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Including Recommended Dietary Intakes

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## VITAMIN C

### BACKGROUND

Vitamin C (L-ascorbic acid or ascorbate) is the generic descriptor for compounds having antiscorbutic activity. Most animals can synthesise vitamin C from D-glucose but humans and other primates, together with guinea pigs, fruit bats, some passeriform birds, some fish and some insects, are exceptions. Humans and primates lack a key enzyme, L-3 gulonolactone oxidase, necessary for the biosynthesis of vitamin C (Nishikimi et al 1994).

Vitamin C is a reducing agent (antioxidant) and it is likely that all of its biochemical and molecular functions relate to this property. In humans, vitamin C acts as an electron donor for eight enzymes, of which three are involved in collagen hydroxylation (including aspects of norepinephrine, peptide hormone and tyrosine metabolism) and two are involved in carnitine biosynthesis (Dunn et al 1984, Eipper et al 1993, 1992, Kaufmann 1974, Kirirkko & Myllyla 1985, Levine et al 1991, Procop & Kiviikko 1995, Peterkovsky 1991, Rebouche 1991). Vitamin C is found in high concentrations in gastric juices (Schorah et al 1991) where it may prevent the formation of N-nitroso-compounds, which are potential mutagens (Correa 1992).

Vitamin C has been shown to protect lipids in human plasma and low density lipoprotein in *ex vivo* experiments against oxidative damage (Frei 1991). But there is no evidence of *in vivo* protection. Vitamin C also interacts with other nutrients. It aids in the absorption of iron and copper (Hallberg 1985, Harris & Perceval 1991), the maintenance of glutathione in the reduced form (Henning et al 1991, Johnston et al 1993), the regeneration, or sparing, of alpha-tocopherol (Halpner et al 1998) and the stabilisation of folate (Stokes et al 1975).

Ascorbate is found widely in fruits and vegetables. Fruits such as blackcurrants, guava, citrus, and kiwi fruit and vegetables such as broccoli and sprouts are good sources. The Australian bush food *terminalia ferdinandiana* is the richest source (Brand et al 1982). However, because of their longer periods of availability, vegetables often contribute more ascorbate to the diet than fruits. In Australia, some 40% of the vitamin C comes from vegetables and 19% from fruits and a further 27% from fruit and vegetable juices (ABS 1998). Vitamin C is very labile and its content in foods varies. Vitamin C content can be affected by season, transport, shelf life, storage time, cooking practices and chlorination of water. Cutting, bruising, heating and exposure to copper, iron or mildly alkaline conditions can destroy ascorbate. It can also be leached into water during cooking.

Intestinal absorption of vitamin C occurs through a sodium-dependent active transport process that is saturable and dose dependent (Rumsey & Levine 1998, Tsao 1997). Kallner et al (1979) showed that some 70–90% of usual intake is absorbed and that absorption fell to 50% or less with increasing doses above 1 g/day. Dose-dependent absorption and renal regulation of ascorbate allow conservation of vitamin C in the body during periods of low intake and regulation of plasma levels at high intakes.

There is a sigmoidal relationship between intake and plasma concentration of vitamin C (Levine et al 1996, Newton et al 1983). Newton et al (1983) showed that for intakes up to 30 mg/day, plasma concentrations are about 11  $\mu\text{mol/L}$  (or 0.2 mg/dL). Above this intake, plasma concentrations increase steeply to 60  $\mu\text{mol/L}$  and plateau at 80  $\mu\text{mol/L}$ , the renal threshold. Levine et al (1996) found that the steep portion of the plasma concentration curve occurred with a daily dose of vitamin C of between 30 and 100 mg and that complete saturation occurred at 1,000 mg daily. Close to steady states, plateau concentrations are reached above 200 mg/day. Absorption is also to some extent dependent on the dosing regimen of vitamin C. For example, there would be better absorption with 250 mg as supplements taken four times daily than 1,000 mg taken once daily.

High levels of vitamin C are found in the pituitary and adrenal glands, leukocytes, eye tissues and fluids and the brain (Horning et al 1975). The biologic half-life of vitamin C is 8–40 days (Kallner et al 1979) and catabolic turnover varies widely, averaging 2.9% over a wide range of intakes (Baker et al 1971). A body pool of less than 300–400 mg is associated with the symptoms of scurvy (Baker et al 1969).

At saturation, the whole body content in males is about 20 mg/kg or 1,500 mg (Baker et al 1969, Kallner et al 1979).

Plasma vitamin C concentrations are reduced by 40% in male smokers. This may be partly due to smokers tending to eat less fruits and vegetables, but after correcting for intakes of fruit and vegetables, smokers still show lower plasma ascorbate than non-smokers (Lykkesfeldt et al 2000). The metabolic turnover of ascorbate is markedly accelerated in smokers (Kallner et al 1981).

Vitamin C deficiency causes scurvy, symptoms of which include skeletal and vascular lesions with gingival changes, pain in the extremities, haemorrhage, oedema, ulcerations and death. In adults, clinical signs occur at intakes of 7–8 mg/day or less (Goldsmith 1961, Rajajalakshmi et al 1965, van Eekelen 1953). In infantile scurvy, the changes are mainly at the sites of active bone growth and include a pseudoparalysis of the limbs (McLaren 1992).

There are several potential indices of vitamin C requirements in humans, including assessment of clinical outcomes, vitamin C turnover and biochemical indices of status (eg plasma, urine, leukocyte). Some studies have raised the question of whether vitamin C has beneficial effects on normal human subjects at intakes, and tissue levels, considerably greater than those needed to prevent or cure scurvy. However, the evidence has been conflicting. There is potential confounding in food intake studies related to the issue of concomitant intakes of other protective nutrients in fruits and vegetables, such as phytochemicals. In addition, studies generally do not provide the dose-response data on which average requirements can be ascertained (COMA 1991, FNB:IOM 2000, FAO:WHO 2002).

As a result, the estimates of vitamin C requirements in this report are based on prevention of scurvy, vitamin C turnover studies and biochemical indices of vitamin C status in man.

## RECOMMENDATIONS BY LIFE STAGE AND GENDER

<b>Infants</b>	<b>AI</b>	<b>Vitamin C</b>
0–6 months	25 mg/day	
7–12 months	30 mg/day	

**Rationale:** Breast milk concentration varies widely according to maternal intake and does not necessarily reflect infant needs (Irwin & Hutchins 1976, Olson & Hodges 1987, van Zoeren-Grobbe et al 1987). Human milk generally can vary from 30 mg/L to 80 mg/L or more, depending on the intake of the mother (Bates & Prentice 1988, WHO 1998). Clinical scurvy has not been observed in fully breast-fed infants, even in communities where the vitamin C intakes of the mothers are low. Scurvy is seen only at intakes of about 7–8 mg/day or less, generally in non-breast-fed babies. The AI for 0–6 months was therefore calculated by multiplying together the average intake of breast milk (0.78 L/day) and a breast milk concentration of 30 mg/L, and rounding up. The AI for 7–12 months was calculated on a body weight basis from that of younger infants.

<b>Children &amp; adolescents</b>	<b>EAR</b>	<b>RDI</b>	<b>Vitamin C</b>
<b>All</b>			
1–3 yr	25 mg/day	35 mg/day	
4–8 yr	25 mg/day	35 mg/day	
<b>Boys</b>			
9–13 yr	28 mg/day	40 mg/day	
14–18 yr	28 mg/day	40 mg/day	
<b>Girls</b>			
9–13 yr	28 mg/day	40 mg/day	
14–18 yr	28 mg/day	40 mg/day	

**Rationale:** In the absence of adequate data for children and following the approach of the FAO/WHO (2002), the EARs were interpolated from the adult and infant recommendations, although these figures are somewhat arbitrary. The RDI was set assuming a CV of 20% for the EAR, as for adults.

<b>Adults</b>	<b>EAR</b>	<b>RDI</b>	<b>Vitamin C</b>
<b>Men</b>			
19–30 yr	30 mg/day	45 mg/day	
31–50 yr	30 mg/day	45 mg/day	
51–70 yr	30 mg/day	45 mg/day	
>70 yr	30 mg/day	45 mg/day	
<b>Women</b>			
19–30 yr	30 mg/day	45 mg/day	
31–50 yr	30 mg/day	45 mg/day	
51–70 yr	30 mg/day	45 mg/day	
>70 yr	30 mg/day	45 mg/day	

**Rationale:** The EAR for adult men was set on the assumption that the best indicator of adequacy currently available is the intake at which body content is halfway between tissue saturation and the point at which clinical signs of scurvy appear. This equates to 900 mg body content. Assuming an absorption efficiency of 85%, a catabolic rate of 2.9%, and rounding, the EAR for adults was set at 30 mg/day ( $900 \times 2.9/100 \times 100/85$ ). This EAR provides enough vitamin C for smokers. There is a known CV for catabolism of 21% (2.9%/day, SD = 0.6%) (Baker et al 1971) which, with rounding, gives an RDI of 45 mg/day. Plasma concentrations of vitamin C fall more rapidly in women than men (Blanchard 1991), so the male recommendation was retained for women although women have lower body sizes.

<b>Pregnancy</b>	<b>EAR</b>	<b>RDI</b>	<b>Vitamin C</b>
14–18 yr	38 mg/day	55 mg/day	
19–30 yr	40 mg/day	60 mg/day	
31–50 yr	40 mg/day	60 mg/day	

**Rationale:** There is a moderate drain on vitamin C during pregnancy, particularly in the last trimester, probably due to haemodilution as well as transfer to the fetus. Given that 7 mg/day will prevent scurvy in young infants, (Goldsmith 1961, Rajalalakshmi et al 1965, van Eekelen 1953), an extra 10 mg/day in pregnancy should enable reserves to accumulate to meet the extra demands of the growing fetus. The EAR is therefore set at 40 (or 38) mg/day and the RDI set assuming a CV for the EAR of 20%, and rounding up.

<b>Lactation</b>	<b>EAR</b>	<b>RDI</b>	<b>Vitamin C</b>
14–18 yr	58 mg/day	80 mg/day	
19–30 yr	60 mg/day	85 mg/day	
31–50 yr	60 mg/day	85 mg/day	

**Rationale:** The EARs for lactation are estimated from the EAR for non-lactating women plus needs for the infant. The RDI is set assuming a CV for the EAR of 20%.

## UPPER LEVEL OF INTAKE - VITAMIN C

**It is not possible to establish a UL for vitamin C, but 1,000 mg/day is a prudent limit.**

**Rationale:** It is not possible to establish with any certainty a UL for supplementary vitamin C, as data are too inconclusive. However, expert bodies have suggested that intakes of no more than 1,000 mg/day for adults would be prudent (UK Expert Group on Vitamins and Minerals 2003, German Nutrition Society 2002).

The UK Expert Group on Vitamins and Minerals (2002) has suggested a guidance level of 1,000 mg based on a LOAEL of 3,000–4,000 mg/day from the study of Cameron & Campbell (1974), applying an UF of 3 to extrapolate to a NOAEL of 1,000 mg/day. The US Food and Nutrition Board used the same data but applied an UF of only 1.5 to give a NOAEL of 2,000 mg which it adopted as the Tolerable Upper Intake for adults ranging down to 400 mg in children aged 1–3 years.

Gastrointestinal effects are the most common adverse effects associated with acute, high doses of vitamin C given over a short period of time. Other reported effects include metabolic acidosis, changes in prothrombin activity and 'conditioned need' scurvy (low ingestion in pregnancy conditioning the need for higher amounts in the infant). It has also been suggested that vitamin C consumption may increase oxalate excretion. However, studies in humans have not revealed a substantial increase in urinary oxalate stones with high intakes of vitamin C. Key studies include those of Auer et al (1998), Cameron & Campbell (1974), Cook et al (1984), Gokce et al (1999), Levine et al (1996, 1999), Mai et al (1990), Morton et al (2001), Urivetsky et al (1992), and Wandilak et al (1994). These studies suggest that vitamin C is not associated with significant adverse effects and there are no obvious specific key toxic endpoints.

Vitamin C can also enhance non-haem iron absorption and thus may increase iron-induced tissue damage in individuals with haemochromatosis (McLaran et al 1982). Haemochromatosis is a condition of glucose-6-phosphate dehydrogenase deficiency that occurs in about 1 in 300 people of northern European descent (George & Powell 1997). However, the possibility of such adverse effects in this group has not been systematically examined.

## REFERENCES

- Auer BL, Auer D, Rodgers AL. The effect of ascorbic acid ingestion on the biochemical and physiochemical risk factors associated with calcium oxalate kidney stone formation. *Clin Chem Lab Med* 1998;36:143–8.
- Australian Bureau of Statistics: Department of Health and Aged Care. *National nutrition survey. Nutrient intakes and physical measurements. Australia, 1995*. Canberra: Australian Bureau of Statistics, 1998.
- Baker EM, Hodges RE, Hood J, Sauberlich HE, March SC. Metabolism of ascorbic-1-<sup>14</sup>C acid in experimental human scurvy. *Am J Clin Nutr* 1969;22:549–58.
- Baker EM, Hodges RE, Hood J, Sauberlich HE, March SC. Metabolism of <sup>14</sup>C and <sup>3</sup>H labelled L-ascorbic acid in human scurvy. *Am J Clin Nutr* 1971;24:444–54.
- Bates CJ, Prentice A. Vitamins, minerals and essential trace elements. In: Bennett P ed. *Drugs and human lactation*. Amsterdam:Elsevier,1988. Pp 433–93.
- Blanchard J. Depletion and repletion kinetics of vitamin C in humans. *J Nutr* 1991;121:170–6.
- Brand JC, Cherikoff V, Lee A, Truswell AS. An outstanding food source of vitamin C. *Lancet* 1982;2:873.
- Cameron E, Campbell A. The ortho-molecular treatment of cancer. II Clinical trial of high dose ascorbic acid supplements in advanced human cancer. *Chem Biol Interact* 1974;9:285–315.

- Committee on Medical Aspects of Food Policy. *Dietary Reference Values for food energy and nutrients for the United Kingdom. Report on the panel on Dietary Reference Values*. London: HMSO, 1991.
- Cook JD, Watson SS, Simpson KM, Lipschitz DA, Skikne BS. The effect of high ascorbic acid supplementation on body iron stores. *Blood* 1984;64:721–6.
- Correa, P. Human gastric carcinogenesis: a multistep and multifactorial process--First American Cancer Society Award Lecture on Cancer Epidemiology and Prevention. *Cancer Res* 1992;52:6735–40.
- Dunn WA, Rettura G, Seifter E, England S. Carnitine biosynthesis from gamma-butyrobetaine and from exogenous protein-bound 6-N-trimethyl-L- Lysine by the perfused guinea pig liver. Effect of ascorbate deficiency on the in situ activity of gamma-butyrobetaine hydroxylase. *J Biol Chem* 1984;259:10764–70.
- Eipper B, Stoffers DA, Mains RE. The biosynthesis of neuropeptides: peptide alpha amidation. *Ann Rev Neurosci* 1992;15:57–85.
- Eipper B, Milgram SL, Husten EJ, Yun H, Mains RE. Peptidylglycine alpha amidating monooxygenase: a multifunctional protein with catalytic, processing and routing domains. *Protein Sci* 1993;2:489–97.
- Expert Group on Vitamins and Minerals. *Safe upper levels for vitamin and minerals*. London: Food Standards Agency, 2003.
- Food and Nutrition Board: Institute of Medicine. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium and Carotenoids*, Washington, DC: National Academy Press, 2000.
- Frei B. Ascorbic acid protects lipids in human plasma and low-density lipoprotein against oxidative damage. *Am J Clin Nutr* 1991;54(6 Suppl):1113S–1118S.
- George DK, Powell LW. The screening, diagnosis and optimal management of haemochromatosis. *Aliment Pharmacol & Therap* 1997;11:631–9.
- German Nutrition Society (DGE), Austrian Nutrition Society (ÖGE), Swiss Society for Nutrition Research (SGE) Swiss Nutrition Association (SVE) *Reference Values for Nutrient Intake*. Bonn: German Nutrition Society, 2002.
- Gokce N, Keaney JF Jr, Frei B, Holbrook M, Olesiak M, Zachariah BJ, Leeuwenburgh C, Heinecke JW, Vita JA. Long-term ascorbic acid administration reverses endothelial vasomotor dysfunction in patients with coronary artery disease. *Circulation* 1999;99:3234–40.
- Goldsmith GA. Human requirements for vitamin C and its use in clinical medicine. *Ann NY Acad Sci* 1961;92:230–45.
- Hallberg L. The role of vitamin C in improving the critical iron balance situation in women. *Int J Vitam Nutr Res* 1985;27:177–87.
- Halpner AD, Handelman GJ, Belmont CA, Harris JM, Blumberg JB. Protection by vitamin C of oxidant-induced loss of vitamin E in rat hepatocytes. *J Nutr Biochem* 1998;9:355–9.
- Harris ED, Perceval SS. A role for ascorbic acid in copper transport. *Am J Clin Nutr* 1991;54:1193S–1197S.
- Henning SM, Zhang JZ, McKee RW, Swendseid ME, Jacob RA. Glutathione blood levels and other oxidant defence indices in men fed diets low in vitamin C. *J Nutr* 1991;121:1969–75.
- Hornig D. Distribution of ascorbic acid, metabolites and analogues in man and animals. *Ann NY Acad Sci* 1975;258:103–18.
- Irwin MI, Hutchins BK. A conspectus of research on vitamin C requirements in man. *J Nutr* 1976;106:821–79.
- Johnston CS, Meye CG, Srilakshmi JC. Vitamin C elevates red blood cell glutathione in healthy adults. *Am J Clin Nutr* 1993;58:103–5.
- Kallner A, Hartmann D, Hornig D. Steady-state turnover and body pool of ascorbic acid in man. *Am J Clin Nutr* 1979;32:530–9.

- Kallner A, Hartmann D, Hornig D. On the requirements of ascorbic acid in man: steady-state turnover and body pool in smokers. *Am J Clin Nutr* 1981;34:1347–55.
- Kaufmann S. Dopamine-beta-hydroxylase. *J Psychiatr Res* 1974;11:303–16.
- Kirirkko KI, Myllyla RS. Post-translational processing of procollagens. *Ann NY Acad Sci* 1985;460:187–201.
- Levine M, Dhariwal KR, Washko PW, Butler JD, Wang YH, Bergsten P. Ascorbic acid and in situ kinetics: a new approach to vitamin requirements. *Am J Clin Nutr* 1991;54:1157S–1162S.
- Levine M, Conry-Cantilena C, Wang Y, Welch RW, Washko PW, Dhariwal KR, Park JB, Lazarev A, Graumlich JK. Vitamin C pharmacokinetics in healthy volunteers: evidence for a Recommended Dietary Allowance. *Proc Natl Acad Sci* 1996; 93:3704–9.
- Levine M, Rumsey SC, Daruwala R, Park JB, Wang Y. Criteria and recommendations for vitamin C intake. *JAMA* 1999;281:1415–23.
- Lykkesfeldt J, Christen S, Wallock LM, Change HH, Jacob RA, Ames BN. Ascorbate is depleted by smoking and repleted by moderate supplementation: a study in male smokers and non-smokers with matched dietary antioxidant intakes. *Am J Clin Nutr* 2000;71:530–6.
- Mai J, Sorensen Z, Hansen JC. High dose antioxidant supplementation to MS patients. Effects on glutathione peroxidase, clinical safety and absorption of selenium. *Biol Tr Elem Res* 1990;24:109–17.
- McLaran CJ, Bett JHN, Nye JA, Halliday JW. Congestive cardiomyopathy and haemochromatosis – rapid progression possibly accelerated by excessive ingestion of ascorbic acid. *Aust NZ J Med* 1982;12:187–9
- McLaren DS. *A colour atlas of nutritional disorders*. London: Wolfe Medical Publications, 1992.
- Morton DJ, Barrett-Connor EWL, Schneider DL. Vitamin C supplement use and bone mineral density in postmenopausal women. *J Bone Miner Res* 2001;16:135–40.
- Newton HMV, Morgan DB, Schorah CJ, Hullin RP. Relation between intake and plasma concentration of vitamin C in elderly women. *Br Med J* 1983;287:1429.
- Nishikimi M, Fukuyama R, Minoshima S, Shimizu N, Yagi K. Cloning and chromosomal mapping of the human non-functional gene for L-gulonogamma-lactone oxidase, the enzyme for L-ascorbic acid biosynthesis missing in man. *J Biol Chem* 1994;269:13685–8.
- Olson JA, Hodges RE. Recommended dietary intakes (RDI) of vitamin C in humans. *Am J Clin Nutr* 1987;45:693–703.
- Peterkovsky B. Ascorbate requirement for hydroxylation and secretion of procollagen: relationship to inhibition of collagen synthesis in scurvy. *Am J Clin Nutr* 1991;54:1135S–1140S.
- Procop DJ, Kiviikko KI. Collagens: molecular biology, diseases and potential for therapy. *Annu Rev Biochem* 1995;64:403–34.
- Rajalakshmi R, Deodhar AD, Ramakrishnan CV. Vitamin C secretion during lactation. *Acta Paediatr Scand* 1965;54:375–82.
- Rebouche CJ. Ascorbic acid and carnitine biosynthesis. *Am J Clin Nutr* 1991;54:1147S–1152S.
- Report of a joint FAO:WHO expert consultation, Bangkok Thailand. *Human Vitamin and Mineral Requirements*. Rome: Food and Agricultural Organization, 2002.
- Rumsey SC, Levine M. Absorption, transport and disposition of ascorbic acid in humans. *J Nutr Biochem* 1998;9:116–30.

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- Schorah CJ, Sobala GM, Sanderson M, Collis N, Primrose JM. Gastric juice ascorbic acid: effects of disease and implications for gastric carcinogenesis. *Am J Clin Nutr* 1991;53:287S–293S.
- Stokes PL, Melikian V, Leeming RL, Portman-Graham H, Blair JA, Cooke WT. Folate metabolism in scurvy. *Am J Clin Nutr* 1975;28:126–9.
- Tsao CS. An overview of ascorbic acid chemistry and biochemistry. In: Packer L, Fuchs J eds. *Vitamin C in health and disease*. New York: Marcel Dekker, 1997. Pp 25–58.
- Urivetsky M, Kessar D, Smith AD. Ascorbic acid overdosing: a risk for calcium oxalate nephrolithiasis. *J Urol* 1992;147:1215–8.
- Van Zoeren-Grobbe D, Schrijver J, van den Berg GJ, Berger HM. Human milk vitamin content after pasteurisation, storage or tube feeding. *Arch Dis Child* 1987;62:161–5.
- Van Eekelen M. Occurrence of vitamin C in foods. *Proc Nut Soc* 1953;12:228–32.
- Wandilak TR, D'Andre SD, Davis PA, Williams HE. Effect of high dose vitamin C on urinary oxalate levels. *J Urol* 1994;156:834–7.
- World Health Organization. Complementary feeding of young children in developing countries: a review of current scientific knowledge. Geneva: World Health Organization, 1998.