plements to protect against malignancy, see under Prophylaxis of Malignant Neoplasms, p.1927.

Effects on mortality. A systematic review of the effect of antoxidant supplements on mortality in randomised primary and secondary prevention studies found that betacarotene, used either singly or with other antoxidants, significantly increased all-cause mortality.[1] In another review and meta-analysis, betacarotene supplementation showed a trend towards increased cancer mortality.[2]

1. Bjelakovic G, *et al.* Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2008 (accessed 18/06/08).
2. Bardia A, *et al.* Efficacy of antioxidant supplementation in reducing primary cancer incidence and mortality: systematic review and meta-analysis. *Mayo Clin Proc* 2008; **83:** 23–34.

Effects on the skin. Yellow pigmentation of the skin may result from an unusually high consumption of carrots or other source of carotene,[1] or from a defect in the enzyme that normally metabolises betacarotene to vitamin A.[2] Hypercarotenaemia can be distinguished from jaundice by the fact that the sclerae retain their normal white colour. Pigmentation occurs first on the palms and soles and may extend to the nasolabial folds. Although it has been stated that the condition is harmless as the body converts carotene to retinol only as required,[1] others consider that long-standing hypercarotenaemia can have clinical sequelae:[2] neutropenia[3] and amenorrhoea[4] have been reported to be associated with the condition.

1. Sharman IM. Hypercarotenaemia. *BMJ* 1985; **290:** 95.
2. Vaughan Jones SA, Black MM. Metabolic carotenaemia. *Br J Dermatol* 1994; **131:** 145.
3. Shoenfeld Y, *et al.* Neutropenia induced by hypercarotenaemia. *Lancet* 1982; **i:** 1245.
4. Kemmann E, *et al.* Amenorrhoea associated with carotenemia. *JAMA* 1983; **249:** 926–9.

Pharmacokinetics

Gastrointestinal absorption of betacarotene depends on the presence of bile and is increased by dietary fat. About 20 to 60% of betacarotene is metabolised to retinol in the intestinal wall, and a small amount is converted to vitamin A in the liver. The proportion of betacarotene converted to vitamin A decreases as the intake of betacarotene increases, and high doses of betacarotene do not lead to abnormally high serum concentrations of vitamin A. Unchanged betacarotene is distributed to various tissues including fat, the adrenal glands, and ovaries.

◊ References.

1. Wang X-D. Review: absorption and metabolism of β-carotene. *J Am Coll Nutr* 1994; **13:** 314–25.

Human Requirements

Carotenes, of which betacarotene has the highest activity, are major dietary sources of vitamin A—see p.1972.

UK and US recommended dietary intake. There is currently no UK dietary reference value (see p.1925) for betacarotene, and in the USA recommended dietary allowances or dietary reference intakes (see p.1925) have not been set. However, the Expert Group on Vitamins and Minerals[1] has established a safe upper level (SUL) for betacarotene of 7 mg daily, or about 0.11 mg/kg daily for a 60-kg adult.

1. Expert Group on Vitamins and Minerals. Safe Upper Levels for vitamins and minerals (May 2003). Available at: http://www.food.gov.uk/multimedia/pdfs/vitmin2003.pdf (accessed 06/01/06)

Uses and Administration

Betacarotene is a carotenoid precursor of vitamin A (p.1971). In the *treatment* of vitamin A deficiency, vitamin A is preferred to betacarotene. However, betacarotene has been used for the *prevention* of vitamin A deficiency at a dose of 6 to 15 mg daily for adults and 3 to 6 mg daily for children.

Betacarotene may be given by mouth to reduce the severity of photosensitivity reactions in patients with erythropoietic protoporphyria (see also Porphyria, below). Doses are in the range of 30 to 300 mg daily for adults and 30 to 150 mg daily for children, depending upon severity; they may be taken as either single daily doses or divided doses but should preferably be taken with meals. The protection offered by betacarotene is not total and generally 2 to 6 weeks of treatment resulting in a yellow coloration of palms and soles is necessary before patients should attempt to increase their exposure to sunlight.

Betacarotene and other carotenoids (alphacarotene and gammacarotene) are used as colouring agents for foods and medicinal products.

Betacarotene has antoxidant activity and has been studied for its possible protective benefit in a number of disorders (but see Effects on Mortality, above).

Age-related macular degeneration. A study in patients with age-related macular degeneration (p.785) indicated that the risk of developing this disorder (a leading cause of irreversible blindness among elderly persons) was markedly decreased amongst those with the highest dietary carotenoid intake;[1] in particular, lutein and zeaxanthin, or green leafy vegetables (which contain high concentrations of these carotenoids) were associated with a lower risk. Increasing the dietary intake of these carotenoids may be of benefit in reducing the development of this disorder. Despite this, systematic reviews found no evidence that antoxidant vitamin and mineral supplementation would either prevent[2,3] or delay the onset of macular degeneration. However, one study[4] has shown modest benefit from vitamin C, vitamin E, betacarotene, and zinc supplementation in those with moderate to severe signs of the disease. A systematic review to assess the effects of antoxidant vitamin or mineral supplementation on the progression of age-related macular degeneration included this study, and noted that the generalisability of these findings to other populations (with differing nutritional status) was unknown. Long-term harm from supplementation could not be ruled out.[5]

1. Seddon JM, *et al.* Dietary carotenoids, vitamins A, C, and E, and advanced age-related macular degeneration. *JAMA* 1994; **272:** 1413–20.
2. Evans JR, Henshaw K. Antioxidant vitamin and mineral supplements for preventing age-related macular degeneration. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2008 (accessed 11/03/08).
3. Chong EW-T, *et al.* Dietary antioxidants and primary prevention of age related macular degeneration: systematic review and meta-analysis. *BMJ* 2007; **335:** 755–9.
4. Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no.8. *Arch Ophthalmol* 2001; **119:** 1417–36.
5. Evans JR. Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 11/03/08).

Deficiency states. A study in Senegalese children with vitamin A deficiency found that supplementation with betacarotene (in a single dose equivalent to 200 000 units of vitamin A) was as effective as a single 200 000 unit dose of vitamin A palmitate in reversing ocular changes.[1] Since betacarotene is less toxic than vitamin A itself it would have some advantages for supplementation, either as an oral supplement or by encouraging the consumption of carotenoid-rich fruit and vegetables. A study in anaemic Indonesian women found that a supplement containing betacarotene with iron, vitamin C, and folate improved vitamin A status, whereas an additional daily portion of dark-green leafy vegetables containing a similar amount of betacarotene did not.[2] However, others contended that consumption of food sources of carotenoids were effective in improving vitamin A status in deficiency states,[3,4] and that it might not be appropriate to extrapolate these findings in adults (not necessarily deficient in vitamin A) to vitamin A deficient children.[3,5] WHO policy was to promote dietary adjustment wherever vitamin A deficiency was endemic.[5] Despite further studies confirming improved vitamin A status among those given foods high in betacarotene,[6,7] a review[8] considered the bioavailability of betacarotene from plant foods to be low, and questioned the retinol equivalency determined by WHO (see Units, above). Another study[9] found that increasing dietary fat consumption and eliminating helminthic infection further increased serum retinol concentrations in children given food high in betacarotene.

For a trial reporting improved vitamin A status with betacarotene plus zinc compared with betacarotene or zinc alone, and the suggestion that zinc may have a role in the conversion of betacarotene to retinol, see Vitamin A Deficiency, under Zinc, p.2001.

For further discussion of vitamin A deficiency and the value of supplementation in various disease states, see under Vitamin A Substances, p.1973.

1. Carlier C, *et al.* A randomised controlled trial to test equivalence between retinyl palmitate and β carotene for vitamin A deficiency. *BMJ* 1993; **307:** 1106–10.
2. de Pee S, *et al.* Lack of improvement in vitamin A status with increased consumption of dark-green leafy vegetables. *Lancet* 1995; **346:** 75–81.
3. Reddy V. Vitamin A status and dark green leafy vegetables. *Lancet* 1995; **346:** 1634–5.
4. Underwood BA. Vitamin A status and dark green leafy vegetables. *Lancet* 1995; **346:** 1635.
5. WHO. Vitamin A status: is dietary replacement practicable. *WHO Drug Inf* 1995; **9:** 141.
6. Ncube TN, *et al.* Supplementing lactating women with puréed papaya and grated carrots improved vitamin A status in a placebo-controlled trial. *J Nutr* 2001; **131:** 1497–1502.
7. Vuong LT, *et al.* Plasma β-carotene and retinol concentrations of children increase after a 30-d supplementation with the fruit Momordica cochinchinensis (gac). *Am J Clin Nutr* 2002; **75:** 872–9.
8. West CE, *et al.* Consequences of revised estimates of carotenoid bioefficacy for dietary control of vitamin A deficiency in developing countries. *J Nutr* 2002; **132** (suppl): 2920S–2926S.
9. Jalal F, *et al.* Serum retinol concentrations in children are affected by food sources of β-carotene, fat intake, and anthelmintic drug treatment. *Am J Clin Nutr* 1998; **68:** 623–9.

Ischaemic heart disease. There are results from epidemiological studies suggesting the potential benefits of dietary betacarotene in preventing ischaemic heart disease, particularly in smokers; however, randomised placebo-controlled studies of betacarotene supplements have returned negative results, as discussed on p.1926.

Malignant neoplasms. Some evidence from epidemiological studies suggested that higher dietary intakes of carotenoids and especially betacarotene had a protective effect against cancer. Consequently several randomised placebo-controlled trials examining the use of betacarotene supplements in the primary or secondary prevention of malignancy were instigated. However, the results of studies so far published have generally been disappointing. Moreover, some results suggest that supplementation with betacarotene may actually be harmful (see Prophylaxis of Malignant Neoplasms, p.1927 and Effects on Mortality, above).

Porphyria. Despite a lack of robust evidence, betacarotene is the most widely used systemic drug for the management of erythropoietic protoporphyria,[1,2] a non-acute porphyria characterised by cutaneous photosensitivity (p.1448). It has been given with canthaxanthin to reduce the skin discoloration caused by betacarotene alone.

1. Todd DJ. Erythropoietic protoporphyria. *Br J Dermatol* 1994; **131:** 751–66.
2. Todd DJ. Therapeutic options for erythropoietic protoporphyria. *Br J Dermatol* 2000; **142:** 826.

Preparations

USP 31: Beta Carotene Capsules.

Proprietary Preparations (details are given in Part 3)
Arg.: B-Caroteno; ***Austria:*** Carotaben; ***Braz.:*** Vitcaroten†; Vitizin Beta; Zirvit Beta; ***Cz.:*** Carotaben; ***Ger.:*** Carotaben; Carotana†; Carotinora; ***Ital.:*** Tannisol; ***Switz.:*** Carotaben; ***Turk.:*** Carovit; ***UK:*** Biocarotine.

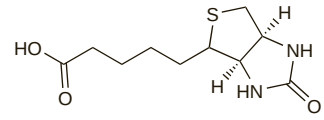
Multi-ingredient: ***Arg.:*** Bronsul; Natubrown; Sigmasol; Sol Bronce Vital; ***Austral.:*** Antioxidant Forte Tablets; Antioxidant Tablets; Beta A-C; Eye Health Herbal Plus Formula 4; Lifesystem Herbal Plus Formula 5 Eye Relief†; Lifesystem Herbal Plus Formula 8 Echinacea†; Odourless Garlic†; ***Austria:*** Oleovit A; Oleovit A + D; ***Braz.:*** Purpuralin†; ***Chile:*** Unitone; ***Fr.:*** Difrarel; Phytolongbronze; Phytosolaire; ***Ger.:*** Carotin; ***Hong Kong:*** Purpuralin†; Sanjukei Panax Ginseng; ***India:*** Rovigon†; ***Indon.:*** Bioretin; Lesifit; Matase; Matovit; Nu-Derm Sunblock; Retivit; ***Ital.:*** Agedin Plus; Angstrom Viso; Ecamannan; Keratolip; Levudin†; Mirtilene; Solecin; Tannidin Plus; ***Mex.:*** Unitone; ***Neth.:*** Difrarel; ***Philipp.:*** Pynocare 40 Actisome; ***Pol.:*** Biovision; ***Port.:*** Rilastil Dermo Solar; ***Rus.:*** Strix (Стрикс); ***Spain:*** Aceite Acalorico; Mirtilus; ***Switz.:*** Visaline; ***Turk.:*** Dervanol; ***Venez.:*** Unitone†.

Biotin *(rINN)*

Biotiini; Biotina; Biotinas; Biotine; Biotinum; Coenzyme R; Vitamin H. *cis*-5-(Hexahydro-2-oxo-1*H*-thieno[3,4-*d*]imidazol-4-yl)valeric acid.

Биотин

$C_{10}H_{16}N_2O_3S$ = 244.3.
CAS — 58-85-5.
ATC — A11HA05.
ATC Vet — QA11HA05.



Pharmacopoeias. In *Eur.* (see p.vii) and *US.*

Ph. Eur. 6.2 (Biotin). A white or almost white, crystalline powder or colourless crystals. Very slightly soluble in water and in alcohol; practically insoluble in acetone. It dissolves in dilute solutions of alkali hydroxides. Protect from light.

USP 31 (Biotin). A practically white crystalline powder. Very slightly soluble in water and in alcohol; insoluble in other common organic solvents. Store in airtight containers.

Profile

Biotin is traditionally considered to be a vitamin B substance. It is an essential coenzyme in fat metabolism and in other carboxylation reactions. Biotin deficiency may result in the urinary excretion of organic acids and changes in skin and hair. Deficiency of biotin is very unlikely in man because of its widespread distribution in food. Egg-yolk and offal are especially good sources. Biotin deficiency has been reported however during long-term parenteral nutrition and in patients with biotinidase deficiency, an inherited metabolic disorder. For dosage in biotinidase or isolated carboxylase deficiency see below. A combination of biotin and chromium tripicolinate (p.1934) has been promoted as an adjunct for the management of diabetes mellitus.

Biotin combines with avidin, a glycoprotein present in raw egg-white, to form an inactive compound.

Adverse effects. For reference to life-threatening eosinophilic pleuropericarditis in a patient receiving biotin and pantothenic acid see p.1959.

Deficiency states. Biotin has been used to treat deficiency of biotinidase or holocarboxylase synthetase, enzymes responsible for the recycling and incorporation of biotin. In the UK, the *BNFC* suggests the following doses:

- for isolated carboxylase defects, biotin may be given to neonates in a dose of 5 mg once daily by mouth or slow intravenous injection, adjusted according to response; older patients may be given 10 mg daily. The usual maintenance dose ranges from 10 to 50 mg daily, though up to 100 mg daily may be needed
- for defects of biotin metabolism, 10 mg once daily may be given by mouth or slow intravenous injection, adjusted according to response. Usual maintenance doses are 5 to 20 mg daily but higher doses may be needed

References.

1. Baumgartner ER, Suormala T. Multiple carboxylase deficiency: inherited and acquired disorders of biotin metabolism. *Int J Vitam Nutr Res* 1997; **67:** 377–84.
2. Tsao CY, Kien CL. Complete biotinidase deficiency presenting as reversible progressive ataxia and sensorineural deafness. *J Child Neurol* 2002; **17:** 146.
3. Wolf B. Biotinidase deficiency: new directions and practical concerns. *Curr Treat Options Neurol* 2003; **5:** 321–8.
4. Seymons K, *et al.* Dermatologic signs of biotin deficiency leading to the diagnosis of multiple carboxylase deficiency. *Pediatr Dermatol* 2004; **21:** 231–5.
5. Grünewald S, *et al.* Biotinidase deficiency: a treatable leukoencephalopathy. *Neuropediatrics* 2004; **35:** 211–16.
6. Puertas Bordallo D, *et al.* Neuropatía óptica por déficit de biotinidasa. *Arch Soc Esp Oftalmol* 2004; **79:** 393–6.
7. Hoffman TL, *et al.* Biotinidase deficiency: the importance of adequate follow-up for an inconclusive newborn screening result. *Eur J Pediatr* 2005; **164:** 298–301.
8. Wilson CJ, *et al.* Severe holocarboxylase synthetase deficiency with incomplete biotin responsiveness resulting in antenatal insult in Samoan neonates. *J Pediatr* 2005; **147:** 115–18.

Human requirements. In the UK neither a reference nutrient intake (RNI) nor an estimated average requirement (EAR—see p.1925) has been set for biotin although it was considered that an intake of between 10 and 200 micrograms daily was both safe and adequate.[1] Similarly in the USA an adequate intake of 30 micrograms daily has been set for adults.[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 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)
Arg.: Aminosam; Panabiotin; ***Austria:*** Bio-H-Tin; Curatin; Medobiotin; Merzbiotin; ***Canad.:*** D Biotin†; ***Chile:*** Hvit; ***Fin.:*** Biotisan; ***Ger.:*** Bio-H-Tin; Biokur†; Biotin-Asmedic; Deacura; Gabunat; Medobiotin†; Natubiotin; Natuderm†; Rombellin†; ***Hung.:*** Bio-H-Tin; ***Ital.:*** Biodermatin; Diathynil; Nebiotin; ***Spain:*** Medebiotin; ***Switz.:*** Bio-H-Tin; Rombellin; ***USA:*** Appearex; Hard Nails.

Multi-ingredient: ***Arg.:*** Folimax B; Megaplus; Tersoderm Anticaspa†; ***Fr.:*** Zeniac LP†; Zeniac†; ***Ger.:*** Carotin; ***Indon.:*** Alicron; ***Spain:*** Doctodermis; Lacerdermol.

Calcium Ferrous Citrate

Ferrous Calcium Citrate. Dicalcium iron(2+) bis(2-hydroxypropane-1,2,3-tricarboxylate).

$C_{12}H_{10}Ca_2FeO_{14}$ = 514.2.
CAS — 53684-61-0.

Profile

Calcium ferrous citrate is used as a source of iron (p.1949) for iron-deficiency anaemia (p.1951).

Preparations

Proprietary Preparations (details are given in Part 3)
Israel: Ferrocal.

Multi-ingredient: ***India:*** Raricap; Raricap L.

Calcium Fluoride

Fluoruro cálcico.

CaF_2 = 78.07.
CAS — 7789-75-5.

Pharmacopoeias. In *Ger.*

Profile

Calcium fluoride is used as a fluoride supplement (see Sodium Fluoride, p.1962) for the prevention of dental caries. Calcium fluoride is also used as a source of calcium.

Homoeopathy. Calcium fluoride has been used in homoeopathic medicines under the following names: Calcarea Fluorica; Calc. Fluor; Calcium Fluoratum; Cal. fl.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Calcifluor†.

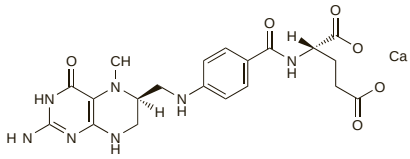
Multi-ingredient: ***Cz.:*** Bifluorid†; ***Denm.:*** Bifluorid; ***India:*** Calcinol; ***Ital.:*** Bifluorid†; ***Pol.:*** Bifluorid; ***Swed.:*** Bifluorid.

Calcium Mefolinate

Calcii Mefolinas; Calcio Mefolinato; Calcium L-Methylfolate; Calcium (6S)-5-Methyltetrahydrofolate.

Кальция L-Метилфолат

$C_{20}H_{23}CaN_7O_6$ = 497.5.
CAS — 26560-38-3.



NOTE. Metafolin is a trade name that has been used for calcium mefolinate.

Profile

Calcium mefolinate is the calcium salt of 5-methyltetrahydrofolate, the biologically active metabolite of folic acid (p.1940). It is used as a food supplement and also has similar uses to folic acid.

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Biofolic; Furoic; Prefolic; ***USA:*** Deplin.

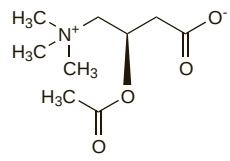
Multi-ingredient: ***USA:*** Cerefolin; Metanx.

Carnitine Derivatives

Acetylcarnitine Hydrochloride

Acetilcarnitina, hidrocloruro de; Acetyl-L-carnitine Chloride; Levacecarnine Hydrochloride; Levocarnitinum acetilum hydrochloricum; ST-200. (3-Carboxy-2-hydroxypropyl)trimethylammonium acetate (ester) chloride.

$C_9H_{17}NO_4$,HCl = 239.7.
CAS — 5080-50-2.
ATC — N06BX12.
ATC Vet — QN06BX12.



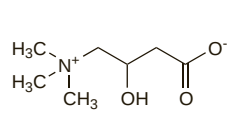
(acetyl-L-carnitine)

Carnitine *(rINN)*

Carnitina; Carnitinum; Karnitin; ST-198; Vitamin B_T. (3-Carboxy-2-hydroxypropyl)trimethylammonium hydroxide, inner salt; 3-Hydroxy-4-trimethylammoniobutyrate.

Карнитин

$C_7H_{15}NO_3$ = 161.2.
CAS — 461-06-3.

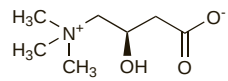


Levocarnitine *(BAN, USAN, rINN)*

L-Carnitine; L-Karnitin; Levocarnitina; Lévocarnitine; Levocarnitinum; Levokarnitiini; Levokarnitin; Levokarnitinas. (*R*)-(3-Carboxy-2-hydroxypropyl)trimethylammonium hydroxide, inner salt; (*R*)-3-Hydroxy-4-trimethylammoniobutyrate.

Левокарнитин

$C_7H_{15}NO_3$ = 161.2.
CAS — 541-15-1.
ATC — A16AA01.
ATC Vet — QA16AA01.



Pharmacopoeias. In *Eur.* (see p.vii) and *US.*

Ph. Eur. 6.2 (Levocarnitine). A white or almost white, hygroscopic, crystalline powder or colourless crystals. Freely soluble in water; soluble in warm alcohol; practically insoluble in acetone. A 5% solution in water has a pH of 6.5 to 8.5. Store in airtight containers.

USP 31 (Levocarnitine). White, hygroscopic, crystals or crystalline powder. Freely soluble in water and in hot alcohol; practically insoluble in acetone, in ether, and in benzene. pH of a 5% solution in water is between 5.5 and 9.5. Store in airtight containers.

Levocarnitine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de levocarnitina; Lévocarnitine, Chlorhydrate de; Levocarnitini Hydrochloridum. (*R*)-3-Hydroxy-4-trimethylammoniobutyrate hydrochloride.

Левокарнитина Гидрохлорид

$C_7H_{15}NO_3$,HCl = 197.7.
CAS — 6645-46-1.

Levocarnitine Propionate *(rINNM)*

L-Carnitine propionate; Lévocarnitine, Propionate de; Levocarnitini Propionas; Propionato de levocarnitina; Propionylcarnitine; L-Propionylcarnitine; Propionyl-L-carnitine; ST-261.

Левокарнитина Пропионат

$C_{10}H_{19}NO_4$ = 217.3.
CAS — 20064-19-1.

Levocarnitine Propionate Hydrochloride *(USAN)*

Propionyl-L-carnitine Hydrochloride; STI-261. (2*R*)-3-Carboxy-*N*,*N*,*N*-trimethyl-2-(propanoyloxy)propan-1-aminium chloride.

$C_{10}H_{20}ClNO_4$ = 253.7.
CAS — 119793-66-7.

Adverse Effects and Precautions

Gastrointestinal disturbances such as nausea, vomiting, diarrhoea, and abdominal cramps have been reported after the use of levocarnitine. Body odour has also been noticed in some patients, possibly due to the formation of the metabolite trimethylamine (see Fish Odour Syndrome, p.1923). Decreasing the dosage may reduce or eliminate these effects; oral levocarnitine should be consumed slowly to decrease gastrointestinal disturbances. Seizures have been reported.

Patients with severe renal impairment should not be given high oral doses of levocarnitine for long periods, because of the accumulation of the metabolites trimethylamine and trimethylamine-*N*-oxide. This is said not to occur to the same extent after intravenous dosage. Diabetic patients given carnitine while receiving insulin or hypoglycaemic drugs should be monitored for hypoglycaemia.

Renal impairment. Of 30 patients given DL-carnitine intravenously after dialysis sessions 3 developed myasthenia-like symptoms but when these 3 were given only levocarnitine the symptoms did not occur.[1] It was considered that in anuric uraemic patients the D-isomer was not excreted adequately and that accumulation had blocked neuromuscular transmission. It was therefore suggested that levocarnitine, rather than the DL-form, should be used. (High and prolonged oral doses of levocarnitine should, however, be avoided—see above.)

1. Bazzato G, *et al.* Myasthenia-like syndrome after but not - carnitine. *Lancet* 1981; **i:** 1209.

Pharmacokinetics

Oral doses of levocarnitine are absorbed slowly and incompletely from the small intestine. Bioavailability has been reported to be only about 10 to 15%, with peak plasma concentrations attained about 3 to 4 hours after an oral dose. Plasma concentrations after oral doses represent the sum of endogenous and exogenous material. Levocarnitine does not appear to bind to plasma proteins. It is mainly eliminated by the kidneys, undergoing extensive tubular reabsorption. After intravenous doses, levocarnitine appears to undergo minimal metabolism. Levocarnitine given orally may undergo degradation in the gastrointestinal tract, leading to the