nitine in relieving complications of HIV infection and adverse effects of antiretroviral drugs,[2] notably toxic neuropathy.[3,4]

1. Vilaseca MA, *et al.* Low serum carnitine in HIV-infected children on antiretroviral treatment. *Eur J Clin Nutr* 2003; **57:** 1317–22.
2. Ilias I, *et al.* -Carnitine and acetyl- -carnitine in the treatment of complications associated with HIV infection and antiretroviral therapy. *Mitochondrion* 2004; **4:** 163–8.
3. Herzmann C, *et al.* Long-term effect of acetyl-L-carnitine for antiretroviral toxic neuropathy. *HIV Clin Trials* 2005; **6:** 344–50.
4. Osio M, *et al.* Acetyl-l-carnitine in the treatment of painful antiretroviral toxic neuropathy in human immunodeficiency virus patients: an open label study. *J Peripher Nerv Syst* 2006; **11:** 72–6.

MALE INFERTILITY. Increases in sperm motility have been reported in some infertile men treated with carnitine,[1-3] although clinical benefit needs to be further evaluated.[4]

1. Lenzi A, *et al.* Use of carnitine therapy in selected cases of male factor infertility: a double-blind crossover trial. *Fertil Steril* 2003; **79:** 292–300.
2. Lenzi A, *et al.* A placebo-controlled double-blind randomized trial of the use of combined -carnitine and -acetyl-carnitine treatment in men with asthenozoospermia. *Fertil Steril* 2004; **81:** 1578–84.
3. Vicari E, Calogero AE. Effects of treatment with carnitines in infertile patients with prostato-vesiculo-epididymitis. *Hum Reprod* 2001; **16:** 2338–42.
4. Agarwal A. Carnitines and male infertility. *Reprod Biomed Online* 2004; **8:** 376–84.

NEUROLOGICAL DISORDERS. A meta-analysis of 21 studies concluded that acetylcarnitine improved mild cognitive impairment and prevented deterioration in patients with mild *Alzheimer's disease*.[1] However, a systematic review of 11 of these trials concluded that, although some evidence of benefit on clinical global impression exists, use of acetylcarnitine could not be routinely recommended in the treatment of Alzheimer's disease.[2]

Although no differences were found in serum carnitine concentrations in *multiple sclerosis* patients with or without disabling fatigue,[3] there is some suggestion of benefit with acetylcarnitine treatment for those patients with fatigue.[4] Carnitine has been reported to be of benefit in other cases of fatigue (see above).

In *Rett syndrome*, a severe neurodevelopmental disorder, supplementation with levocarnitine led to improvements in sleep efficiency, energy levels, and communication skills.[5] Parental and medical assessment of patient well-being improved in another study;[6] girls with classical Rett syndrome also improved in motor behaviour as assessed medically.

1. Montgomery SA, *et al.* Meta-analysis of double-blind randomized controlled clinical trials of acetyl- -carnitine versus placebo in the treatment of mild cognitive impairment and mild Alzheimer's disease. *Int Clin Psychopharmacol* 2003; **18:** 61–71.
2. Hudson S, Tabet N. Acetyl-l-carnitine for dementia. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2003 (accessed 08/11/05).
3. Fukazawa T, *et al.* Serum carnitine and disabling fatigue in multiple sclerosis. *Psychiatry Clin Neurosci* 1996; **50:** 323–5.
4. Tomassini V, *et al.* Comparison of the effects of acetyl -carnitine and amantadine for the treatment of fatigue in multiple sclerosis: results of a pilot, randomised, double-blind, crossover trial. *J Neurol Sci* 2004; **218:** 103–8.
5. Ellaway CJ, *et al.* Medium-term open label trial of L-carnitine in Rett syndrome. *Brain Dev* 2001; **23** (suppl): S85–S89.
6. Ellaway C, *et al.* Rett syndrome: randomized controlled trial of -carnitine. *J Child Neurol* 1999; **14:** 162–7.

Preparations

USP 31: Levocarnitine Injection; Levocarnitine Oral Solution; Levocarnitine Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Albicar; Fertilix; Neurex; Neuroactil; ***Braz.:*** Levocarnin†; ***Canad.:*** Carnitor; ***Chile:*** Actigeron; Carnicor; ***Fr.:*** Levocarnil; ***Ger.:*** Biocarn; L-Carn; Nefrocarnit; ***Gr.:*** Aveptol; Bitobionil; Carnidose; Carnil; Corubin; Ensial; Frutenor; Growart; Inestom; Intelecta; Koptilan; Levalastine; Levamin; Levars; Levocarnil; Levosan; Lisefor; Listover; Lofostin; Maledrol; Merlit; Mevamyst; Minartine; Minoa; Oskana; Phacovit; Soludamin; Superamin; Tonovit; Trian; Trinalin; ***Hong Kong:*** Carnitene; Carnitor; ***India:*** Carnitor; L-Tine†; ***Ital.:*** Branigen; Branitil; Cardiobil†; Cardiogen†; Carnitene; Carnitolo; Carnitop†; Carnovis†; Carnum†; Carrier†; Dromos; Elleci; Eucar; Eucarnil; Farnitin; Karrer†; Kernit; Lefcar; Levocarvit; Medocarnitin; Megavis; Metina†; Miocardin; Miocor; Miotonal; Neo Cardiol; Nicetile; Normobren; Transfert†; Zibren; ***Mex.:*** Cardispan; Provicar; ***Neth.:*** Nefrocarnit; ***Philipp.:*** Carnicor; ***Pol.:*** Carnivit; ***Port.:*** Cartine; Disocor; Lacetilina; ***Rus.:*** Carniten (Карнитен); Elcar (Элькар); ***Spain:*** Carnicor; Secabiol; ***Turk.:*** Carnitene; ***UK:*** Carnitor; ***USA:*** Carnitor; VitaCarn; ***Venez.:*** Carnisin; Kativil; Lixi; Provicar.

Multi-ingredient: ***Arg.:*** Enlinea†; Garcinol Max; Herbaccion Diet; Metabolic; Reductase; Silueta Plus; Tonekin Plus†; ***Braz.:*** Pepsivit†; ***Chile:*** Grisetin Con Carnitina†; ***Indon.:*** Car-Q; Corsel; Naturica DFM; Procardio; Vitaslim; ***Ital.:*** Biocarnil†; Carfosid; Carpantin†; Co-Carnetina B12; Memorandum; ***Mex.:*** Lipovitasi-Or; Redumed; Slim-D; ***Philipp.:*** Fitrum; Godex; Nutrafit; ***Spain:*** Hepadif; Malandil; Pranzo.

Casein

Kazeina.
CAS — 9000-71-9.

Profile

Casein is a protein found in milk and has been used as a source of protein in preparations for enteral and parenteral nutrition; it may be used in the production of protein hydrolysate injection. Calcium caseinate has also been used.

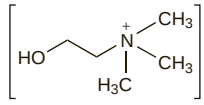
Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Secalbum; ***Canad.:*** Casec†; ***Israel:*** Casec; ***Mex.:*** Calsein; Caseincal†; K-Sein; ***USA:*** Casec.

Multi-ingredient: ***Mex.:*** Calciyodina; ***Switz.:*** Cicafissan; Fissan†; Vitafissan N.

Choline Bitartrate

Bitartarato de Colina; Choline Acid Tartrate; Choline Hydrogen Tartrate; Cholinii Tartras; Colina, bitartrato de. 2-Hydroxyethyltrimethylammonium hydrogen tartrate.
$C_9H_{19}NO_7$ = 253.2.
CAS — 87-67-2.



(choline)

Pharmacopoeias. In *US*.
USP 31 (Choline Bitartrate). A white, hygroscopic, crystalline powder; odourless or with a faint trimethylamine odour. Clear and colourless in solution. Freely soluble in water; slightly soluble in alcohol; insoluble in chloroform and in ether. pH of a 10% solution in water is between 3.0 and 4.0.

Choline Chloride *(rINN)*

Choline, Chlorure de; Cholini Chloridum; Cholinii Chloridum; Choliny chlorek; Cloruro de colina; Koliinikloridi; Kolinklorid. 2-Hydroxyethyltrimethylammonium chloride.

Холина Хлорид
$C_5H_{14}ClNO$ = 139.6.
CAS — 62-49-7 (choline); 67-48-1 (choline chloride).

Pharmacopoeias. In *Fr.* and *US*.
USP 31 (Choline Chloride). Hygroscopic, colourless or white crystals or crystalline powder, usually having a slight odour of trimethylamine. Clear and colourless in solution. Soluble in water and in alcohol. pH of a 10% solution in water is between 4.0 and 7.0.

Profile

Choline is an acetylcholine precursor. It is involved in lipid metabolism and acts as a methyl donor in various other metabolic processes. Choline has traditionally been considered to be a vitamin B substance although its functions do not justify its classification as a vitamin. Choline can be synthesised in the body. However, its absence in total parenteral nutrition causes hepatic steatosis, and it is also thought to be a requirement in the diet of neonates. Sources of choline, which occurs mostly as lecithin, include egg-yolk and vegetable and animal fat.

Choline is used as a dietary supplement and has been used to treat liver disorders such as fatty liver and cirrhosis. It has been tried in the management of Alzheimer's disease (see Dementia, p.362) but without success. Choline is used as the dihydrogen citrate, and orotate salts as well as the bitartrate and the chloride.

Human requirements. In the USA, an adequate intake (see p.1925) of 550 mg daily in men and 425 mg daily in women has been determined for choline.[1] The tolerable upper intake level for adults is 3.5 g daily.[1]

1. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board. *Dietary Reference Intakes for thiamin, riboflavin, niacin, vitamin B , folate, vitamin B , pantothenic acid, biotin, and choline*. Washington, DC: National Academy Press, 2000. Also available at: http://www.nap.edu/openbook.php?isbn=0309065542 (accessed 21/07/08)

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: neurotropan†.

Multi-ingredient: ***Arg.:*** Bil 13; GB 100; ***Austral.:*** Gingo A†; Liv-Detox†; ***Austria:*** Orocholin; ***Braz.:*** Alcafelol†; Aminotox†; Anekron; B-Vesil; Betaliver†; Biohepax; Enterofigon; Epativan; Epocler; Extrato Hepatico Composto; Extrato Hepatico Vitaminado†; Hecrosine B12†; Hepacitron†; Hepalin; Hepatobe†; Hepatotris†; Hepatox; Hormo Hepatico†; Jurubileno†; Lisotox; Metiocolin B12; Metiocolin Composto; Necro B-6; Olocynan†; Olohepat†; Panvitrop; Xantina B12†; Xantinon B12; Xantinon Complex; ***Chile:*** Hepabil; ***Cz.:*** Lipovitan†; ***Fr.:*** Citrocholine; Desintex-Choline; Hepacholine†; Hepagrume; ***Ger.:*** Lipovitan†; ***Hong Kong:*** Bilsan; Hepatofalk; ***India:*** Delphicol; Livocip; Mecolin; Sorbiline; Sorliv; ***Indon.:*** Curliv; Curliv Plus; Hepatin; Lipagent; Methicol; Methioson; Naturica DFM; ***S.Afr.:*** Hepavite; Prohep; ***Spain:*** Hepato Fardi†; ***Thai.:*** Liporon; ***UK:*** Lipotropic Factors.

Chondroitin Sulfate–Iron Complex

Chondroitin Sulphate–Iron Complex; Ferropolichondrum; Hierro y sulfato de condroitina, complejo de.
CAS — 54391-57-0.
ATC — B03AB07.
ATC Vet — QB03AB07.

Profile

Chondroitin sulfate-iron complex is used as a source of iron (p.1949) for iron-deficiency anaemia (p.1951). It is given orally in doses of up to 900 mg daily, equivalent to up to 90 mg of iron daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Condrofer†; Isairon.

Chromium

Chrom; Chrome; Cromo.
Cr = 51.9961.

Chromium Trichloride

Chromic Chloride; Cromo, tricloruro de.
$CrCl_3,6H_2O$ = 266.4.
CAS — 10025-73-7 (anhydrous chromium trichloride); 10060-12-5 (chromium trichloride hexahydrate).

Pharmacopoeias. In *US*.
USP 31 (Chromic Chloride). Dark green, odourless, slightly deliquescent crystals. Soluble in water and in alcohol; slightly soluble in acetone; practically insoluble in ether. Store in airtight containers.

Chromium Tripicolinate

Chromium Picolinate; Cromo, tripicolinato de.
$C_{18}H_{12}N_3O_6Cr$ = 418.3.

Pharmacopoeias. In *US*.
USP 31 (Chromium Picolinate). Store in airtight containers.

Adverse Effects

Trivalent salts of chromium, such as chromium trichloride, are generally considered to produce few adverse effects. However, hexavalent forms of chromium are notably toxic (see under Chromium Trioxide, p.2281).

Effects on the kidneys. Two cases of renal failure were attributed to ingestion of excessive doses of chromium tripicolinate in women with no history of renal dysfunction.[1,2] Acute renal failure with features of acute tubular necrosis, and requiring haemodialysis, has been reported after ingestion of a chromium picolinate-containing supplement. The amount of chromium in the supplement could not be determined.[3] For mention of decreases in glomerular filtration rate in children receiving chromium-supplemented total parenteral nutrition, see Supplementation, below.

1. Wasser WG, *et al.* Chronic renal failure after ingestion of over-the-counter chromium picolinate. *Ann Intern Med* 1997; **126:** 410.
2. Cerulli J, *et al.* Chromium picolinate toxicity. *Ann Pharmacother* 1998; **32:** 428–31.
3. Wani S, *et al.* Acute tubular necrosis associated with chromium picolinate-containing dietary supplement. *Ann Pharmacother* 2006; **40:** 563–6.

Effects on the skin. There have been rare reports[1,2] of cutaneous reactions to oral chromium tripicolinate, including one of acute generalised exanthematous pustulosis.

1. Young PC, *et al.* Acute generalized exanthematous pustulosis induced by chromium picolinate. *J Am Acad Dermatol* 1999; **41:** 820–3.
2. Fowler JF. Systemic contact dermatitis caused by oral chromium picolinate. *Cutis* 2000; **65:** 116.

Uses and Administration

Chromium is an essential trace element that potentiates insulin action and thus influences carbohydrate, lipid, and protein metabolism. Dietary sources rich in chromium include brewers' yeast, meat, whole grains, and nuts. Chromium trichloride has been given as a chromium supplement in total parenteral nutrition. Chromium tripicolinate is used as a chromium supplement, and is being investigated for improving glycaemic control in patients with diabetes mellitus.

Diabetes mellitus. A review[1] of trivalent chromium in the management of diabetes mellitus (p.431) concluded that it may have an adjunctive role. A meta-analysis[2] found no effect of chromium on glucose or insulin concentrations in non-diabetic subjects; data for diabetic patients were inconclusive. A systematic review[3] found no significant effect with chromium supplementation on lipid or glucose metabolism in non-diabetic subjects, but it may have a modest beneficial effect on glycaemia and dyslipidaemia in those patients with diabetes. Meta-analysis was hampered by the overall poor quality and heterogeneity of available studies,[3] and further research was considered necessary.[1-3]

1. Ryan GJ, *et al.* Chromium as adjunctive treatment for type 2 diabetes. *Ann Pharmacother* 2003; **37:** 876–85.
2. Althuis MD, *et al.* Glucose and insulin responses to dietary chromium supplements: a meta-analysis. *Am J Clin Nutr* 2002; **76:** 148–55.
3. Balk EM, *et al.* Effect of chromium supplementation on glucose metabolism and lipids: a systematic review of randomized controlled trials. *Diabetes Care* 2007; **30:** 2154–63.

Human requirements. In the UK neither a reference nutrient intake (RNI) nor an estimated average requirement (EAR—see p.1925) has been set for chromium although a safe and adequate