VITAMIN C (ASCORBIC ACID)

Also Known As:

Acide Ascorbique, Acide Cévitamique, Acide Iso-Ascorbique, Acide L-Ascorbique, Acido Ascorbico, Antiscorbutic Vitamin, Ascorbate, Ascorbate de Calcium, Ascorbate de Sodium, Ascorbyl Palmitate, Calcium Ascorbate, Cevitamic Acid, Iso-Ascorbic Acid, L-Ascorbic Acid, Magnesium Ascorbate, Palmitate d'Ascorbyl, Selenium Ascorbate, Sodium Ascorbate, Vitamina C, Vitamine Antiscorbutique, Vitamine C.

Scientific Name:

Ascorbic acid.

Benefits

Orally, vitamin C is used for preventing and treating scurvy; preventing deficiency in people with gastrointestinal diseases and those on chronic total parenteral nutrition or chronic hemodialysis; increasing iron absorption from the gastrointestinal tract; and increasing the healing rate of wounds, burns, fractures, ulcers, and pressure sores. It is used for urine acidification, treating idiopathic methemoglobinemia, correcting tyrosinemia in premature infants on high-protein diets, increasing iron excretion (in combination with deferoxamine), preventing and treating the common cold and other viral infections, bronchitis, human immunodeficiency virus (HIV) disease, Helicobacter pylori infection, tuberculosis, dysentery, furunculosis, hematuria, retinal hemorrhages, hemorrhagic states, and anemia. Vitamin C is also used orally for atherosclerosis, preventing vascular thrombosis, myocardial infarction, stroke, hypertension, lowering cholesterol, glaucoma, preventing cataracts, preventing gallbladder disease, dental caries, pyorrhea, gum infections, constipation, peptic ulcer, acne, dermatitis, improving immune function, swine flu, allergic rhinitis (hayfever), asthma, bronchitis, cystic fibrosis, cystitis, prostatitis, infertility, and diabetes. It is also used orally for mental depression, cognitive impairment, dementia, Alzheimer's disease, physical and mental stress, fatigue, attention deficit-hyperactivity disorder (ADHD), chronic fatigue syndrome (CFS), autism, collagen disorders, arthritis and bursitis, back pain and disc inflammation, cancer, osteogenesis imperfecta, osteoporosis, and gout. Other uses include improving physical endurance, Lyme disease, reducing aging, heat prostration, for counteracting the side effects of cortisone and related drugs, aiding drug withdrawal in addiction, and in the treatment of levodopa, succinylcholine, interferon, aspirin, and arsenic toxicity. Other uses include use as an adjunct to radiation therapy and treating chronic radiation proctitis. It is also used to prevent human immunodeficiency virus (HIV) transmission to breast-fed babies.

Topically, vitamin C is used for improving skin conditions, protecting against free radicals and pollutants, and for improving photo-aged skin. It is also applied topically for ulcerative mucositis associated with radiation therapy.

Parenterally, vitamin C is used for preventing and treating vitamin C deficiency and correcting tyrosinemia in premature infants on high-protein diets.

Safety

LIKELY SAFE ...when used orally, topically, intramuscularly, or intravenously and appropriately. Vitamin C is safe when taken orally in doses below the tolerable upper intake level (UL). Tell patients not to exceed the UL of 2000 mg per day (1959, 4713, 4714, 4844). ...when used intravenously or intramuscularly and appropriately. Injectable vitamin C is an FDA-approved prescription product (15).

POSSIBLY UNSAFE ...when used orally in excessive doses. Doses greater than the tolerable upper intake level (UL) of 2000 mg per day can significantly increase the risk of adverse effects such as osmotic diarrhea and gastrointestinal upset (4844).

CHILDREN: LIKELY SAFE ...when used orally and appropriately (4844, 10352, 14443). POSSIBLY UNSAFE ...when used orally in excessive amounts. Tell patients not to use doses above the tolerable upper intake level (UL) of 400 mg per day for children ages 1 to 3 years, 650 mg per day for children 4 to 8 years, 1200 mg per day for children 9 to 13 years, and 1800 mg per day for adolescents 14 to 18 years. Higher doses can cause osmotic diarrhea and gastrointestinal upset (4844).

PREGNANCY AND LACTATION: LIKELY SAFE ...when used orally and appropriately (4844). POSSIBLY UNSAFE ...when used orally in excessive doses. Tell patients not to use doses exceeding the UL of 2000 mg per day for pregnant or breast-feeding women over age 19; and 1800 mg per day for pregnant and breast-feeding women 14 to 18 years. Higher doses can cause osmotic diarrhea and gastrointestinal upset. Large doses of vitamin C during pregnancy can also cause newborn scurvy (4844); avoid using.

Indications

Vitamin C deficiency. Administering vitamin C orally or intramuscularly prevents and treats vitamin C deficiency, including scurvy. Vitamin C administration can reverse complications of scurvy within two days to three weeks (4844).

Iron absorption. Concurrent administration of at least 200 mg vitamin C per 30 mg iron increases iron absorption (3042, 9518).

Tyrosinemia. Administering vitamin C orally or intramuscularly improves tyrosinemia in premature infants on high protein diets (15).

Age-related macular degeneration (AMD). Taking vitamin C 500 mg orally, in combination with elemental zinc 80 mg, vitamin E 400 IU, and beta-carotene 15 mg daily seems to provide a risk reduction of 27% for visual acuity loss and a risk reduction of 25% for progression of AMD in patients with advanced AMD (7303, 11326). There isn't enough evidence to know if this combination is beneficial for people with less advanced macular disease or for preventing AMD. Vitamin C with other antioxidants, but without zinc, doesn't seem to have any effect on AMD (7303, 7304).

Some epidemiological evidence suggests that increased vitamin C dietary intake and supplements might actually increase the risk of age-related maculopathy (9823). Other evidence suggests that increasing dietary vitamin C alone does not significantly reduce the risk of AMD (14007, 14257);

however, consuming above average amounts of dietary vitamin C along with other nutrients such as vitamin E, beta-carotene, and zinc might reduce risk of AMD by up to 35% (14257).

Albuminuria. Taking vitamin C plus vitamin E can reduce the excretion of albumin by about 19% when given for 4 weeks in patients with type 2 diabetes. This might also reduce the risk of end-stage renal disease in patients with type 2 diabetes (10434).

Atherosclerosis and peripheral arterial disease. Taking vitamin C orally seems to decrease the risk of atherosclerosis and peripheral arterial disease. Patients with peripheral arterial disease appear to have lower levels of vitamin C and higher levels of C-reactive protein, a marker of inflammation (9813). In women, there is some epidemiological evidence suggesting that dietary vitamin C can decrease the risk of peripheral arterial disease. However, it does not seem to have this effect in men (10130). However, other research suggests that slow release vitamin C 250 mg in combination with vitamin E 136 IU twice daily might slow the progression of atherosclerosis of the carotid artery. This combination appears to benefit both smoking and nonsmoking men, but has a marginal effect in postmenopausal women (1918, 10473). Epidemiological evidence also suggests that dietary intake of vitamin C doesn't affect atherosclerotic markers such as carotid artery wall thickness or carotid artery plaque (9814). In children with familial hypercholesterolemia, vitamin C and vitamin E may increase flow mediated dilation, when used with a National Cholesterol Education Program Step II (NCEP-II) diet (10352). There's also some evidence that the combination of vitamin C and vitamin E might help prevent cardiac transplant-associated arteriosclerosis (5197). Overall, vitamin C appears to slow progression of atherosclerosis. The effects of dietary and supplemental vitamin C on atherosclerosis requires further study to determine if it is generally beneficial or more useful in specific patient populations (9815).

Cancer. Dietary vitamin C might decrease the risk of developing mouth cancer and other cancers (10819, 10821). Some evidence suggests that a diet low in vitamin C might increase the risk of mortality due to cancer in men, but not in women (3910, 5878). Other research suggests a combination of vitamin C 125 mg/day with vitamin E, beta carotene, selenium and zinc can lower cancer incidence in men, but not women. Researchers speculate that men have lower intake of dietary antioxidants and therefore might benefit more from supplements (14109). Research on the protective effects of vitamin C against developing breast cancer is mixed. Some research suggests that dietary vitamin C reduces breast cancer risk (1444, 10823, 10824); other research suggests no association between vitamin C intake and breast cancer risk (10825, 10826). There is currently no evidence that vitamin C from supplements has any effect on breast cancer risk. Some researchers project that plasma ascorbic acid increases to theoretically protective levels against cancer with an increase of one serving of fruits and vegetables per day (3910). The use of high-dose vitamin C as adjunctive therapy, in combination with other antioxidants to treat cancer, is controversial. Some experts think these supplements might increase the sensitivity of tumor cells to radiation and reduce toxicity in normal cells. Other experts worry that antioxidants might protect cancer cells from the effects of radiation (9826). Preliminary evidence suggests that vitamin C might reduce the effectiveness of some chemotherapy drugs, including doxorubicin, cisplatin, vincristine, methotrexate, and imatinib (16407).

High dose oral vitamin C, 10 grams daily in patients with advanced cancer regardless of prior chemotherapy, does not seem to improve survival or decrease disease progression (4842, 4843).

Preliminary clinical evidence suggests high doses of vitamin C given intravenously might have a beneficial effect on survival rate in patients with terminal cancer. Thus far, this has not been tested in well-designed clinical trials (9809). Some observational research in children with lymphoblastic leukemia suggests that greater dietary vitamin C intake is associated with fewer delays in chemotherapy, less toxicity, and fewer hospitalization days (11997).

Common cold. There is a lot of controversy about the effectiveness of vitamin C for treating the common cold (1969, 1989, 7100, 9835, 9836). However, the majority of evidence shows that taking high doses of vitamin C orally might decrease the duration of cold symptoms by 1-1.5 days in some patients (1966, 1967, 1968, 1987, 6458, 7102, 9832). Other studies have found no effect with doses up to 3 grams daily (9833). Some research suggests vitamin C may be more effective for treating cold symptoms in children than in adults. There may also be a dose-dependent response; doses of at least 2 grams per day seem to work better than 1 gram doses (9834). Tell patients that the high doses used for treating the common cold, 1-3 grams daily, can increase the risk of side effects. Some patients might not think the modest benefit is worth the risk. Explain to patients that taking vitamin C supplements prophylactically does not decrease the risk of catching a cold (1966, 1967, 1968, 1987, 3042, 6458, 7101, 9832). Dietary intake of vitamin C also doesn't seem to affect the risk of getting a cold (10780).

Complex regional pain syndrome (reflex sympathetic dystrophy). Taking vitamin C 500 mg daily for 50 days after a wrist fracture seems to significantly decrease the risk of developing complex regional pain syndrome (2045, 16302).

Contrast-mediated nephropathy. Taking vitamin C before and after coronary angiography seems to reduce the risk of developing contrast-mediated nephropathy compared to placebo (12234).

Erythema. There is some evidence that an aqueous formulation of topical vitamin C can decrease the degree and duration of erythema following cutaneous carbon dioxide laser resurfacing for scar and wrinkle removal (1959).

Exercise-induced respiratory infections. Some evidence suggests that prophylactic use of vitamin C in doses of 600 mg to 1 gram per day before heavy physical exercise, such as a marathon, might prevent upper respiratory infections that sometimes follow heavy exercise (9831).

Gallbladder disease. There is some evidence that vitamin C supplementation and increased vitamin C serum levels decrease the risk of developing gallbladder disease in women; however, it doesn't seem to have this effect in men (5877).

Helicobacter pylori (H pylori). Taking vitamin C orally seems to decrease gastritis associated with acid suppressive therapy in patients with H. pylori infection (10359). After H. pylori is eradicated, vitamin C appears to decrease the incidence of precancerous changes in stomach tissue (10360).

HIV transmission. Taking vitamin C orally during pregnancy and breast-feeding seems to reduce HIV transmission. Supplementation of mothers with HIV disease with vitamin B, vitamin C, and vitamin E seems to reduce child mortality and HIV transmission through breast milk (9801).

Hypertension. Taking vitamin C orally along with conventional antihypertensive medications appears to modestly decrease systolic blood pressure, but does not seem to decrease diastolic pressure

(2044, 13162). In patients with type 2 diabetes, vitamin C 500 mg taken daily for 4 weeks, in addition to antihypertensives, seems to reduce arterial blood pressure and decrease arterial stiffness (9822). But supplemental vitamin C 500 mg per day taken without antihypertensives doesn't seem to reduce systolic or diastolic blood pressure (9821). Dietary restriction of vitamin C is associated with increases in both diastolic and systolic blood pressure (10354).

Lead toxicity. Consuming vitamin C from dietary sources seems to lower blood concentrations of lead (3097, 3098, 3099).

Nitrate tolerance. Taking vitamin C orally seems to prevent the development of nitrate tolerance in patients taking sublingual nitroglycerin. There is some evidence that short-term vitamin C supplementation can prevent attenuation of tolerance to the vasodilatory effects of nitrates (1441, 1961).

Osteoarthritis. Consuming vitamin C from dietary sources seems to reduce the risk of cartilage loss and disease progression in people with osteoarthritis (5881).

Physical performance. Population research suggests that higher intake of dietary vitamin C is associate with improved physical performance and muscle strength in elderly people (14006).

Pre-eclampsia. Taking vitamin C orally with vitamin E seems to prevent pre-eclampsia in high-risk pregnancies (3236).

Sunburn. Taking vitamin C orally in combination with vitamin E seems to prevent ultraviolet (UV) radiation-induced erythema (sunburn) (4715, 4716). Vitamin C in combination with high dose oral RRR-alpha-tocopherol (natural vitamin E) seems to protect against skin inflammation after exposure to ultraviolet (UV) radiation (1416, 4715). This effect is not found when vitamin C is used without vitamin E (1417). Applying vitamin C topically, in combination with vitamin E and melatonin, also seems to prevent ultraviolet (UV) radiation-induced erythema (sunburn). Topical vitamin C in combination with topical vitamin E and melatonin seems to provide modest photo-protective effects when used prior to UV exposure. However, it has no effect when used during or after UV exposure (4713, 4714).

Wrinkled skin. Topical preparations containing 5% to 10% vitamin C seem to improve the appearance of wrinkled skin. In one trial, a topical preparation containing 10% vitamin C as L-ascorbic acid and acetyl tyrosine, zinc sulfate, sodium hyaluronate, and bioflavonoids (Cellex-C High Potency Serum) used for 3 months and applied to photo-aged facial skin improved fine and coarse wrinkling, yellowing and sallowness, roughness, and skin tone compared to placebo (6155). There is also some evidence that vitamin C 3% applied for 12 weeks might reduce facial wrinkles (14008).

Acute bronchitis. Taking vitamin C orally 500 mg on day 1, then 250 mg on days 2 through 5 (similar to an azithromycin regimen) doesn't seem to have any effect on acute bronchitis duration or symptoms (9827).

Alzheimer's disease or vascular dementia. Consuming vitamin C from dietary sources, as a supplement alone, or in combination with vitamin E, doesn't seem to affect the risk of developing Alzheimer's disease or vascular dementia (4636, 9824, 10131, 13165). However, some epidemiological research suggests that long-term use of vitamin C and vitamin E supplements in

combination, and in higher doses than typically found in multivitamins, is associated with a reduced prevalence and incidence of Alzheimer's disease (11390).

Diabetes. Population research suggests that increasing intake of dietary vitamin C does not decrease the risk of developing type 2 diabetes (14004).

Interferon-related retinopathy. Taking vitamin C 600 mg per day orally doesn't seem to reduce the risk of retinopathy associated with interferon therapy in patients with chronic hepatitis C (10355).

Overall mortality. Population research suggests that plasma vitamin C levels are positively associated with a reduced risk of mortality from all causes (3910). Clinical research shows that taking vitamin C 125 mg/day in combination with vitamin E, beta carotene, selenium, and zinc does not significant reduce all-cause mortality in men and women; however, it might lower all-cause mortality just in men, but not women (14109). Other clinical research shows that, in high-risk patients, vitamin C 250 mg in combination with vitamin E 600 mg and beta-carotene 20 mg daily does not seem to affect overall mortality risk. Additionally, this combination doesn't seem to reduce mortality rate or illness from vascular disease in people with diabetes, coronary disease, or occlusive arterial disease. This vitamin combination also doesn't seem to reduce the risk of cancer or hospitalization for any other nonvascular cause (9817). Overall, the best evidence suggests that taking vitamin C supplements does not reduce overall mortality.

Pancreatic cancer. Clinical research shows that taking vitamin C in combination with beta-carotene plus vitamin E does not reduce the risk of pancreatic cancer (12185).

Prostate cancer. A large-scale clinical study (The SU.VI.MAX study) shows that a combination of vitamin C 120 mg, vitamin E (alpha-tocopherol) 30 mg, beta-carotene 6 mg, selenium 100 mcg, and zinc 20 mg daily for an average of 8 years does not reduce the risk of prostate cancer overall. However, it might reduce the risk of prostate cancer in men who have normal PSA levels. It does not seem to be beneficial for reducing the risk of prostate cancer in patients with PSA levels above 3 mcg/L (14135).

Another large scale study (Physician's Health Study II) shows that taking vitamin C 500 mg daily for an average of 8 years does not significantly reduce the risk of prostate cancer compared to placebo (16708).

Overall, the best evidence indicates that taking vitamin C supplements does not significantly reduce the risk of developing prostate cancer.

Radiation dermatitis. Applying a 10% vitamin C solution does not appear to have a protective effect when applied to the scalps of patients treated with radiation for intracranial tumors (789).

Stroke. Most population studies show that taking vitamin C orally doesn't seem to affect the risk of ischemic or hemorrhagic stroke (1449, 1958, 7390, 7716). Lower plasma levels of vitamin C have been associated with increased stroke risk (1957, 7714). Higher consumption of fruits and vegetables has been associated with reduced ischemic stroke risk (7394). Suggest a diet high in fruits and vegetables rather than vitamin C supplements to reduce stroke risk.

Allergic rhinitis (hayfever). There is conflicting evidence about the effects of vitamin C on symptoms of allergic rhinitis (15201, 15202, 15203). Epidemiological research shows that higher vitamin C plasma levels are not associated with a decreased risk of allergic rhinitis (15200).

Aspirin-associated gastric damage. Some clinical evidence suggests that vitamin C might prevent gastric damage associated with aspirin therapy by decreasing blood loss and preventing decreased gastric blood flow (10357).

Asthma. There is some evidence that low levels of vitamin C are associated with certain conditions. Vitamin C levels might be decreased in some asthmatics (5873). Some clinical evidence also suggests that taking vitamin C supplements might decrease exercise-induced asthma (1443). However, population research suggests that vitamin C intake in 5-year-old children is not associated with risk of asthma (15006).

Attention deficit-hyperactivity disorder (ADHD). Some evidence suggests that taking megadose vitamins including vitamin C does not seem to help ADHD symptoms (9957, 9958, 9959). Other preliminary evidence suggests that a lower dose, vitamin C 25 mg, in combination with flaxseed oil providing alpha-linolenic acid 200 mg, twice daily might improve measures of attention, impulsivity, restlessness, and self-control in children with ADHD (14443).

Bladder cancer. Epidemiological research suggests that supplemental vitamin C use does not affect mortality rate associated with bladder cancer (9839).

Cardiovascular disease. Using antioxidants such as vitamin C for preventing heart disease and cardiovascular events such as myocardial infarction (MI) is controversial. There have been lots of studies, but results have been mixed (11001, 14108). In populations with relatively low or deficient vitamin C intake, vitamin C seems to lower the risk of death from coronary heart disease, although not all studies have shown benefit (1958, 7714, 7715, 10815, 11001). Some large population studies have shown a reduction in mortality from coronary heart disease either from dietary sources or supplements (3910, 7394, 10358, 10814, 10816, 10817, 11003), but similar studies have shown no effect on mortality risk with increased vitamin C intake (1958, 3933, 3934, 3938, 7724). According to one analysis, supplemental vitamin C, but not dietary vitamin C, is associated with a reduced risk of cardiovascular disease (14108). Interestingly, two of the positive studies found a 25% to 28% reduction of cardiovascular disease and cardiovascular disease mortality in women only who took vitamin C supplements (10358, 11002). Some population studies that found benefit have been criticized for not considering concurrent vitamin E intake (7715, 11002). Some research suggests that a combination of vitamin C and vitamin E might offer additional benefit for preventing coronary heart disease (3938). In people with coronary heart disease, the few studies that have been done haven't shown vitamin C to be beneficial (10817, 10818, 11000). Vitamin C in combination with selenium, beta-carotene, and vitamin E also doesn't seem to protect against cardiovascular disease progression and related events such as MI (7388). Studies investigating serum vitamin C concentrations and cardiovascular mortality risk are inconclusive. One study found decreased mortality with increasing concentrations (3910); the other found no effect (5878). A Science Advisory from the American Heart Association also states that the evidence does not justify use of antioxidants such as vitamin C for reducing the risk of cardiovascular disease (12142). Tell patients more research is needed before supplemental vitamin C can be recommended for preventing

coronary heart disease. Increasing fruit and vegetable intake by one serving per day in the average person could boost plasma ascorbic acid to theoretically protective levels (3910).

Cataracts. There is conflicting information about the use of vitamin C to prevent cataracts. Vitamin C plus vitamin E and beta-carotene doesn't seem to have any significant effect on age-related loss of vision due to cataracts in well-nourished people who took the supplement for an average of 6.3 years (7304). However, population research suggests that vitamin C use in multivitamins or any supplement containing vitamin C for 10 years appears to reduce the incidence of nuclear and cortical cataracts by 60%. Use of supplements for shorter periods doesn't appear to reduce the risk for cataract development (4208).

Chronic radiation proctitis. Preliminary clinical research suggests that vitamin C 500 mg plus vitamin E 400 IU three times daily might improve symptoms of chronic radiation proctitis (9825).

Colorectal cancer. Taking vitamin C in combination with beta-carotene plus vitamin E doesn't seem to reduce the risk of colorectal cancer (12185).

Esophageal cancer. Taking vitamin C in combination with beta-carotene plus vitamin E doesn't seem to reduce the risk of esophageal cancer (12185).

Gastric cancer. There is contradictory evidence from population studies on the effects of dietary and supplemental vitamin C intake on the risk of developing gastric cancer (9194, 9838, 10819, 10822). Taking vitamin C supplements in combination with beta-carotene or beta-carotene plus vitamin E does not seem to reduce the risk of gastric cancer (12185). Some evidence suggests that taking vitamin C orally 1 gram daily might promote regression of precancerous gastric lesions in people at high risk for gastric cancer (2579). However, another study suggests that taking vitamin C 250 mg in combination with selenium 37.5 mcg and vitamin E 100 IU twice daily for about 7 years does not seem to reduce the risk of developing precancerous gastric lesions (14447).

Gout. Population research shows that increased intake of vitamin C is associated with a significantly decreased risk of gout in men. Ingesting vitamin C 500-1500 mg daily from the diet and/or supplements is associated with 17% to 34% reduced risk of gout compared to men consuming less than 250 mg daily (16755). Higher vitamin C intake is also associated with lower levels of serum uric acid in men. Men who ingest more than 500 mg/day of vitamin C from the diet and supplements have serum uric acid levels that are 0.5-0.6 mg/dL lower than men who consume less than 90 mg daily (16820).

HIV/AIDS. Taking vitamin C 250 mg daily in combination with vitamin A, beta-carotene, vitamin E, selenium, and coenzyme Q-10 seems to improve markers of oxidative defense and oxidative stress in men with human immunodeficiency virus (HIV) disease. However, higher doses of vitamin C, 1000 mg, and the other antioxidants don't seem to provide any additional effect. Neither high-dose nor low-dose antioxidants affect viral load (9830).

Hypercholesterolemia. Taking vitamin C 50 mg daily or 500 mg daily for up to 5 years does not seem to decrease serum lipid levels in people with normal lipid levels (14011). The effect of vitamin C on lipid levels in patients with hyperlipidemia is not known.

Infertility. There is preliminary evidence that women with infertility, due to luteal phase defect, might increase their progesterone levels by taking vitamin C 750 mg daily (12010). Other preliminary clinical research suggests that taking 400-1000 mg daily might improve fertility, resulting in ovulation and pregnancy in anovulatory women (14016, 14018).

Leukemia. There is some evidence that vitamin C might have a synergistic effect with arsenic trioxide (Trisenox) on myeloid leukemia cells. Preclinical evidence suggests that vitamin C might enhance the apoptotic effect of arsenic trioxide in patients with acute myeloid leukemia (9837).

Mental stress. Preliminary evidence suggests that vitamin C might reduce blood pressure and subjective symptoms during psychological or mental stress (10353).

Nonalcoholic steatohepatitis (NASH). Preliminary research suggests vitamin C in combination with vitamin E might improve hepatic fibrosis in patients with NASH. However, it does not seem to decrease liver inflammation (14005).

Osteoporosis. Some evidence suggests that vitamin C intake might be related to bone mineral density in premenopausal women and men. In postmenopausal women who use estrogen and smoke, higher vitamin C levels might reduce fracture risk. However, in postmenopausal women without a history of smoking or estrogen use, higher serum vitamin C levels have been associated with lower bone mineral density. At present, there is not enough information to make recommendations about vitamin C and bone density (9828).

Ovarian cancer. Epidemiological research suggests that dietary vitamin C does not affect risk of developing ovarian cancer (9193).

Sickle cell disease. Vitamin C, in combination with aged garlic extract and vitamin E might be useful for sickle cell disease (5056).

Pharmacological Action

Vitamin C is a commonly used water-soluble vitamin. Although many mammals can produce vitamin C, humans must obtain vitamin C from foods and other sources (1964). It's contained in high concentration in fresh fruits and vegetables, especially citrus fruits. Vitamin C is labile, and the amount in foods can decrease significantly with cooking and storage (3042). Vitamin C has a role in several physiological functions. It is involved in tyrosine metabolism and is a cofactor in the synthesis of carnitine, thyroxin, norepinephrine, dopamine, and tryptophan (3042). Vitamin C is also involved in a variety of metabolic processes including oxidation-reduction reactions and cellular respiration, carbohydrate metabolism, synthesis of lipids and proteins, catabolism of cholesterol to bile acids, conversion of folic acid to folinic acid, and iron metabolism (5877). Vitamin C is probably best known for its effects as an antioxidant and its role in maintaining proper immune function (15). Normal plasma vitamin C levels typically exceed 0.3 mg/dL. When plasma levels exceed 1.4 mg/dL, excretion of vitamin C greatly increases (1965, 1969). Concentrations below 0.2 mg/dL indicate significant deficiency (1964).

Vitamin C deficiency can cause fatigue, personality changes, and decline in psychomotor performance and motivation within 84 to 97 days. Some evidence suggests that subclinical vitamin C deficiency is more common in healthy people than generally recognized (9810). Since the nonspecific symptom of fatigue is often the first symptom of deficiency, vitamin C depletion may go undiagnosed (9809). Sustained vitamin C deficiency over 3 to 5 months results in symptomatic scurvy characterized by gingival swelling and bleeding, loosening of the teeth, hyperkeratosis, perifollicular hemorrhages, petechial hemorrhages in the viscera, and hemorrhages into the muscles of the arms, legs, and joints (1964). Severe scurvy may progress to neuritis, jaundice, fever, dyspnea, and death. In infants, vitamin C deficiency is initially manifested by listlessness, anorexia, irritability, and failure to thrive. Later symptoms result from hemorrhage and collagen deficiency, with seizures, shock, and death if left untreated (1965).

Because of vitamin C's role in maintaining normal immune function, a lot of people use it for treating and preventing infectious conditions such as the common cold. T-lymphocyte activity, phagocyte function, leukocyte mobility, and possibly antibody and interferon production seem to be increased by vitamin C (1963, 1965). Vitamin C levels in phagocytes and lymphocytes are up to 100 times greater than in plasma (7101). Some researchers think that vitamin C levels in white blood cells decrease at the onset of a cold and that boosting vitamin C intake might be beneficial. There is some evidence vitamin C might have other effects in patients with the common cold. Vitamin C might protect normal tissues against reactive oxygen species that are produced by phagocytes during a viral infection. It might also enhance the proliferative responses of T-lymphocytes (1988). There is preliminary evidence vitamin C excretion might actually decrease during a cold, indicating that patients may retain vitamin C. However, absorption of vitamin C is unchanged during a cold (1986).

There is interest in using vitamin C for allergies such as allergic rhinitis. Some evidence suggests that low vitamin C levels are associated with higher plasma histamine levels (10611). Theoretically, people with low vitamin C levels might have worse symptoms of allergic rhinitis. There is also some evidence that vitamin C might also have weak antihistamine properties (1969).

Vitamin C is used for gout because it is thought to have a uricosuric effect and lower serum levels of uric acid. Some research shows that healthy subjects who take vitamin C 4 grams have uric acid clearance increased by over 200% within 2-6 hours. Vitamin C might compete with uric acid for renal reabsorption via the proximal tubules (16755, 16756, 16757, 16758, 16759).

Some researchers think vitamin C supplements might be useful to prevent other respiratory viral infections, such as severe acute respiratory syndrome (SARS), but there are no reliable clinical studies to support this hypothesis (14015).

Other potentially beneficial effects of vitamin C are attributed primarily to antioxidant and free radical scavenging effects. Vitamin C readily undergoes reversible oxidation and reduction in the body (1963). Vitamin C decreases oxidants in gastric juice, lipid peroxidation, and oxidative DNA and protein damage (3042). Damage by reactive oxygen species are thought to be a contributing factor to a number of diseases including dementia, asthma, hypertension, osteoarthritis, and cancer. Researchers theorized that antioxidants such as vitamin C might protect against some diseases associated with oxidative damage. For example, in hypertension, endothelium-derived nitric oxide (NO), which causes vasodilation, might be inhibited by superoxide anions. Vitamin C can scavenge the superoxide anions and theoretically might help patients with hypertension. However, in this case

there is some evidence that oral doses might not reach concentrations high enough for this effect (5879).

In people with chronic heart failure, intra-arterial vitamin C seems to improve endothelial dysfunction and flow-dependent dilation of the arteries. Vitamin C appears to prevent inactivation of NO-mediated vasodilation. Four weeks of oral vitamin C 1 gram twice daily appears to produce a similar effect (2434). In patients with coronary artery disease and type 2 diabetes, vitamin C 2 grams daily seems to improve endothelium-dependent vasodilation (14009). Vitamin C also seems to improve endothelial function and vascular resistance in patients with chronic renal failure (14014, 14017).

There's also some evidence that vitamin C might suppress the apoptosis (death) of endothelial cells of patients with congestive heart failure, but the clinical relevance of this isn't known (9816). Intracoronary infusion of vitamin C has been shown to enhance the inotropic response to dobutamine (Dobutrex), possibly by reducing oxidative stress caused by beta-adrenergic stimulation of the ventricle (2432). Some researchers think vitamin C might prevent or slow atherosclerosis by inhibiting low-density lipoprotein (LDL) cholesterol; by impairing the products of reactive oxygen species from vascular cells; and by limiting the cellular responses to oxidized LDL, such as production of endothelium-derived NO (9812). In patients with coronary spastic angina, vitamin C seems to improve endothelial function when given by intravenous infusion as a single 2 gram dose (9819). Some research suggests that endothelial function may relate to insulin resistance in patients with hypertension. Single-dose intravenous vitamin C seems to improve endothelial function and restore insulin-mediated vasodilatation, but doesn't seem to improve glucose uptake (9820). Oral vitamin C seems to improve endothelial function in healthy young smokers, short term; the improvements in endothelial function diminish within 8 weeks, even though vitamin C levels remain elevated (9818).

In smokers, a single 3 gram dose given by intravenous infusion appears to restore coronary microcirculatory responsiveness and impaired coronary flow reserve induced by the oxidant effects of smoking. Vitamin C might reduce oxidative stress caused by the large number of oxidants in cigarette smoke (1956). Whether these effects are sustained when vitamin C is taken chronically is unknown. Pulmonary function is also positively related to dietary vitamin C intake in smokers and nonsmokers (2400).

Some research suggests vitamin C 515 mg daily can reduce C-reactive protein levels in people who are actively or passively exposed to cigarette smoke (14010).

For radiation-induced oral mucositis, the reduced form of vitamin C might be beneficial due to its antioxidant effect and role in maintaining connective tissue integrity (6103). Vitamin C may also reduce toxicity of reactive oxygen during radio-immunotherapy due to its antioxidant effects (5878).

Some researchers theorize that antioxidants, such as vitamin C, might make chemotherapy more effective by reducing oxidative stress that could interfere with apoptosis (cell death) of cancer cells (14012, 14013). However, vitamin C could also reduce the activity of chemotherapy drugs that generate free radicals (391). Preliminary data from a mouse lymphoma model indicate that vitamin C pretreatment reduces the efficacy of doxorubicin (16407). Leukemia and lymphoma cell culture studies also suggest that vitamin C pretreatment can reduce the cytotoxicity of doxorubicin, cisplatin, vincristine, methotrexate, and imatinib. Since this list includes drugs which do not generate

free radicals, mechanisms other than the antioxidant effects of vitamin C may be involved. This might include prevention of the mitochondrial membrane depolarization caused by many chemotherapy drugs, which is involved in regulating cell death (16407).

Research in marathon runners suggests vitamin C might help post-race immune suppression. Vitamin C 1500 mg taken daily for 7 days before running seems to reduce post exercise serum cortisol and cytokines (11961).

Free radicals are also generated in the skin by exposure to ultraviolet light and cause photo-aging. Vitamin C in the skin is believed to play a key role in neutralizing these free radicals and reducing UV skin damage. Topical application of vitamin C is thought to prevent skin damage when applied prior to UV exposure due to vitamin C's antioxidant effects (6062, 6155). Topical preparations are thought to help treat photo-aged and wrinkled skin due to vitamin C's antioxidant properties and by possibly by increasing collagen production and improving collagen organization (6155, 14008). Topical preparations containing 10% vitamin C might be most effective for increasing vitamin C concentrations in the skin. Because vitamin C is water soluble, oral supplementation of vitamin C might not produce high enough concentrations in the skin to treat photo-aged skin (6064, 6155).

Vitamin C is well absorbed orally at lower does, but absorption decreases as the dose increases. Approximately 87% of a 30 mg oral dose is absorbed, 80% of a 100 mg dose is absorbed, 63 % of a 500 mg dose is absorbed, and less than 50% of a 1250 mg does is absorbed. Most of what is absorbed is excreted in the urine. Decreased bioavailability with increasing dosages and increased renal excretion limits the plasma levels attainable with oral vitamin C supplementation (9809).

Side Effects

Orally, the adverse effects of vitamin C are dose-related (3042) and include nausea, vomiting, esophagitis, heartburn, abdominal cramps, gastrointestinal obstruction, fatigue, flushing, headache, insomnia, sleepiness, and diarrhea. Doses greater than the tolerable upper intake level (UL) of 2000 mg per day can increase the risk of significant adverse effects such as osmotic diarrhea and gastrointestinal upset (4844).

Vitamin C may also cause precipitation of urate, oxalate, or cysteine stones or drugs in the urinary tract (10356). Hyperoxaluria, hyperuricosuria, hematuria, and crystalluria have occurred in people taking 1 gram or more per day (3042). In people with a history of oxalate kidney stones (the most common type of nephrolithiasis), supplemental vitamin C 1 gram per day appears to increase stone risk by 40% (12653).

Large amounts of vitamin C are associated with deep vein thrombosis. Prolonged use of large amounts of vitamin C can also result in increased metabolism of vitamin C, and scurvy can occur when vitamin C intake is reduced (15).

High doses of vitamin C might not be safe for some people. In postmenopausal women with diabetes, supplemental vitamin C in doses greater than 300 mg per day is associated with increased risk of cardiovascular mortality (12498). Oral supplementation with vitamin C has also been associated with an increased rate of carotid inner wall thickening in men. There is preliminary

evidence that supplemental intake of vitamin C 500 mg daily for 18 months can cause a 2.5-fold increased rate of carotid inner wall thickening in non-smoking men and a 5-fold increased rate in men who smoked. The men in this study were 40-60 years old. This effect was not associated with vitamin C from dietary sources (1355). There is also some concern that supplements of vitamin C 200 mg might increase production reactive oxygen molecules capable of damaging DNA. This is based on very preliminary in vitro evidence that vitamin C can induce decomposition of lipid hydroperoxides to reactive molecules. More evidence is needed to determine if this is clinically relevant in humans taking vitamin C supplements (7088).

Topically, vitamin C might cause tingling or irritation at the site of application (6166).

Interactions with Herbs & Supplements

ACEROLA: Acerola contains high concentrations of vitamin C (12651). Advise people to avoid taking large amounts of acerola along with vitamin C, which together could exceed the tolerable upper intake level of 2000 mg vitamin C per day for adults.

CHEROKEE ROSEHIP: Cherokee rosehip contains high concentrations of vitamin C (12652). Advise people to avoid taking large amounts of cherokee rosehip along with vitamin C, which together could exceed the tolerable upper intake level of 2000 mg vitamin C per day for adults.

CHROMIUM: Limited data suggests that vitamin C increases chromium absorption. The amount of chromium absorbed from a 1000 mcg dose approximately doubled when vitamin C 100 mg was given at the same time (10600). Advise people to avoid taking large doses of chromium and vitamin C together. It isn't known whether separating the doses by several hours avoids this interaction.

COPPER: High doses of vitamin C (1500 mg daily) can decrease serum levels of copper and the copper transport protein, ceruloplasmin, in young men. The acidity of vitamin C may convert copper in the gut to a less absorbable form, and vitamin C may directly interfere with transport of copper across the intestinal wall. It's also suggested that vitamin C can stimulate tissue copper utilization (710, 11538). It's unlikely that this interaction is clinically significant unless dietary copper intake is low (710).

GRAPE: Preliminary evidence suggests that patients with hypertension who take both vitamin C 500 mg/day plus grape seed polyphenols 1000 mg/day have significantly increased systolic and diastolic blood pressure (13162). The potential mechanism of this interaction is not known.

IRON: Supplemental or dietary vitamin C improves absorption of supplemental or dietary non-heme (plant-derived) iron when ingested at the same time (9518, 9571, 9586, 11571). The amount of vitamin C in the diet is a factor in dietary iron absorption and iron status (9570, 9572). Vitamin C can counteract the effects of substances which inhibit iron absorption such as dietary phytates, polyphenols, and tannins, possibly by chemically reducing iron and preventing the formation of less soluble ferric compounds (9518, 9573, 9586, 11571). Taking a vitamin C supplement to improve absorption of dietary or supplemental iron probably isn't necessary for most people, especially if their diet contains plenty of vitamin C (9571).

ROSEHIP: Rosehips contain high concentrations of vitamin C (12652). Advise people to avoid taking large amounts of rosehip along with vitamin C, which together could exceed the tolerable upper intake level of 2000 mg vitamin C per day for adults.

VITAMIN B12: Preliminary evidence suggests that vitamin C supplements can destroy dietary vitamin B12. However, other components of food, such as iron and nitrates, might counteract this effect (9511). It isn't clear whether this interaction is clinically significant, and it can likely be avoided if vitamin C supplements are taken at least 2 hours after meals.

Interactions with Drugs:

ACETAMINOPHEN (Tylenol, others)

High doses of vitamin C (3 grams) competitively inhibits sulfate conjugation of acetaminophen. However, to compensate, elimination of acetaminophen glucuronide and unconjugated acetaminophen increases. Overall, the elimination rate is slightly slower, increasing the half-life from around 2.3 hours to 3.1 hours (6451). This isn't likely to be clinically significant.

ALUMINUM

Vitamin C can increase the amount of aluminum absorbed from aluminum compounds. It's thought that vitamin C chelates aluminum, keeping it in solution and available for absorption (10549, 10550, 10551). In people with normal renal function, urinary excretion of aluminum likely increases, making aluminum retention and toxicity unlikely (10549). Patients with renal failure who take aluminum-containing compounds chronically such as phosphate binders should avoid vitamin C supplements in doses above the recommended dietary allowances.

ASPIRIN

It's been suggested that acidification of the urine by vitamin C could increase reabsorption of salicylates by the renal tubules, and increase plasma salicylate levels (3046). However, short-term use of up to 6 grams/day of vitamin C doesn't seem to affect urinary pH or salicylate excretion (10588, 10589), suggesting this interaction isn't clinically significant. Some preliminary clinical research suggests that that addition of vitamin C to buffered aspirin causes less gastric irritation. Aspirin might cause formation of free radicals that cause gastric lesions, which theoretically might be blocked by the antioxidant effects of vitamin C (14019).

CHEMOTHERAPY

The use of antioxidants like vitamin C during chemotherapy is controversial. There's concern that antioxidants could reduce the activity of chemotherapy drugs which generate free radicals, such as cyclophosphamide, chlorambucil, carmustine, busulfan, thiotepa, and doxorubicin (391). Preliminary data from an animal lymphoma model indicate that vitamin C pretreatment reduces the efficacy of doxorubicin (16407). Leukemia and lymphoma cell culture studies also suggest that vitamin C pretreatment can reduce the cytotoxicity of doxorubicin, cisplatin, vincristine, methotrexate, and imatinib. Since this list includes drugs which do not generate free radicals, mechanisms other than the antioxidant effects of vitamin C might be involved. This might include prevention of the mitochondrial membrane depolarization caused by many chemotherapy drugs, which is involved in

regulating cell death (16407). In contrast, some researchers theorize that antioxidants might make chemotherapy more effective by reducing oxidative stress that could interfere with apoptosis (cell death) of cancer cells (14012, 14013). More evidence is needed to determine what effects vitamin C has on chemotherapy. Advise patients to consult their oncologist before using vitamin C supplements, especially in high doses.

CHOLINE MAGNESIUM TRISALICYLATE (Trilisate)

It's been suggested that acidification of the urine by vitamin C could increase reabsorption of salicylates by the renal tubules, and increase plasma salicylate levels (3046, 4531). However, short-term use of up to 6 grams/day of vitamin C doesn't seem to affect urinary pH or salicylate excretion (10588, 10589), suggesting this interaction probably isn't clinically significant.

ESTROGENS

Increases in plasma estrogen levels of up to 55% occur under some circumstances when vitamin C is taken concurrently with oral contraceptives or hormone replacement therapy, including topical products (129, 130, 11161). It's suggested that vitamin C prevents oxidation of estrogen in the tissues, regenerates oxidized estrogen, and reduces sulfate conjugation of estrogen in the gut wall (129, 11161). When tissue levels of vitamin C are high, these processes are already maximized and supplemental vitamin C doesn't have any effect on estrogen levels. Increases in plasma estrogen levels may occur when women who are deficient in vitamin C take supplements (11161). Monitor these patients for estrogen-related side effects.

FLUPHENAZINE (Prolixin)

In one patient there was a clinically significant decrease in fluphenazine levels when vitamin C (500 mg twice daily) was started (11017). The mechanism isn't known and there's no further data to confirm this interaction.

HMG-CoA REDUCTASE INHIBITORS ("Statins")

A combination of simvastatin (Zocor) and niacin effectively raises HDL cholesterol ("good cholesterol") levels in people with coronary disease and low HDL levels. A combination of antioxidants (vitamin C, vitamin E, beta-carotene, and selenium) seems to blunt this rise in HDL, specifically the HDL-2 and apolipoprotein A1 fractions (7388, 11537). HDL-2 is considered to be the most cardioprotective component of HDL (7388). It isn't known whether this adverse effect is due to a single antioxidant such as vitamin C, or to the combination. It also isn't known whether it will occur in other patient populations, or when antioxidant vitamins are combined with other lipid-altering regimens. Monitor lipid levels closely in people taking lipid-altering drugs and antioxidant vitamin supplements, including vitamin C. Other "statin" drugs include lovastatin (Mevacor), pravastatin (Pravachol), fluvastatin (Lescol), and atorvastatin (Lipitor).

NIACIN

A combination of niacin and simvastatin (Zocor) effectively raises HDL cholesterol ("good cholesterol") levels in people with coronary disease and low HDL levels. A combination of antioxidants (vitamin C, vitamin E, beta-carotene, and selenium) seems to blunt this rise in HDL,

specifically the HDL-2 and apolipoprotein A1 fractions (7388, 11537). HDL-2 is considered to be the most cardioprotective component of HDL (7388). It isn't known whether this adverse effect is due to a single antioxidant such as vitamin C, or to the combination. It also isn't known whether it will occur in other patient populations, or when antioxidant vitamins are combined with other lipid-altering regimens. Monitor lipid levels closely in people taking lipid-altering drugs and antioxidant vitamin supplements, including vitamin C.

NICARDIPINE (Cardene)

Dihydropyridine calcium channel blockers (DCCBs) including nicardipine inhibit uptake of vitamin C by intestinal cells in-vitro (9808). This likely occurs with other DCCBs such as amlodipine (Norvasc), felodipine (Plendil), isradipine (DynaCirc), and nisoldipine (Sular). Whether this causes a clinically significant reduction in vitamin C absorption in humans isn't known.

NIFEDIPINE

Dihydropyridine calcium channel blockers (DCCBs) including nifedipine inhibit uptake of vitamin C by intestinal cells in-vitro (9808). This likely occurs with other DCCBs such as amlodipine (Norvasc), felodipine (Plendil), isradipine (DynaCirc), and nisoldipine (Sular). Whether this causes a clinically significant reduction in vitamin C absorption in humans isn't known.

PROTEASE INHIBITORS (PIs)

Vitamin C seems to modestly reduce indinavir (Crixivan) levels. Vitamin C 1 gram daily for 7 days reduces the area under the concentration/time curve by 14%. The mechanism of this interaction is unknown, but it's unlikely to be clinically significant in most patients. However, the effect of higher doses of vitamin C is unknown (11300). It's also not known whether an interaction could occur with other protease inhibitors, such as amprenavir (Agenerase), nelfinavir (Viracept), ritonavir (Norvir), or saquinavir (Fortovase, Invirase).

SALSALATE (Disalcid)

It's been suggested that acidification of the urine by vitamin C could increase reabsorption of salicylates by the renal tubules, and increase plasma salicylate levels (3046). However, short-term use of up to 6 grams/day vitamin C doesn't seem to affect urinary pH or salicylate excretion (10588, 10589), suggesting this interaction probably isn't clinically significant.

WARFARIN (Coumadin)

High doses of vitamin C may reduce the response to warfarin, possibly by causing diarrhea and reducing warfarin absorption (11566). This occurred in two people who took up to 16 grams/day of vitamin C (9804, 9806). Lower doses of 5 to 10 grams/day can also reduce warfarin absorption, but this doesn't seem to be clinically significant (9805, 9806, 11566, 11567).

Drug Influences on Nutrient Levels and Depletion

ASPIRIN: Aspirin increases elimination of vitamin C. It reduces tissue and leukocyte uptake of vitamin C, leaving more in the plasma to be filtered into the urine (10590, 10591, 10592). It may also reduce absorption of vitamin C from the gut (11526, 11527). These effects are dose-related (10590, 11526). Vitamin C supplementation has been suggested for people taking high-dose aspirin chronically, such as was used in the past for rheumatoid arthritis (10591). Supplements aren't needed with low doses of aspirin used for cardiovascular indications.

DIURETIC DRUGS: In people with chronic renal failure, a 20 mg intravenous dose of furosemide (Lasix) increases urinary losses of vitamin C, probably due to increased water excretion (9525). Significant vitamin C depletion hasn't been reported with chronic oral use of furosemide or other diuretics.

ESTROGENS: Data regarding the effects of oral contraceptives and hormone replacement therapy on vitamin C levels is conflicting (10548, 10583, 10585, 10586, 11528, 11875, 11876). It's suggested that estrogens can reduce vitamin C absorption or increase its breakdown, and that vitamin C stores are used to prevent oxidation of estrogens in the tissues (10548, 10583, 10587, 11161, 11875). This probably only contributes to vitamin C depletion in women with very low intake of vitamin C (10548, 11161, 11528). Supplements aren't necessary for women on estrogens who have an adequate dietary intake of vitamin C.

PROTON PUMP INHIBITORS (PPIs): Preliminary data suggests omeprazole reduces vitamin C levels, possibly due to increased destruction of vitamin C at higher gastric pH levels (10572). It isn't known if this is clinically significant. Other proton pump inhibitors include lansoprazole (Prevacid), rabeprazole (Aciphex), pantoprazole (Protonix), and esomeprazole (Nexium).

Interactions with Lab Tests

ACETAMINOPHEN: Vitamin C can cause false-negative urine results with methods based on hydrolysis and formation of an indophenol blue chromogen (275).

ASPARTATE AMINOTRANSFERASE (AST, SGOT): Large amounts of ascorbic acid can cause a false increase in results of serum tests relying on color reactions (Redox reactions) and Technicon SMA 12/60 (275).

BILIRUBIN: Large amounts of vitamin C can cause a false increase in serum test results measured by Technicon SMA 12/60 or colorimetric methods (275).

CALCIUM/SODIUM: Daily vitamin C 3-6 grams can cause an increase in urinary calcium and test results, and a decrease in urinary sodium and test results (15).

CARBAMAZEPINE (Tegretol): Large doses of vitamin C can cause falsely increased serum assay results measured by Ames ARIS method (275).

CREATININE: Vitamin C can cause a false increase in serum creatinine or urine test results (275).

GLUCOSE: Large amounts of vitamin C can cause false increases in urine test results measured by copper reduction methods (e.g., Clinitest), and false decreases in results measured by glucose oxidase methods (e.g., Clinistix, Tes-Tape) (15).

HIGH-DENSITY LIPOPROTEIN-2 (HDL-2): Vitamin C in combination with beta-carotene, selenium, and vitamin E seems to lower HDL-2 levels. This combination can lower HDL-2 levels by 15% in people with heart disease (7388).

IRON: Vitamin C can increase the absorption of iron and measures of iron status, such as serum iron and ferritin (9518).

LACTIC DEHYDROGENASE (LDH): Vitamin C can cause a false decrease in test results measured by Technicon SMA 12/60 and Abbott 100 methods (275).

OCCULT BLOOD: False-negative guaiac results occur with 250 mg or more of vitamin C per day (3042).

THEOPHYLLINE: Large amounts of vitamin C can cause a false decrease in serum assay results when measured by the ARIS system or Ames Seralyzer photometer (275).

URIC ACID: Large amounts of vitamin C can cause a decrease in serum uric acid concentrations and test results measured by enzymatic method assays (15).

VITAMIN B12: Large amounts of vitamin C can interfere with vitamin B12 assay, resulting in false decrease in vitamin B12 levels (1965).

Interactions with Diseases or Conditions

ANGIOPLASTY: There is some concern that when antioxidant vitamins, including vitamin C, are used in combination they might have harmful effects in patients after angioplasty. A combination of beta-carotene 30,000 IU, vitamin C 500 mg, and vitamin E 700 IU daily started 30 days before angioplasty, and continued for 6 months thereafter, seems to prevent beneficial vascular remodeling in patients by promoting fibrosis at the site of angioplastic intervention (11000). Tell patients to avoid taking supplements containing these vitamins immediately before and following angioplasty without the supervision of a healthcare professional.

CANCER: Cancerous cells accumulate high concentrations of vitamin C. Cancer cells uptake the oxidized form of vitamin C, dehydroascorbic acid, then convert it back to vitamin C (4838, 4839, 4840, 4841). However, it is not yet known if this benefits growth of cancer cells or has any detrimental effect of cancer treatments. Until more is known, patients with cancer should only use high doses of vitamin C under the direction of their oncologist.

DIABETES: Vitamin C can affect glycogenolysis and increase blood sugar, but this effect remains controversial (15). In postmenopausal women with diabetes, supplemental vitamin C in doses greater than 300 mg per day is associated with increased risk of cardiovascular mortality (12498).

GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY: Large amounts of vitamin C can cause hemolysis in individuals with glucose-6-phosphate dehydrogenase deficiency (15).

IRON OVERLOAD, HEMOCHROMATOSIS, THALASSEMIA, SIDEROBLASTIC ANEMIA: Vitamin C can increase iron absorption, which might worsen these conditions (1960). Theoretically, large doses of vitamin C given intravenously might trigger the release of free radicals and have a prooxidant effect in iron-overloaded uremic patients (14014).

KIDNEY STONES (Nephrolithiasis): Large amounts of vitamin C can increase the risk of oxalate stone formation. Vitamin C is metabolized to oxalic acid, so increased consumption increases the urinary concentration of oxalic acid (10356). In people with a history of oxalate kidney stones (the most common type of nephrolithiasis), supplemental vitamin C 1 gram per day appears to increase stone risk by 40% (12653). Tell patients prone to kidney stone formation to avoid high doses of vitamin C.

MYOCARDIAL INFARCTION (MI): Vitamin C levels are significantly reduced during the acute phase after a MI. However, low plasma levels of vitamin C have not been associated with an increased risk of MI (5876).

SICKLE CELL DISEASE: Vitamin C can decrease blood pH, which can rarely precipitate sickle cell crisis (15).

NICOTINE and SMOKING: Smokers have lower plasma levels of vitamin C than nonsmokers with similar dietary intake of vitamin C. This is likely due to increased use of vitamin C to counteract oxidizing free radicals in cigarette smoke (5875, 11501). Advise smokers to consume a diet rich in vitamin C, or recommend a supplement if this isn't possible. Smokers may need between 124 and 200 mg/day to maintain normal plasma levels (11546). There doesn't seem to be an effect of nicotine on vitamin C levels and depletion hasn't been reported with nicotine replacement products (e.g., patches, gum, etc).

SMOKELESS TOBACCO USE: Users of chewing tobacco tend to have lower plasma levels of vitamin C than non-users with similar dietary intakes (11501). This may increase their risk of precancerous oral lesions, because the antioxidant effects of vitamin C are needed to prevent formation of carcinogenic nitrosamines from nitrates and nitrites in smokeless tobacco (11502). Advise tobacco users to consume a diet rich in vitamin C.

Dosage

ORAL: For scurvy, 100-250 mg once or twice daily for several days is commonly used (15).

For treating the common cold, 1-3 grams daily has been used (6458).

For preventing the common cold, in people under physical stress, vitamin C 600-1000 mg daily has been used (9831).

During acute stress, vitamin C 1 gram 3 times daily, as a sustained release preparation, has been used for up to 14 days (10353).

For preventing contrast-mediated nephropathy, vitamin C 3 grams is given before coronary angiography and then 2 grams is given after the procedure in the evening and again the following morning (12234).

For chronic hemodialysis in adults, 100-200 mg per day is recommended (15).

For preventing nitrate tolerance, 3-6 grams of vitamin C daily has been used (1961).

For preventing sunburn, 2 grams of vitamin C in combination with RRR-alpha-tocopherol (natural vitamin E) 1000 IU has been used (4716).

For treatment of premalignant gastric lesions, vitamin C 1 gram twice daily has been used (2579).

For slowing progression of atherosclerosis, slow release vitamin C 250 mg in combination with 91 mg (136 IU) of vitamin E has been given twice daily for up to 6 years (1918, 10473).

For treatment of familial hypercholesterolemia in children, vitamin C 500 mg daily and vitamin E 400 IU daily have been used for up to 6 months with a National Cholesterol Education Program Step II (NCEP-II) diet (10352).

For tyrosinemia in premature infants on high protein diets, 100 mg of vitamin C has been used (15).

For reducing albuminuria in patients with type 2 diabetes, vitamin C 1250 mg with vitamin E 680 IU daily has been used for 4 weeks (10434).

For prostate cancer, vitamin C 120 mg in combination with vitamin E (alpha-tocopherol) 30 mg, beta-carotene 6 mg, selenium 100 mcg, and zinc 20 mg has been used (14135).

For infertility associated with luteal phase defect, 750 mg per day has been used (12010).

For attention-deficit hyperactivity disorder (ADHD), vitamin C 25 plus flaxseed oil providing 200 mg alpha-linolenic acid twice daily has been used (14443).

For preventing complex regional pain syndrome in patients with wrist fractures, vitamin C 500 mg daily for 50 days has been used (2045, 16302).

For preventing gout, vitamin C 500-1500 mg daily from food and/or supplements has been used (16755, 16820).

The daily recommended dietary allowances (RDAs) are: Infants 0 to 12 months, human milk content (older recommendations specified 30-35 mg); Children 1 to 3 years, 15 mg; Children 4 to 8 years, 25 mg; Children 9 to 13 years, 45 mg; Adolescents 14 to 18 years, 75 mg for boys and 65 mg for girls; Adults age 19 and greater, 90 mg for men and 75 mg for women; Pregnancy and Lactation: age 18 or younger, 115 mg; ages 19 to 50 years 120 mg. People who use tobacco should take an additional 35 mg per day (4844).

The tolerable upper intake levels (UL) for vitamin C are 400 mg per day for children ages 1 to 3 years, 650 mg per day for children 4 to 8 years, 1200 mg per day for children 9 to 13 years, and 1800 mg per day for adolescents and pregnant and lactating women 14 to 18 years, and 2000 mg per day for adults and pregnant and lactating women (4844).

TOPICAL: Most topical preparations used for aged or wrinkled skin are applied daily. Studies have used creams containing 5% to 10% vitamin C (6155). In one study a specific vitamin C formulation (Cellex-C High Potency Serum) used 3 drops applied daily to areas of facial skin (6155). Avoid application to eye area or eyelids. Also avoid contact with hair or clothes. It can cause discoloration (6166).

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