrome.²

- Thys-Jacobs S, et al. Calcium carbonate and the premenstrual syndrome: effects on premenstrual and menstrual symptoms. *Am J Obstet Gynecol* 1998; **179**: 444–52.
- Ward MW, Holimon TD. Calcium treatment for premenstrual syndrome. *Ann Pharmacother* 1999; **33**: 1356–8.

Preparations

BP 2008: Calcium and Ergocalciferol Tablets; Calcium Chloride Injection; Calcium Gluconate Injection; Calcium Gluconate Tablets; Calcium Lactate Tablets; Effervescent Calcium Gluconate Tablets;

BPC 1973: Calcium with Vitamin D Tablets;

USP 31: Aluminum Sulfate and Calcium Acetate for Topical Solution; Aluminum and Calcium Acetate Tablets for Topical Solution; Calcium Acetate Tablets; Calcium Chloride Injection; Calcium Glubionate Syrup; Calcium Glucoprotein Injection; Calcium Gluconate Injection; Calcium Gluconate Tablets; Calcium Lactate Tablets; Calcium Levulinate Injection; Calcium with Vitamin D Tablets; Dibasic Calcium Phosphate Tablets; Half-strength Lactated Ringer’s and Dextrose Injection; Lactated Ringer’s and Dextrose Injection; Lactated Ringer’s Injection; Potassium Chloride in Lactated Ringer’s and Dextrose Injection.

Proprietary Preparations (details are given in Part 3)

- Arg:** Calcimax; Calcio Cit Simple; Calcional Citrate; Calcium-Sandoz; Citramar; Findecalc Combi; Ostram; Procalcio; Raffo-C; Regual; Royen; Sigmacal; **Australia:** Calcidos CP 57; Citracal®; Sandoval; **Austria:** Calcium Frenesiun; Calcium-Sandoz; Mono Kalz; Ostram; Phos-E; **Belg:** Sandoz; **Braz:** Calcium-Sandoz; Calcium-Sandoz F; Miocalen; Ostocalcin; **Canada:** Calcject; Calcium-Rougier®; Calcium-Sandoz; Ostecit; **Chile:** Calcim; Elcal I; Kaplus; Ostram; Phoslo; **Cz:** Phosorb; **Denm:** Calcium-Sandoz; Phos-Ex; **Fin:** Calcium-Sandoz; Phos-Ex; **Fr:** CAL Ocean; Calcium-Sandoz; Kalcidol®; Ostram; **Ger:** Calciaret; Calcium-Eifelango®; Calcium Fresenius®; Calcium-Sandoz; Cerisorb; Euobiolac; Phos-Ex; **Gr:** Neocalcit; Osteorol; **Italia:** **Hong Kong:** Calcium Unison; Calcium Vida; Calcium-Sandoz; Citracal; Gluco-Calcium®; Mega-Cal; **Hung:** Ban; Calcimic; Calcium-Sandoz; Citrocalcium; **India:** Calcium-Sandoz; Phosforid; **Indon:** Dumocalin; Licokalk; **Irl:** Calcium-Sandoz; **Malaysia:** Ca Lac; Citracal; Ircium; **Mex:** Bio-Baltron; Bon-Kerf; Calcifox; Calcigen; Dibocalin; Doleco; Calcifem; Calcium-Sandoz; Calvaf; Ostram; **Pol:** Calcium Calft; Calcium Syrop; Ostical; Ostram; Sanosvit Calcium; Satural; **Port:** Calcium-Sandoz; Phosphosorb; Sandoval; **Rus:** Calcium-Sandoz Forte (Кальций-Сандоз Форт); **S Afr:** Calcium-Sandoz Glucal; **Singapore:** Calcium-Sandoz; Citracal; Hydrofluoric Acid Antidote; Os-Cal; Vitacal; **Spain:** Calcio 20 Emulsion; Calcium-Sandoz Forte; Calcium-Sandoz; Ibercal; Oseofort; Ostram; Royen; Tepox Cal; **Swed:** Calcium-Sandoz; Phos-Ex; **Switz:** Calcium-Sandoz; **Thail:** Calcium; Calcium Uni; Calcium-Sandoz; Calsor; Calvin; Kal-Forte; Lo-P-Caps; **Turk:** Anti-Fosfat Ca; Calcium-Sandoz; Phos-Ex; **UK:** BioCalth; Calcium-Sandoz; Ostram; Phos-Ex; Sandoval; **USA:** Cal-C; Cal-Citrate; Cal-G; Cal-Lac; Calphron; Citracal; Oyster Calcium; Phos-Lo; Posture; **Venez:** Calcium; Citracal; Calcium-Sandoz; Citracal; Maxical; Os-Cal; 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