17. Vitamin C

17.1 Functions and essentiality

17.1.1 Essential and undisputed roles of vitamin C (ascorbic acid) in man are to prevent scurvy and to aid wound healing. It also assists in the absorption of non-haem iron, and because of its potential for reaction with destructive free radical containing oxygen, it is an important antioxidant. However, ascorbic acid may exhibit pro-oxidant properties in the presence of certain metal ions and oxygen, and these pro-and anti-oxidant activities are reflected in its role as a cofactor, modulator or protective agent in a senes of essential mixed function oxidase enzyme reactions.

17.1.2 Vitamin C is one of the most labile nutrients in the diet, easily destroyed by oxygen, metal ions, increased pH, heat or light. The richest sources are citrus and soft fruits and the growing points of vegetables, whereas unsprouted cereals and their products contain virtually none.

17.1.3 The most definitive evidence for essentiality has come from experimen tal depletion and repletion studies in adult human volunteers. In the MRC Sheffield study[1] and in Iowa[2] the most characteristic clinical signs of diet-induced vitamin C deficiency were failure of hair follicle eruption, the occurrence of petechial haemorrhages spreading to sheet haemorrhage on the limbs, and bleeding gums. Impairment of connective tissue formation within wound repair tissue was frequently seen, and a wide range of other signs and symptoms was reported, but less often.

17.1.4 Many 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. These studies have included examination of indices as diverse as histamine removal[3]; cholesterol turnover[4]; physical working capacity[5,6]; immune function[7]; male fertility[8]; gingival collagen[9]; nitrosamine and carcinogenesis prevention[10] and selenium or iron utilisation[11,12]. Despite scientific concern about such questions, it is impossible to base estimates of requirements directly upon the evidence of these studies, partly because the evidence is conflicting in many areas, partly because those studies which have noted a positive benefit of vitamin C supplements have not defined the minimum dietary requirement needed to achieve it, and partly because specific design features have made the interpretation difficult in many cases. Because of these and other difficulties, the Panel decided to base their estimates of vitamin C requirements mainly upon the prevention of scurvy, on vitamin C turnover studies, and on biochemical indices of vitamin C status in man.

17.2 **Requirements**

17.2.1 In normal adults, about 2.7 per cent of the exchangeable body pool of ascorbic acid is degraded each day[13,14]. This is independent of body pool size, so that at zero intake there is a first-order rate of loss from the tissues. When the body pool falls to 300 mg or less there is evidence of impaired function[2]. Leukocyte or buffy coat vitamin C levels generally change in parallel with those of most other organs and tissues, and a lower limit of 15 μg/10^8 cells is frequently accepted as an indicator of deficiency. Plasma vitamin C levels are more sensitive to recent intake, with values less than 11 μmol/L (0.2 mg/100 ml) indicating biochemical depletion[15].

17.2.2 The amount of vitamin C required by human adults (mainly males) to prevent and cure scorbutic signs and symptoms has been carefully investigated. Nearly all individuals who received no morp than 1 mg/d for 3-6 months from a specially vitamin C-depleted but otherwise adequate diet developed mild clinical signs of scurvy, whereas those who received 10 mg/d did not. 10 mg/d was also sufficient to cure clinical signs of scurvy in an already-depleted group[1]. Although three subjects who received 10 mg/d for 23 weeks and then only 3.2-4.5 mg/d for 28 weeks showed no clinical signs, a recent study has indicated that an intake of 5 mg/d may be insufficient for gum protection[16].

17.2.3 These studies indicated that the requirement to prevent and cure scurvy in men is less than 10 mg/d. The minimum requirement of women has not been determined, but as women maintain higher blood levels of vitamin C for a given intake than men, their requirements, except perhaps during reproduction, are likely to be less. However, although 10 mg/d is sufficient to protect against scurvy, it is not sufficient to maintain measurable amounts of ascorbate in the plasma, and it leads to a low buffy coat ascorbate level. The Panel therefore judged the safety margin to be insufficient with this intake, and turned to the consideration of biochemical indices.

17.2.4 *Adults* Figure 17.1 shows the sigmoidal relationship between vitamin C intake and plasma ascorbate levels[17,19]. Both men and women exhibit very low plasma levels at intakes between 0 and 30 mg/d, which rise steeply between 30 and 70 mg/d, and approach an upper plateau between 70 and 100 mg/d. Measurable amounts of ascorbic acid begin to circulate in the plasma of most people at an intake of 40 mg/d, and this is available for transfer between the tissues and to sites of depletion or damage. The Panel therefore selected this as the RNI for both men and women. Women probably need less when not in a reproductive cycle, but more during reproduction, including the periconceptual period. An adult will maintain an exchangeable body pool of about 900 mg at this intake, which can provide at least 1 month's safety interval, even on a zero intake, before the pool falls to 300 mg[20]. An LRNI of 10 mg/d for adults is compatible with studies of scurvy prevention in the UK[1], and elsewhere, on the basis that protection against clinical deficiency signs is provided but no margin of safety against further loss. By interpolation, the EAR was calculated as 25 mg/d (Table 17.1).

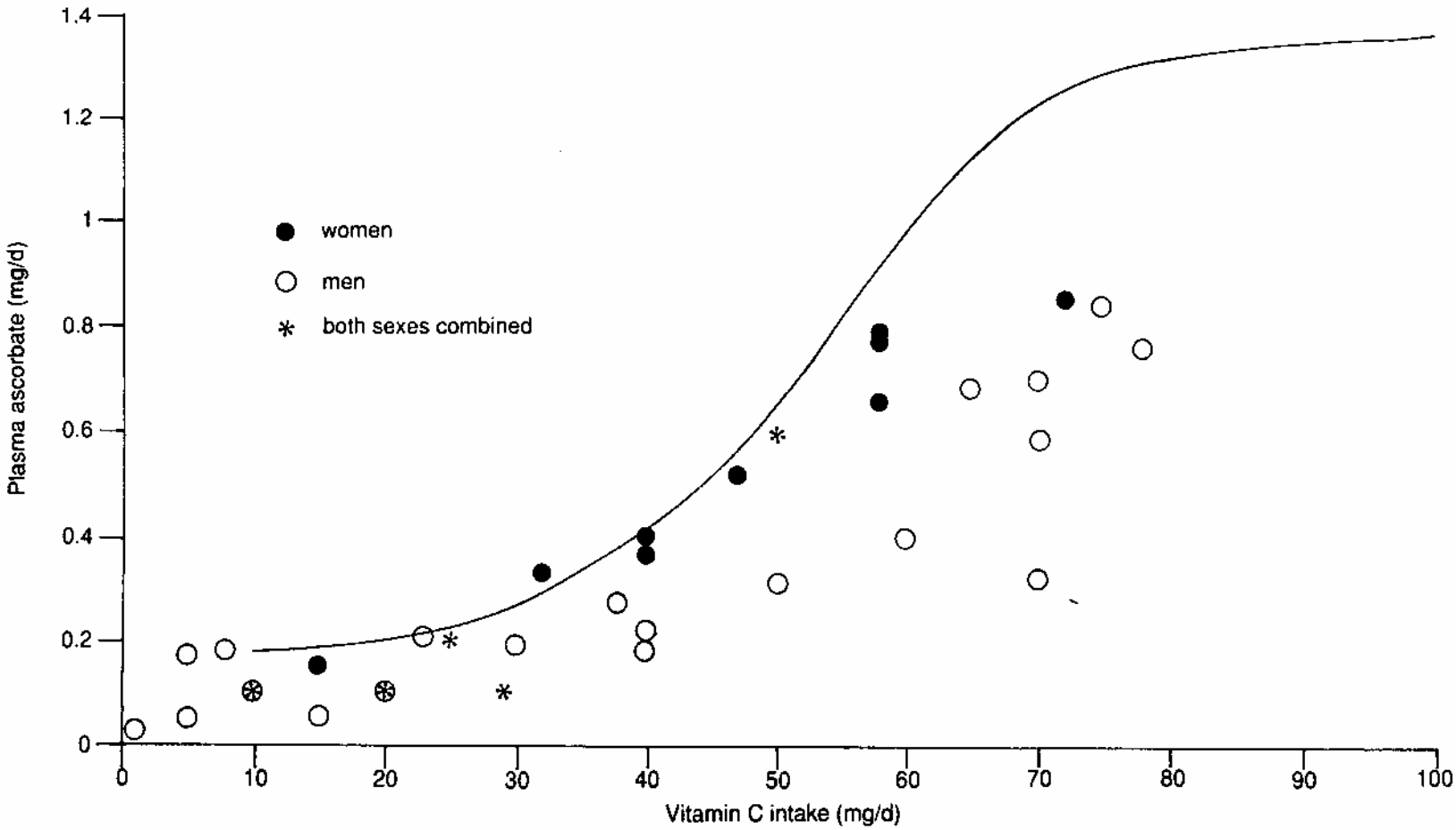

Figure 17.1 Relationship between plasma ascorbic acid concentration and vitamin C intake, in adult human subjects

The continuous line represents a study of elderly women by Newton *et al*[23]. The individual points are mean values compiled from other published studies on this relationship in adult subjects (the data from these represented only part of the range being considered).

●: women ○:men

X: both sexes combined.

17.2.5 *Pregnancy and lactation* During pregnancy there is a moderate extra drain on tissue stores, especially towards the final stages of pregnancy, since the fetus concentrates the vitamin at the expense of maternal stores and circulating vitamin levels. The Panel has increased the RNI by 10 mg/d during the third trimester for this purpose. During lactation, an intake of 70 mg/d ensures that maternal stores are maintained and that breast milk levels are in the upper half of the physiological range for human milk. This represents an increase in the DRVs of 30 mg/d throughout lactation.

17.2.6 *Children* Clinical scurvy has not been observed in fully breast-fed infants, even in communities where mothers' vitamin C intakes are extremely low. Although ascorbate in breast milk may vary from 30 to 80 mg/L depending on the intake of the mother[21], the provision of 25 mg/d from breast milk appears to be adequate for infants, and the Panel has set this as the RNI for infants. RNIs for children were interpolated between this and the RNI for adults (Table 17.1). Infants fed on dried milks providing 5 mg/d do not develop scurvy, and this, together with their body pool size estimates, support an LRNI of 6 mg/d for infants. Values for children have been scaled down proportionately from those for adults (Table 17.1).

17.2.7 *The elderly* In the UK, elderly people may have low blood vitamin C levels, low body stores, and occasionally even overt clinical deficiency signs.

Table 17.1 *Dietary Reference Values for Vitamin C* (mg/d)

Age	Lower Reference Nutrient Intake	Estimated Average Requirement	Reference Nutrient Intake
0-3 months	6	15	25
4-6 months	6	15	25
7-9 months	6	15	25
10-12 months	6	15	25
1-3 years	8	20	30
4-6 years	8	20	30
7-10 years	8	20	30
Males			
11-14 years	9	22	35
15-18 years	10	25	40
19-50 years	10	25	40
50+ years	10	25	40
Females			
11-14 years	9	22	35
15-18 years	10	25	40
19-50 years	10	25	40
50+ years	10	25	40
Pregnancy			+ 10
Lactation:			
0-4 months			+ 30
4+ months			+ 30

However, most deficient individuals have persistently low intakes, and there is no compelling evidence for an increased requirement in old age[23,24].

17.2.8 *Smokers* Several recent studies have indicated that smokers have an increased turnover of vitamin C. To maintain their body pool and circulating levels near those of non-smokers, their intake would need to be greater by up to 80 mg/d[25,26].

17.3 **Guidance on high intakes** Claims that intakes of vitamin C above those necessary to cure scurvy can protect from, or cure, various diseases, tissue damage or improve general health, are still being assessed. Possible risks associated with high intakes include diarrhoea at intakes of grams/d; increased production of oxalate, and hence of kidney stones in a small group of individuals with an unusually high propensity for oxalate synthesis[27]; and 'systemic conditioning', whereby the sudden cessation of high intakes may precipitate scurvy, through enhanced turnover.

17.4 **Research needs** Future research effort should include a) further classi fication of the biological functions of vitamin C; b) further studies on vitamin C turnover; c) studies of the requirements of different groups within the population, and d) identification of possible benefits or detrimental effects of high intakes.

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