Water-Soluble Vitamins

VITAMIN C (ASCORBIC ACID)

Two forms of vitamin C are recognized, ascorbic acid and dehydro-ascorbic acid. Although most of the vitamin exists as ascorbic acid, both forms appear to be utilized similarly by the human (Sabry *et al.*, 1958). Many species of animals are able to synthesize ascorbic acid and do not require it in the diet. When deprived of a dietary source of vitamin C for a sufficient length of time, man, along with other primates and several other species, develops scurvy, a potentially fatal disease characterized by weakening of collagenous structures, which results in widespread capillary hemorrhaging (Vilter, 1967; Hornig, 1975; Woodruff, 1975). Well-defined scurvy is not now common in the United States; it occurs chiefly in infants fed diets deficient in ascorbic acid, such as diets consisting exclusively of cows' milk, and in aged persons on limited diets. In adults the occurrence of scurvy is usually associated with poverty, alcoholism, and nutritional ignorance. Specific biochemical functions of vitamin C have not been well defined. Vitamin C has been implicated in the hydroxylation of proline in the formation of collagen (Barnes, 1975; Myllyla *et al.*, 1978), and ascorbic acid deficiency is associated with impaired wound healing (Schwartz, 1970; Levenson *et al.*, 1971). Vitamin C may also be involved in the metabolic reactions of amino acids such as tyrosine (Steele *et al.*, 1952; La Du and Zannoni, 1961), in microsomal drug metabolism (Zannoni and Sato, 1975), in the synthesis of epinephrine and anti-inflammatory steroids by the adrenal gland (Stone and Townsley, 1973; Deana *et al.*, 1975), in folic acid metabolism (Thien

et al., 1977; Stokes *et aL*, 1975), and in leucocyte functions (Shilotri, 1977a, 1977b). The absorption of iron is increased by dietary ascorbic acid when the two nutrients are ingested simultaneously. This enhancement of iron absorption is observed when the ascorbic acid content of the meal is 25-75 mg or more (Monsen *et al.*, 1978) (see the section on Iron).

Vitamin C is present in relatively large amounts in fresh, canned, and frozen citrus fruits and in important amounts in other fruits, tomatoes, potatoes, and leafy vegetables. Vitamin C in foods is heat labile and easily destroyed by oxidation. Therefore, prolonged cooking at high temperatures and undue exposure to oxygen, copper, and iron should be avoided. Isoascorbic acid (erythroascorbic acid), which possesses little if any vitamin C biological value for the human, is often used as a preservative in foods (LSRO, 1978). Commonly used analytical procedures do not distinguish this compound from ascorbic acid.

Basis for Allowance

The human requirement for vitamin C has been estimated from the amount of vitamin C necessary to prevent or cure scurvy, the amount metabolized by the body daily, and the amount necessary to maintain adequate reserves (Irwin and Hutchins, 1976).

A daily intake of 10 mg of ascorbic acid has been observed to be adequate to alleviate and cure the clinical signs of scurvy in human subjects (Bartley *et al.*, 1953; Hodges *et al.*, 1969, 1971). However, this amount does not provide for acceptable reserves of the vitamin.

In the absence of a functional biochemical measurement that relates to vitamin C status, evaluation of adequacy has been derived from measuring ascorbate levels in serum or plasma, leukocytes, whole blood, red cells, and urine. These measurements correlate with vitamin C intake, but studies seeking to establish the dietary ascorbic acid required to maintain "acceptable" levels have resulted in a wide range of recommendations (see Irwin and Hutchins, 1976).

At the onset of scurvy, plasma ascorbate levels range from 0.13 to 0.24 mg/dl (Hodges *et al.*, 1971). Serum ascorbate levels of approximately 0.75mg/dl are attained with vitamin C intakes of 60-75mg/day (Dodds and McLeod, 1947; Hodges *et al.*, 1971; Sauberlich, 1975). Higher serum levels are attainable with higher intakes of ascorbic acid. Maximal serum ascorbic acid appears to be about 1.4 mg/dl, at which point renal clearance of the vitamin rises sharply (Friedman *et al.*, 1940). Intakes of vitamin C of over 60 mg/day are required for satu-

ration of the leukocytes of the adult human (Burch, 1961; Davey *et al.*, 1952; Morse et al., 1956; Sauberlich, 1975).

Use of radioactive ascorbic acid has permitted detailed studies on metabolism, turnover rates, elimination rates, and size of body pool of ascorbic acid. Healthy male adults have a body ascorbate pool in excess of 1500 mg (Baker *et al*, 1971; Hodges *et al*, 1971; Kallner *et al.*, 1979). Males with intakes of approximately 200 mg of vitamin C per day were observed to have an ascorbate body pool of 2300-2800 mg (Baker *et al*, 1966). In subsequent studies also utilizing radioactive ascorbic acid, adult males receiving a constant vitamin C intake of 77.5 mg/day had a body pool of 1490-1560 mg of ascorbic acid (Baker *et al.*, 1971; Hodges *et al.*, 1971).

In depletion studies, when the body pool fell below 300 mg, clinical symptoms of scurvy were observed. However, psychological changes were observed when the pool had been depleted to 600 mg (Kinsman and Hood, 1971). During depletion, vitamin C was catabolized at a rate of approximately 3 percent of the body pool per day, with a biological variation from subject to subject (range, 2.2-4.1 percent) (Baker *et al.*, 1969, 1971; Hodges *et al.*, 1971). Thus the subject with an ascorbate pool of 1500 mg and a utilization rate of 2.2 percent catabolized 34 mg of ascorbic acid daily. With a utilization rate of 4.4 percent, 61.5 mg of ascorbic acid would be catabolized daily (Baker *et al*, 1968; 1969). Using a pharmacokinetic approach, Kallner *et al* (1979) reported a similar total turnover of about 60 mg/day to maintain a body pool of 1500 mg.

Baker *et al.* (1969, 1971) reported that, in vitamin C-depleted subjects, the rate of repletion was proportional to the daily ascorbic acid intake, and the body ascorbate pool returned to 1500 mg before ascorbic acid was detected in the urine, although symptoms of scurvy receded in the majority of subjects when the body pool reached 300 mg.

A number of factors may alter the need for vitamin C. Under acute emotional or environmental stress, such as exposure to elevated temperatures, increased intakes of vitamin C are required to maintain normal plasma levels of the vitamin (Sauberlich and Baker, 1967; Visagie *et al.*, 1974, 1975; Bondarev *et al.*, 1975; Vallance, 1975; Irwin and Hutchins, 1976). South African mineworkers required vitamin C intakes of 200-250 mg/day in order to maintain serum ascorbate levels of 0.75 mg/dl (Visagie *et al*, 1975). Such serum ascorbate levels are generally attained with vitamin C intakes of 60-75 mg/day (Dodds and MacLeod, 1947; Hodges *et al.*, 1971; Sauberlich, 1975). Whether this

is the result of an increased loss or enhanced turnover of vitamin C by the body has not been established.

The magnitude of effects of such factors as individual variation, age, sex, drugs, smoking, and oral contraceptive agents on vitamin C requirements is equivocal (Irwin and Hutchins, 1976). The use of cigarettes and the ingestion of oral contraceptive agents have been observed to lower plasma levels of vitamin C, but the significance of these effects in terms of vitamin C requirements has not been clarified (Brook and Grimshaw, 1968; Bailey *et al.*, 1970; Loh and Wilson, 1971; Briggs and Briggs, 1972; Rivers and Devine, 1975; McLeroy and Schendel, 1973; Pelletier, 1977). Age and sex may affect the ascorbic acid requirement. Little is known concerning the vitamin C requirement of the adult female, and it is generally assumed to be no greater than that of the adult male. However, there appears to be a physiological difference in the metabolism or retention of vitamin C in the two sexes (Dodds, 1969; Milne *et al.*, 1971; Burr *et al.*, 1974). Plasma and leucocyte vitamin C concentrations in women have been observed to be higher than those in men on similar intakes and may be related to ovarian hormone activity (Dodds, 1969; Loh and Wilson, 1971; Sauberlich, 1975). Blood vitamin C levels tend to be lower in elderly people but can be elevated with ascorbic acid supplements (Brook and Grimshaw, 1968; Salvatore *et al.*, 1969; Burr *et al.*, 1975; Roine *et al.*, 1975; Irwin and Hutchins, 1976).

At intakes of 100 mg/day or less, ascorbic acid is absorbed at an efficiency of 80-90 percent (Kallner *et al.*, 1977). Higher intakes of ascorbic acid are absorbed less efficiently (Mayersohn, 1972).

Recommended Allowance for Adults

A dietary allowance of 60 mg of vitamin C per day is recommended for adults of both sexes. With an average ascorbate catabolism rate of 2.9 ± 0.6 percent (Baker *et al.*, 1971) and an average ascorbate absorption efficiency of 85 percent (Kallner *et al.*, 1977), a daily intake of 60 mg of vitamin C would be required to maintain an ascorate body pool of 1500 mg. A pool of this magnitude will protect against overt signs of scurvy in the adult male for a period of 30-45 days (Hodges *et al.*, 1971). Although there is some evidence that larger intakes, approximating 200 mg/day, may produce a larger body pool (Baker *et al.*, 1966), the Committee on Dietary Allowances believes that efforts to attain such pool sizes are unnecessary in view of the decreased effi-

ciency of absorption and increased rate of excretion of unmetabolized ascorbic acid at these higher intakes.

The allowance recommended here, 60 mg/day, is higher than that provided in the previous edition of *Recommended Dietary Allowances,* Review of existing information justified an increased allowance that will permit the maintenance of a satisfactory ascorbate body pool, sufficient for several weeks, and allow for an ascorbate catabolism rate of 3-4 percent and absorption efficiency of approximately 85 percent. This increased allowance is not difficult to achieve from the foods available in the United States (LSRO, 1978) and may enhance the nutritional status for iron in some groups (see the section on Iron).

Recommended Allowances for Infants, Children, and Adolescents

The requirement for vitamin C during infancy and early childhood is not known precisely. Human milk contains 30-55 mg/liter of vitamin C and varies with the mother's dietary intake of the vitamin (Selleg and King, 1936; Ingalls *et al.,* 1938; Tarjan *et al.,* 1965). Since the breast-fed infant receives approximately 850 ml of milk per day, 35 mg is the recommendation for the infant. This amount should provide an adequate margin of safety since breast-fed infants with vitamin C intakes of 7-12 mg/day and bottle-fed infants with vitamin C intakes of 7 mg/day have been protected from scurvy (Van Eekelan, 1953; Goldsmith, 1961; Rajalakshmi *et at.,* 1965). However, newborn infants, especially if they are premature, may exhibit during the first week of life an increased requirement for the metabolism of tyrosine (Light *et al.,* 1956; A very *et al.,* 1967; Irwin and Hutchins, 1976). To protect against possible adverse effects of the transient tyrosinemia, an intake of 100 mg/day of ascorbic acid is recommended during this period.

On a weight basis, the vitamin C requirement of children appears to be higher than that of adults (Ritchey, 1965; Fidanza and Baldesserini, 1974; Irwin and Hutchins, 1976). For children up to the age of 11 years, an allowance of 45 mg/day of vitamin C is recommended. For older children, an allowance of up to 60 mg/day is recommended as adequate to meet individual needs and to provide a margin of safety.

Recommended Allowances for Pregnancy and Lactation

During pregnancy, plasma vitamin C levels fall (Martin *et al.,* 1957; Mason and Rivers, 1971; Morse *et al.,* 1975; Vobecky *et al.,* 1974).

Whether this is due in part to physiological responses of pregnancy or entirely to increased demands of pregnancy is uncertain (Darby *et al.*, 1953; McLeroy and Schendei, 1973; Rivers and Devine, 1975). Enhanced intakes of ascorbic acid may prevent the fall in plasma vitamin C during pregnancy (Martin *et al.*, 1957; Vobecky *et al.*, 1974). The placenta normally transmits ascorbic acid from mother to fetus against a concentration gradient, resulting in fetal levels 50 percent greater than maternal at term (Hamil *et al.*, 1947; Kattab *et al.*, 1970). To provide for this fetal need, an additional allowance of 20 mg of ascorbic acid per day is recommended for pregnant women, particularly for the second and third trimester of pregnancy.

Human milk from well-nourished women is relatively high in ascorbic acid (30-55 mg/liter) and varies with the mother's dietary intake of the nutrient (Selleg and King, 1936; Tarjan *et al.*, 1965). During lactation, a daily loss of 25-45 mg of vitamin C may occur in a secretion of 850 ml of milk. For lactating women, an additional allowance of 40 mg/day of vitamin C is recommended in order to assure a satisfactory level of the vitamin in breast milk.

Pharmacological Intakes of Ascorbic Acid

Intakes of ascorbic acid far in excess of physiological requirements (1 g/day or more) have been reported to have some effect in reducing the frequency and severity of symptoms of the common cold and other winter illness (Pauling, 1971; Anderson *et al.*, 1972, 1974, 1975; Wilson *et al.*, 1973; Coulehan *et al.*, 1974; Karlowski *et al.*, 1975). In carefully controlled, double-blind trials, however, the effect of ascorbic acid was considerably smaller than had been previously reported (Anderson, 1975) or was not reproducible (Coulehan *et al.*, 1976). In addition, Karlowski *et al.* (1975) found that when those subjects who had guessed the nature of their medication (ascorbic acid or placebo) were eliminated from consideration, the differences between the vitamin and placebo groups were not significant. In general, these investigators (Anderson, 1975; Coulehan *et al.*, 1976; Karlowski *et al.*, 1975) and several reviewers (Chalmers, 1975; Dykes and Meier, 1975) believe that these benefits of large doses of ascorbic acid are too small to justify recommending routine intake of large amounts by the entire population.

Large doses of ascorbic acid have also been reported to lower serum cholesterol in some hypercholesterolemic subjects (Ginter *et al.*, 1977) but not in others (Hodges *et al.*, 1971; Peterson *et al.*, 1975). Ascorbic acid supplements can prevent the reduced platelet and plasma con-

centrations of ascorbic acid observed in aspirin-treated rheumatoid-arthritis patients (Sahud and Cohen, 1971) and have been reported to increase the human serum levels of IgA, IgM, and complement component C-3 (Prinz *et al.*, 1977). Thus ascorbic acid in large doses may have some pharmacological or drug-like effects that are not related to the normal functioning of the vitamin.

Large doses of ascorbic acid have generally been considered nontoxic, except for gastrointestinal symptoms experienced by some subjects. However, a number of adverse effects of excessive intakes of ascorbic acid have been reported, such as ascorbic acid-induced uricosuria (Stein *et al.*, 1976), absorption of excessive amounts of food iron (Cook and Monsen, 1977), and impaired bactericidal activity of leucocytes (Shilotri and Bhat, 1977).

Since many of the claims for significant beneficial effects of large intakes of ascorbic acid have not been sufficiently substantiated, and since excessive intakes may have some adverse effects, routine consumption of large amounts of ascorbic acid is not recommended without medical advice.

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THIAMIN

Prolonged intake of diets low in thiamin will eventually lead to clinical signs of a thiamin deficiency traditionally referred to as the disease, beriberi. Apparent inconsistencies in reports of the thiamin intake required to prevent clinical deficiency signs are related not only to differences in experimental protocols but also to individual variability

Contents

Preface

The *Recommended Dietary Allowances* (RDA) were first published in 1943 to "provide standards serving as a goal for good nutrition." Those allowances were not considered permanent but rather were recommendations based on the best scientific knowledge at the time. Since 1943, the report has been revised at approximately 5-year intervals, as additional data have become available.

Initially, the RDA were intended as a "guide for planning and procuring food supplies for national defense." Over the years, this purpose has been extended to such other areas as interpreting food consumption records of groups and evaluating the adequacy of food supplies in meeting nutritional needs, planning and procuring food supplies for groups and establishing guides for public food assistance programs, development of new food products by industry, establishing guidelines for nutritional labeling of foods, and developing nutrition education programs. As the applications of RDA continue to expand, it is increasingly important that their significance and limitations be clearly understood.

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