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Nutrient Reference Values for Australia and New Zealand
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 lands, 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

Infants	AI	Vitamin C
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.

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

Adults	EAR	RDI	Vitamin C
Men			
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	
Women			
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.

Pregnancy	EAR	RDI	Vitamin C
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.

Lactation	EAR	RDI	Vitamin C
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.

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