Vitamin C

SCIENTIFIC NAME
Ascorbic acid

FAMILY

CAUTION: Acerola, and Rose Hip are rich in vitamin C and are sometimes consumed as sources of vitamin C.

Other Common Names

Acide Ascorbique, Acide Cévitamique, Acide Iso-Ascorbique, Acide L-Ascorbique, Acido Ascorbico, Antiscorbutic Vitamin, Ascorbate, Ascorbate de Calcium, Ascorbate de Sodium, Ascorbic Acid, Ascorbyl Palmitate, Ascorbyl Phosphate, Calcium Ascorbate, Cetyl Ascorbate, Cevitamic Acid, Chromium Ascorbate, Copper Ascorbate, Ferrous Ascorbate, Iron Ascorbate, Iso-Ascorbic Acid, L-Ascorbic Acid, Magnesium Ascorbate, Niacin Ascorbate, Niacinamide Ascorbate, Nicotinamide Ascorbate, Palmitate d'Ascorbyl, Phosphate Ascorbate, Potassium Ascorbate, Selenium Ascorbate, Sodium Ascorbate, Strontium Ascorbate, Vitamina C, Vitamine Antiscorbutique, Vitamine C, Zinc Ascorbate.

Overview

Vitamin C is a water-soluble vitamin that is essential for human survival (90946). Unlike many other mammals, humans do not produce vitamin C, so sufficient levels must be obtained from the diet (90946). Dietary sources of vitamin C include various fruits and vegetables, particularly citrus fruits such as oranges (90946).

WARNINGS

Coronavirus disease 2019 (COVID-19): Some experts suggest taking vitamin C 200 mg daily to prevent COVID-19 and other respiratory tract infections, or 1-2 grams daily at the onset of symptoms to improve recovery. These doses are likely safe in most adults, but there is no strong evidence to support the effectiveness of vitamin C for the prevention of COVID-19 or treatment of mild-to-moderate COVID-19. There is some evidence that vitamin C might prevent mortality in critically ill patients hospitalized with COVID-19, but more research is needed to confirm these findings. Ensure that patients considering vitamin C for COVID-19 follow healthy lifestyle choices and proven prevention methods as well.

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 daily (1959,4713,4714,4844). ...when used intravenously or intramuscularly and appropriately. Injectable vitamin C is an FDA-approved prescription product (15) and has been used with apparent safety in clinical trials up to 150 mg/kg daily for up to 4 days (114489) and up to 200 mg/kg daily for up to 2 days (114492).

POSSIBLY UNSAFE ...when used orally in excessive doses. Doses greater than the tolerable upper intake level (UL) of 2000 mg daily 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 daily for children ages 1 to 3 years, 650 mg daily for children 4 to 8 years, 1200 mg daily for children 9 to 13 years, and 1800 mg daily 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 over age 19 not to use doses exceeding the UL of 2000 mg daily when pregnant or breast-feeding and for those 14-18 years of age not to use doses exceeding 1800 mg daily when pregnant or breast-feeding. Higher doses can cause osmotic diarrhea and gastrointestinal upset. Large doses of vitamin C during pregnancy can also cause newborn scurvy (4844); avoid using.

Adverse Effects

General: Orally, intravenously, and topically, vitamin C is well-tolerated.

Most Common Adverse Effects:

Orally: Abdominal cramps, esophagitis, heartburn, headache, osmotic diarrhea, nausea, vomiting. Kidney stones have been reported in those prone to kidney stones. Adverse effects are more likely to occur at doses above the tolerable upper intake level of 2 grams daily.

Topically: Irritation and tingling.

Serious Adverse Effects (Rare):

Orally: There have been rare case reports of carotid inner wall thickening after large doses of vitamin C.

Intravenously: There have been case reports of hyperoxalosis and oxalate nephropathy following high-dose infusions of vitamin C.

Cardiovascular

Evidence from population research has found that high doses of supplemental vitamin C might not be safe for some people. In postmenopausal adults with diabetes, supplemental vitamin C intake in doses greater than 300 mg per day is associated with increased risk of cardiovascular mortality. However, dietary intake of vitamin C is not associated with this risk. Also, vitamin C intake is not associated with an increased risk of cardiovascular mortality in patients without diabetes (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 (1355). This effect was not associated with vitamin C from dietary sources (1355).

There is also some concern that vitamin C may increase the risk of hypertension in some patients. A meta-analysis of clinical research suggests that, in pregnant patients at risk of pre-eclampsia, oral intake of vitamin C along with vitamin E increases the risk of gestational hypertension (83450). Other clinical research shows that oral intake of vitamin C along with grape seed polyphenols can increase both systolic and diastolic blood pressure in hypertensive patients (13162). Three cases of transient hypotension and tachycardia during intravenous administration of vitamin C have also been reported (114490).

Dental

Orally, vitamin C, particularly chewable tablets, has been associated with dental erosion (83484).

Dermatologic

Topically, vitamin C might cause tingling or irritation at the site of application (6166). A liquid containing vitamin C 20%, red raspberry leaf cell culture extract 0.0005%, and vitamin E 1% (Antioxidant and Collagen Booster Serum, Max Biocare Pty Ltd.) has been reported to cause mild tingling and skin tightness (102355). It is unclear if these effects are due to vitamin C, the other ingredients, or the combination.

Gastrointestinal

Orally, the adverse effects of vitamin C are dose-related and include nausea, vomiting, esophagitis, heartburn, abdominal cramps, gastrointestinal obstruction, and diarrhea. Doses greater than the tolerable upper intake level (UL) of 2000 mg per day can increase the risk of adverse effects such as osmotic diarrhea and severe gastrointestinal upset (3042,4844,96707,104450,114493,114490). Mineral forms of vitamin C, such as calcium ascorbate (Ester-C), seem to cause fewer gastrointestinal adverse effects than regular vitamin C (83358). In a case report, high dose intravenous vitamin C was associated with increased thirst (96709).

Genitourinary

Orally, vitamin C may 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 (3042,90943). Supplemental vitamin C over 250 mg daily has been associated with higher risk for kidney stones in males. There was no clear association found in females, but the analysis might not have been adequately powered to evaluate this outcome (104029). In people with a history of oxalate kidney stones, supplemental vitamin C 1 gram per day appears to increase kidney stone risk by 40% (12653). A case of hematuria, high urine oxalate excretion, and the presence of a ureteral stone has been reported for a 9-year-old male who had taken about 3 grams of vitamin C daily since 3 years of age. The condition resolved with cessation of vitamin C intake (90936).

Hematologic

Prolonged use of large amounts of vitamin C can result in increased metabolism of vitamin C; subsequent reduction in vitamin C intake may precipitate the development of scurvy (15). In one case, a patient with septic shock and a large intraperitoneal hematoma developed moderate hemolysis and increased methemoglobin 12 hours after a high-dose vitamin C infusion. The patient received a blood transfusion and the hemolysis resolved spontaneously over 48 hours (112479).

Neurologic/CNS

Orally, the adverse effects of vitamin C are dose-related and include fatigue, headache, insomnia, and sleepiness (3042,4844,83475,83476).

Renal

Hyperoxalosis and oxalate nephropathy have been reported following high-dose infusions of vitamin C. Hyperoxalosis and acute kidney failure contributed to the death of a 76-year-old patient with metastatic adenocarcinoma of the lung who received 10 courses of intravenous infusions containing vitamins, including vitamin C and other supplements over a period of 1 month. Dosages of vitamin C were not specified but were presumed to be high-dose (106618). In another case, a 34-year-old patient with a history of kidney transplant and cerebral palsy was found unresponsive during outpatient treatment for a respiratory tract infection. The patient was intubated for acute hypoxemic respiratory failure, initiated on vasopressors, hydrocortisone, and antibacterial therapy, and received 16 doses of vitamin C 1.5 grams. Serum creatinine level peaked at greater than 3 times baseline and the patient required hemodialysis for oliguria and uncontrolled acidosis. Kidney biopsy revealed oxalate nephropathy with concomitant drug-induced interstitial nephritis (106625). In another case, a 41-year-old patient with a history of kidney transplant presented with fever, nausea, and decreased urine output 4 days after receiving intravenous vitamin C 7 grams for urothelial carcinoma. Serum creatinine levels increased from 1.7 mg/dL to 7.3 mg/dL over those 4 days, and hemodialysis was initiated 3 days after admission due to anuria. Renal biopsy confirmed the diagnosis of acute oxalate nephropathy (109962).

Other

Intravenously, hypernatremia and falsely elevated ketone levels is reported in a patient with septic shock and chronic kidney disease after a high-dose vitamin C infusion. The hypernatremia resolved over 24 hours after cessation of the infusion (112479).

Effectiveness

EFFECTIVE

Vitamin C deficiency. Oral or intramuscular vitamin C is effective for preventing or treating vitamin C deficiency.
Details: Administering vitamin C orally or intramuscularly prevents and treats vitamin C deficiency, including scurvy. Vitamin C administration can reverse complications of scurvy within 2 days to 3 weeks (4844). In newborns with transient tyrosinemia due to vitamin C deficiency, oral or intramuscular vitamin C can correct this condition (15).

POSSIBLY EFFECTIVE

Anemia of chronic disease. Oral vitamin C seems to improve markers of anemia in patients on hemodialysis.
Details: Meta-analyses of clinical research in hemodialysis patients with anemia shows that treatment with vitamin C 200-300 mg three times weekly for 3-6 months increases hemoglobin levels by approximately 0.9 grams/dL, increases transferrin saturation by about 8%, and decreases the required recombinant human erythropoietin dose by 17 U/kg weekly when compared with standard care (83447,83475).

Atrial fibrillation. Oral and intravenous vitamin C seems to help prevent atrial fibrillation after cardiac surgeries.
Details: Meta-analyses of clinical research show that taking vitamin C prior to and after cardiac surgery reduces the risk of postoperative atrial fibrillation by 27% to 53%. Most studies administered vitamin C at doses of 1-2 grams orally daily for 1-3 days prior to cardiac surgery, followed by 1-2 grams in two divided doses daily for 4-5 days after cardiac surgery. Some studies provided vitamin C intravenously at similar doses, but oral vitamin C seems to be more effective (91233,96703,96705). Despite these findings, a meta-analysis of clinical research conducted only in the U.S. does not support the benefit of vitamin C for reducing postoperative atrial fibrillation (96703). These differences may be related to lifestyle factors such as nutrition, as well as differences in hospital treatments.

Vitamin C has also been studied in combination with eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) with evidence of benefit (90701).

Bowel preparation. Powdered vitamin C is approved for use as part of a polyethylene glycol-based bowel preparation for colonoscopy.
Details: Clinical research shows that treatment with 2 liters of oral solution containing polyethylene glycol (PEG) plus vitamin C achieves a similar quality of bowel cleansing as treatment with 4 liters of PEG when administered on the evening prior to colonoscopy or when administered in a split-dose regimen. Patients given 2 liters of PEG plus vitamin C solution also have better adherence and experience fewer adverse events, such as nausea, vomiting, or abdominal bloating, compared to patients treated with 4 liters of PEG solution without vitamin C (90413,90415,90420,90424,90428). This treatment also appears to be effective and tolerable in elderly patients aged 60-79 years, including those with poor bowel habits and a high number of comorbidities (108085). Other clinical research in older adults undergoing bowel preparation for colonoscopy also shows that taking 1 liter of PEG plus vitamin C (CleanViewAL, Taejoon Pharm) results in similar quality of bowel cleansing overall and per segment with similar tolerability and adverse effects as sodium picosulfate 170 mL plus magnesium citrate or oral sulfate solution alone (111297,112476).

The most common PEG plus vitamin C preparation used in clinical research is MoviPrep (Norgine BV), which contains macrogol 3350 100 grams, sodium sulfate 7.5 grams, sodium chloride 2.7 grams, potassium chloride 1 gram, vitamin C 4.7 grams, and sodium ascorbate 5.9 grams per liter of solution (90413,90415,90424). In the U.S., MoviPrep is approved by the Food and Drug Administration (FDA) for bowel preparation prior to a colonoscopy.

Cataracts. Dietary and supplemental intake of vitamin C may reduce the risk of developing cataracts.
Details: Population research suggests that people with the highest total intake of vitamin C have about a 19% reduced risk of developing cataracts when compared with those with the lowest total intake, with the most benefit observed for nuclear cataracts (96711). Additionally, another observational study shows that higher supplemental intake of vitamin C over 10 years is associated with a 60% reduction in the incidence of nuclear and cortical cataracts (4208). Other population research suggests that individuals with the highest blood levels of vitamin C have a 33% lower odds of developing age-related cataract, but any benefit is limited to Asian populations (90944). An umbrella review of meta-analyses also shows that dietary intake of vitamin C is associated with a 27% lower odds of cataract development (112095).

However, a prospective clinical study shows that a combination of vitamin C, vitamin E, and beta-carotene does not prevent age-related loss of vision from cataracts in well-nourished people with an average supplementation duration of 6.3 years (7304).

Common cold. Oral high-dose vitamin C might modestly shorten and reduce cold symptoms; however, taking vitamin C prophylactically does not seem to prevent the development of a cold.
Details: There is substantial controversy about the effectiveness of vitamin C for treating the common cold (1969,1989,7100,9835,9836). 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 (1966,1967,1968,1987,6458,7102,9832,83487). However, other studies have found no effect with doses up to 3 grams daily (9833). A meta-analysis of clinical research in healthy children and adults shows that taking vitamin C 1-4 grams daily for one week to 5 months reduces cold severity by 13%, limits absences from daily activities, and improves the duration of severe symptoms, but does not reduce the duration of mild symptoms, when compared with placebo (113665).

Vitamin C has also been investigated for preventing the common cold. A meta-analysis of clinical research suggests that vitamin C supplementation decreases the incidence of cold in individuals exposed to physical stress, but not in the general population (83487). Other research suggests vitamin C may be more effective for treating cold symptoms in children than in adults. Also, there may be a dose-dependent response; doses of at least 2 grams daily seem to work better than 1 gram doses (9834). 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 does not seem to affect the risk of getting a cold (10780).

Complex regional pain syndrome. Most research shows that taking oral vitamin C after a wrist or distal radius fracture or after orthopedic surgery seems to reduce the risk of developing complex regional pain.
^ Details: Although some research has found no benefit in patients with distal radius (i.e. wrist) fractures (90411,96702), most clinical research shows that taking vitamin C 500 mg daily, and possibly doses of up to 1500 mg daily, for 45-50 days beginning immediately after fracture can reduce the risk of developing complex regional pain syndrome (2045,16302,96700,96706). Reasons for discrepancies are unclear but might relate to differences in diagnostic criteria for complex regional pain syndrome (96702).

Research in patients undergoing orthopedic surgery has also shown benefit with the use of vitamin C for the prevention of complex regional pain syndrome (90422,108076,108087). One meta-analysis of clinical research in patients undergoing wrist, foot, or ankle surgery shows that taking vitamin C 500-1000 mg for 42-50 days following surgery reduces the rate of complex regional pain syndrome, and may improve pain following ankle or foot surgery, when compared with placebo (108076). The validity of these findings is limited by the high heterogeneity of included trials. Another meta-analysis of clinical research in patients undergoing orthopedic surgery (i.e. wrist, knee, ankle, foot, lumbar, rotator cuff) suggests that oral and intravenous vitamin C may have similar effectiveness; however, this evidence is low quality (108087).

Exercise-induced respiratory infections. High-dose oral vitamin C seems to reduce the risk of respiratory infections associated with strenuous exercise.
^ Details: Some preliminary clinical research suggests that prophylactic use of vitamin C in doses of 600 mg to 1 gram daily for 3-8 weeks before heavy physical exercise, such as a marathon, might prevent upper respiratory infections that sometimes follow heavy exercise (9831,83370). More recently, high doses of vitamin C have been studied. A large clinical study in army recruits undergoing basic military training shows that taking vitamin C 6 grams daily for one month reduces the odds of getting a cold by 20% when compared with placebo (102975).

Hypercholesterolemia. Oral vitamin C seems to reduce lipid levels in patients with hypercholesterolemia.
^ Details: A meta-analysis of clinical research in patients with hypercholesterolemia shows that taking vitamin C 500 mg daily for at least 4 weeks reduces low-density lipoprotein (LDL) cholesterol by about 8 mg/dL and reduces triglycerides by about 20 mg/dL when compared with control (83445).

Hypertension. Oral vitamin C seems to modestly reduce blood pressure in patients with hypertension, but some evidence is conflicting.
^ Details: Vitamin C seems to modestly reduce systolic blood pressure (SBP), without meaningful effects on diastolic blood pressure (DBP) (2044,9822,13162,83483,102974). A meta-analysis of 13 clinical trials in patients with hypertension, with or without other comorbidities, shows that taking a median dose of vitamin C 500 mg daily for 8 weeks reduces SBP but not DBP by about 5 mmHg. Some of the studies used vitamin C in combination with other supplements, such as vitamin E and magnesium. When studies assessing vitamin C alone were analyzed, the magnitude of reduction in SBP decreased (83483). A newer meta-analysis of small clinical studies in patients with essential hypertension shows that taking vitamin C 200 mg or more daily reduces SBP by about 4 mmHg and DBP by about 2 mmHg (102974). However, this newer analysis omitted numerous relevant studies and included studies with normotensive patients and those without an adequate control, limiting the validity of its findings.

In contrast, a network meta-analysis of small, low-quality clinical studies comparing five different vitamins in adults with essential hypertension shows that vitamin C does not reduce SBP, DBP, mean 24-hour SBP, mean 24-hour DBP, or heart rate when compared with placebo and when indirectly compared with vitamin B2, vitamin D, vitamin E, and folic acid. However, the included studies were of low quality and high heterogeneity, particularly in dosing, limiting the validity of the results (113668).

Laser skin resurfacing. Topical vitamin C seems to reduce erythema occurring after cosmetic laser skin resurfacing procedures intended to reduce scars and wrinkles.
^ Details: 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).

Lead toxicity. Dietary vitamin C seems to lower concentrations of lead in the blood.
^ Details: Observational research has found that consuming more vitamin C from dietary sources is associated with lower blood concentrations of lead. People who consumed at least 340 mg of vitamin C daily as part of the diet had lower blood lead levels than those who consumed less than 100 mg vitamin C daily (3097,3098,3099).

Nitrate tolerance. Oral vitamin C might prevent nitrate tolerance in some patients.
^ Details: Small clinical studies show that 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 tolerance to the vasodilatory effects of nitrates (1441,1961).

Postoperative pain. Oral or intravenous vitamin C might prevent acute postoperative pain following certain surgeries. It is unclear if vitamin C reduces chronic postoperative pain.
^ Details: A meta-analysis of 7 small clinical studies in adults undergoing elective surgery shows that receiving perioperative vitamin C, either as 1 gram orally, 2-3 grams intravenously, or 50 mg/kg intravenously, modestly reduces acute pain and opioid requirements for up to 24 hours when compared with control (105457). Most surgeries were laparoscopic and included cholecystectomy, colectomy, hysterectomy; two non-laparoscopic surgeries included uvulopalatopharyngoplasty with tonsillectomy and major abdominal surgery (90418,99840,105457).

A meta-analysis of clinical trials in adults undergoing noncardiac surgery (i.e., orthopedic, abdominal, gynecologic, kidney transplantation) shows that administering perioperative vitamin C, either orally or intravenously, reduces postoperative intravenous morphine requirements at 2, 24, and 48 hours after surgery and improves pain scores at 2, 6, and 24 hours after surgery when compared with placebo. The dose of vitamin C did not appear to impact outcomes. However, when only laparoscopic surgeries are included, perioperative vitamin C does not improve pain or morphine use when compared with placebo (108087). A moderate-sized clinical study in adults undergoing transurethral resection of a bladder tumor under general anesthesia shows that administering intravenous vitamin C 1 gram after induction of anesthesia reduces the incidence and severity of catheter-related bladder discomfort immediately after surgery and at 1 and 2 hours postoperatively, but not 6 hours, when compared with placebo. However, vitamin C does not reduce postoperative pain scores or analgesic requirements when compared with placebo (111645).

For dental surgery, a small observational study in adults undergoing surgery for wisdom tooth extraction shows that taking vitamin C 500 mg three times daily for 7 days in addition to standard treatment reduces pain 24, 48, and 72 hours after surgery when compared with control (113664). Further research is needed to determine the effects of vitamin C for acute postoperative pain.

Vitamin C has also been evaluated for reducing chronic pain after surgery. Clinical research in patients undergoing surgery for foot or ankle trauma shows that taking vitamin C 500 mg orally twice daily postoperatively for 6 weeks reduces pain scores when compared with placebo at 2 weeks and 6 weeks. The mean total amount of diclofenac used for pain relief over the 6-week period is also reduced, from 5.7 grams with placebo to 3.4 grams with vitamin C (102131).

Wrinkled skin. Topical vitamin C might reduce the appearance of existing wrinkles.
^ Details: Topical preparations containing vitamin C seem to improve the appearance of wrinkled skin. Some evidence shows that vitamin C 3% applied for 12 weeks might reduce facial wrinkles (14008). A small clinical study shows that applying a dissolving microneedle patch containing vitamin C 5.6% every 4 days for 12 weeks to crow's feet on one side of the face reduces wrinkles when compared to control treatment applied on the other side of the face (98780). Other clinical research in females aged 30-60 years shows that applying an oil-soluble cream containing the vitamin C derivative tetra-isopalmitoyl ascorbic acid 1%, 2%, or 3% to the periorbital area twice daily for 8 weeks reduces visual wrinkle grading when compared with placebo. A dose analysis shows greater improvements in wrinkle parameters, average wrinkle depth, and mean depth with the lower concentration, while greater improvements in maximum roughness and maximum depth are observed with the higher concentration (108072). This study only included individuals defined as having Fitzpatrick skin type III or IV; it effects on other skin types is unclear.

Preparations containing vitamin C in combination with other ingredients have also been investigated. A small low-quality trial in females with moderately photodamaged and hyperpigmented facial skin shows that applying a moisturizer with vitamin C 30%, vitamin E, and coenzyme Q10 once daily in the morning, along with applying retinol 0.5% once daily or once every other day for 12 weeks, seems to improve skin tone, photodamage, and wrinkles when compared to baseline (99085). In another small trial, a topical preparation containing vitamin C 10% as L-ascorbic acid along with acetyl tyrosine, zinc sulfate, sodium hyaluronate, and bioflavonoids (Cellex-C High Potency Serum) applied to photo-aged facial skin for 3 months improves fine and coarse wrinkling, yellowing and sallowness, roughness, and skin tone when compared with placebo (6155). It is unclear if the beneficial effects of these products are due to vitamin C, other ingredients, or the combination.

POSSIBLY INEFFECTIVE
Acute bronchitis. Oral vitamin C doesn't seem to improve symptoms of acute bronchitis.
^ Details: A clinical study in adults with acute bronchitis shows that 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 quality of life or bronchitis duration when compared with azithromycin (9827).

Asthma. Oral vitamin C doesn't seem to prevent asthma or improve lung function.
^ Details: Although some observational research has found that some patients with asthma might have lower serum vitamin C levels (5873), other observational research found that increased dietary vitamin C intake is not associated with a reduced risk of asthma or improved lung function (15006,34567). In addition, clinical research shows that supplemental intake of vitamin C does not reduce asthma symptoms, improve lung function, or reduce the use of inhaled steroids in asthma patients (90409).

Atherosclerosis. Oral vitamin C does not seem to reduce the progression of atherosclerosis.
^ Details: A clinical study shows that taking a specific combination product containing slow-release vitamin C 250 mg and vitamin E 136 IU (CellaVie, Ferrosan A/S) twice daily modestly slows the 3-year progression of atherosclerosis of the carotid artery in males, but not females. This result persisted at a 6-year follow-up of this study (1918,10473). However, when this form of vitamin C is used alone, it does not slow the 3-year progression of atherosclerosis of the carotid artery (1918).

Bladder cancer. Oral vitamin C does not reduce the risk of bladder cancer or mortality from bladder cancer.
^ Details: Epidemiological research has found that supplemental vitamin C intake is not associated with mortality rate in patients with bladder cancer (9839). A secondary analysis of a large clinical trial, the Physicians' Health Study II, in healthy men aged at least 50 years also shows that taking vitamin C 500 mg daily alone or with vitamin E 400 IU daily for up to 10 years does not reduce the risk of developing bladder cancer or bladder cancer-related deaths when compared with placebo (90097).

Cardiovascular disease (CVD). Oral vitamin C does not seem to be beneficial for either primary or secondary CVD prevention.
^ Details: Vitamin C does not seem to be beneficial for primary prevention of CVD. Some population research has found that higher supplemental vitamin C or dietary vitamin C has been associated with a reduced risk of developing CVD (10358,14108,109779), while other observational research has found no benefit (34566,10358,14108). However, meta-analyses of clinical research in healthy patients show that vitamin C supplementation does not prevent CVD or coronary heart disease when compared with control (97308,104025). In 2004, the American Heart Association stated that current evidence does not justify use of antioxidants such as vitamin C for reducing the risk of CVD (12142).

Evidence is also negative for secondary prevention in people with coronary heart disease. Population studies have found that higher serum vitamin C was associated with no effect or decreased CVD mortality from CVD (3910,5878). A meta-analysis of two large clinical trials shows that vitamin C supplementation does not reduce CVD events or CVD mortality when compared with control (97308).

Colorectal cancer. Oral vitamin C does not seem to prevent colorectal cancer.
^ Details: Population research has found that dietary vitamin C intake is not associated with a reduced risk of developing colon cancer. When total vitamin C intake from food and supplements is considered, there is a modest association (34600). However, most clinical trials show that supplemental vitamin C, alone or along with other antioxidants, does not reduce the risk of colorectal cancer development, colorectal cancer or adenoma recurrence, or colorectal cancer-related mortality (34580,34581,34594,90097,90089,92903).

Fetal and premature infant mortality. Oral vitamin C does not seem to prevent neonatal death.
^ Details: Meta-analyses of clinical research show that taking vitamin C alone or with other supplements does not reduce the risk of neonatal death (83472,96707).

Fractures. Oral vitamin C does not seem to improve fracture healing.
^ Details: Clinical research shows that taking vitamin C 500 mg daily for 50 days following an acute distal radial fracture does not improve physical function, symptoms, or healing rates when compared with placebo (90411).

Helicobacter pylori. Oral vitamin C does not seem to improve eradication of H. pylori.
^ Details: Most clinical research shows that treatment with vitamin C, alone or in combination with vitamin E, does not improve the eradication rate of H. pylori when taken with a standard eradication regimen when compared with the eradication regimen alone (83476,90094).

Hereditary motor and sensory neuropathy. Oral vitamin C does not seem to improve neuropathy in these patients.
^ Details: In a meta-analysis of five studies in patients with Charcot-Marie-Tooth disease type 1A, taking vitamin C 1-4 grams orally daily for 1 year did not improve neuropathy when compared with placebo (99084). Continuing vitamin C 4 grams daily for 2 years also does not improve neuropathy in these patients (90419).

Interferon-related retinopathy. Oral vitamin C does not seem to improve retinopathy associated with interferon therapy.
^ Details: A small clinical study in patients with chronic hepatitis C receiving interferon therapy shows that taking vitamin C 600 daily orally does not seem to reduce the risk of retinopathy from interferon therapy when compared with control (10355).

Leukemia. Oral vitamin C does not seem to reduce the risk of leukemia or mortality from leukemia.
^ Details: A large clinical trial in men aged at least 50 years shows that taking vitamin C 500 mg daily, alone or along with vitamin E 400 IU daily, for up to 10 years does not reduce the risk of developing leukemia or leukemia-related deaths when compared with placebo (90097).

Low birth weight. Oral vitamin C does not seem to reduce the risk of infants being born with a low birth weight.
^ Details: Meta-analyses of clinical research show that maternal use of oral vitamin C alone or with other supplements does not reduce the risk of giving birth to infants with low birth weight when compared with control (83450,83472).

Lung cancer. Oral vitamin C does not seem to reduce the risk of lung cancer.
^ Details: Two meta-analyses of clinical research suggest that taking vitamin C, alone or in combination with vitamin E, does not reduce the incidence of lung cancer or lung cancer-related mortality (34528,34632). Also, a clinical study in females shows that taking supplemental vitamin C 500 mg daily, with or without vitamin E and beta carotene, is associated with an INCREASED risk of lung cancer when compared with placebo (34580). However, another large epidemiological cancer screening trial with a mean follow-up of over 12 years suggests that moderate dietary intake of vitamin C around 500 mg daily is protective against lung cancer, but higher doses of vitamin C might increase the risk of lung cancer (112096).

Melanoma. Oral vitamin C does not seem to reduce the risk of melanoma.
^ Details: Clinical research shows that taking vitamin C 500 mg daily, alone or along with vitamin E 400 IU daily, for up to 10 years does not reduce the risk of developing melanoma or melanoma-related deaths when compared with placebo in men aged at least 50 years (90097).

Miscarriage. Oral vitamin C does not seem to reduce the risk of miscarriage.
^ Details: A meta-analysis of clinical research shows that taking vitamin C alone or with other supplements does not reduce the risk of miscarriage when compared with control (94820).

Overall mortality. Oral vitamin C does not reduce overall mortality.
^ Details: Although population research suggests that higher dietary intake and higher plasma vitamin C levels are associated with a reduced risk of mortality from all causes (3910,109779), vitamin C supplementation does not seem to affect overall mortality. Meta-analyses of clinical research show that taking vitamin C supplements does not reduce overall mortality when compared with control (34622,111641). Clinical studies of vitamin C used in combination with vitamin E, beta carotene, and/or selenium and zinc, also show no benefit for overall mortality (9817,14109).

Pancreatic cancer. Oral vitamin C does not seem to prevent pancreatic cancer.
^ Details: Observational research has found that increased dietary vitamin C intake is associated with up to a 30% reduced risk of pancreatic cancer (99083,99086). However, clinical research shows that supplemental vitamin C 500 mg daily does not reduce the risk of pancreatic cancer in females (34580). Also, taking vitamin C in combination with beta-carotene plus vitamin E does not reduce the risk of pancreatic cancer (12185,34581).

Pre-eclampsia. Oral vitamin C does not seem to prevent pre-eclampsia.
^ Details: Despite some early positive research in high-risk pregnancies, the majority of meta-analyses and clinical studies show that taking vitamin C alone or with vitamin E or other supplements does not reduce the risk of pre-eclampsia when compared with control. There is even some concern that vitamin C supplementation may increase the risk of gestational hypertension (3236,83450,83472,83474,96707).

Preterm labor. Oral vitamin C does not seem to prevent preterm labor.
^ Details: Meta-analyses of clinical research show that taking vitamin C alone or with other supplements does not reduce the risk of preterm labor when compared with control (83450,83472,96707).

Prostate cancer. Oral vitamin C does not seem to prevent prostate cancer.
^ Details: 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, taken 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 those 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 when compared with placebo (16708). Similarly, results from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial seem to show that supplemental or dietary intake of vitamin C does not reduce the risk of prostate cancer when compared to individuals not taking vitamin C (14124).

Radiation dermatitis. Topical vitamin C does not seem to prevent radiation dermatitis in cancer patients.
^ Details: A small clinical study shows that applying a 10% vitamin C solution does not appear to protect from radiation dermatitis when applied to the scalps of patients treated with radiation for intracranial tumors (789).

Small for gestational age (SGA). Oral vitamin C does not seem to reduce SGA.
^ Details: Meta-analyses of clinical research show that taking vitamin C alone or with other supplements does not reduce the risk of small for gestational age birth when compared with control (83450,83472).

Stillbirth. Oral vitamin C does not seem to prevent stillbirth.
^ Details: Meta-analyses of clinical research show that maternal use of vitamin C alone or with other supplements does not reduce the risk of stillbirth when compared with control (83472,96707).

LIKELY INEFFECTIVE
Coronavirus disease 2019 (COVID-19). Oral vitamin C, even at high doses, does not seem to speed recovery from COVID-19 in non-hospitalized patients. Most studies show that oral or intravenous vitamin C given to patients hospitalized with COVID-19

does not improve organ function or survival, but the evidence is conflicting. It is unclear whether vitamin C is beneficial for long COVID.

^ Details: A clinical study in adult outpatients with confirmed COVID-19 shows that taking oral vitamin C (ascorbic acid) 8000 mg in 2-3 divided doses daily, alone or with zinc gluconate 50 mg daily, for 10 days does not reduce symptom severity when compared with standard care (104450). The study was terminated prior to complete enrollment due to futility and apparent lack of effect from vitamin C and/or zinc supplementation. Limitations of this study include a lack of placebo control and blinding. Additionally, this study has been criticized for methodologic concerns (106624). Another small clinical trial in adult outpatients with confirmed COVID-19 shows that taking vitamin C 1000 mg daily for 14 days does not improve symptoms or quality of life when compared with placebo (109462).

Vitamin C has also been evaluated in patients hospitalized with COVID-19. A very large analysis of two multinational clinical studies in critical and non-critical adults hospitalized with COVID-19 shows that administering intravenous vitamin C 50 mg/kg every 6 hours for 96 hours does not improve organ support-free days or survival and has a high probability of futility and worsened outcomes when compared with placebo (113666). Individual prospective and retrospective studies in critically ill patients hospitalized with COVID-19 in various countries have found that administering vitamin C, either enterally as 500-1000 mg daily or intravenously as 8-24 grams daily or 50 mg/kg daily, does not significantly reduce in-hospital or short-term mortality, hospital length of stay, or end-organ failure when compared with control groups receiving standard care alone. Additionally, all but one study found no change in the need for mechanical ventilation (105458,105465,106937,106938,108075,108079,108081).

However, a meta-analysis and some small individual studies have found that vitamin C is modestly beneficial for patients hospitalized with COVID-19. A meta-analysis of 10 clinical trials and 9 observational studies in patients hospitalized with COVID-19 shows that receiving oral or intravenous vitamin C daily reduces the odds of in-hospital mortality by 41% when compared with control. When only clinical trials were considered, the odds of in-hospital mortality were decreased by 56%; however, this reduction was only identified in studies using vitamin C 10 grams daily or less. Conversely, supplementation with vitamin C increased the length of intensive care unit (ICU) stay by nearly 2 days and did not impact length of hospital stay or reduce the need for mechanical ventilation, liver injury, or cardiac injury (109955). Similarly, a meta-analysis of 8 clinical studies in primarily hospitalized patients with moderate to severe COVID-19 shows that vitamin C administered orally or intravenously decreases the risk of all-cause mortality by 16% when compared with control (114488). Additionally, a small study found a small improvement in survival when compared with standard care; however, the overall survival rate in this study was low (108075). Another clinical study in patients hospitalized in Turkey with COVID-19 shows that adding high-dose intravenous sodium ascorbate 50 mg/kg to a treatment regimen of hydroxychloroquine, azithromycin, and zinc may improve recovery time, with 57% and 39% of patients achieving total recovery at day 15 in the vitamin C and control groups, respectively (108071). However, the validity of this trial is limited due to unclear reporting.

Vitamin C has also been evaluated in combination with other ingredients in patients with long COVID. Preliminary clinical research in adults with long COVID and persistent fatigue shows that taking a specific combination product containing vitamin C 500 mg and L-arginine 1.66 grams (Bioarginina C, Farmacetici Damor) for 28 days increases 6-minute walk test distance by 10% and reduces self-reported fatigue when compared with placebo (110390). However, it is unclear whether these effects are due to vitamin C, L-arginine, or the combination.

Sepsis. Intravenous vitamin C, alone or in combination with thiamine and/or hydrocortisone, does not prevent organ failure, reduce intensive care or hospital length of stay, or reduce mortality in sepsis or septic shock.

^ Details: Observational research suggests that patients with septic shock are more likely to have low plasma levels of vitamin C (100317). However, three randomized clinical trials in patients with sepsis or septic shock show no benefit with intravenous vitamin C, with or without thiamine, for improving organ function and preventing organ failure when compared with control treatment (102130,104027,114489). A small clinical study in patients with septic shock shows that intravenous vitamin C 50 or 150 mg/kg daily for 4 days does not improve organ dysfunction or failure rates, duration of hospital or intensive care unit (ICU) length of stay, duration of mechanical ventilation, or mortality rate when compared with placebo (114489). Another clinical study in patients with septic shock shows that administering an intravenous bolus of vitamin C 1000 mg followed by a continuous infusion of 250 mg/hour for 96 hours, starting within 24 hours of vasopressor initiation, does not improve 28-day or ICU mortality when compared with placebo. A subgroup analysis shows that the addition of corticosteroids does not affect outcomes in either group (108078). This study may have been inadequately powered to detect a difference between groups. Also, a larger clinical trial in adults with sepsis receiving vasopressor therapy in the ICU shows that intravenous administration of vitamin C 50 mg/kg every 6 hours for up to 4 days increases the risk of death or persistent organ dysfunction at day 28 by 14% to 21% when compared with placebo. There were no differences in mortality at 6 months (109459,111643).

Vitamin C has also been frequently studied in patients with sepsis and septic shock in a specific combination regimen (HAT therapy) which includes intravenous vitamin C 1.5-2 grams with hydrocortisone 50 mg every 6 hours and thiamine 200 mg every 12 hours. While some retrospective research has found HAT therapy to be beneficial in sepsis (100315,102980), high quality, prospective clinical research has not confirmed these findings (105447,106620,109956). Several meta-analyses of randomized controlled trials and small clinical studies in patients with sepsis or septic shock show that intravenous vitamin C, either alone, as a component of HAT therapy, or in combination with thiamine, does not reduce short- or long-term mortality, ICU or hospital length of stay, kidney injury, or duration of mechanical ventilation, but modestly improves duration of vasopressor use and procalcitonin clearance, when compared with placebo or standard care. These analyses also show mixed results with respect to improvement in sequential organ failure assessment (SOFA) scores within 72 hours (105447,106620,106935,108073,109460,111298,111300,111301,111642,112479). Most studies included in the analyses administered HAT therapy for 2-10 days and compared it with normal saline control or with hydrocortisone alone (102129,102998,104027,104028,104032,105446). Although some subgroup analyses suggests that intravenous vitamin C alone in patients with sepsis may improve short-term mortality (106620,111298), other meta-analyses have not shown this benefit in subgroup analyses (111300). In addition, meta-analyses have identified significant publication bias (111298,111300). Long-term follow up from a study in patients with sepsis-induced respiratory and/or cardiovascular dysfunction shows that receiving HAT therapy does not improve cognitive, psychological, or functional status after 6 months and, for some domains, HAT therapy was worse when compared with placebo (111299).

Studies evaluating intravenous vitamin C, either alone, as a component of HAT therapy, or in combination with thiamine, in mixed critically ill populations have also shown mixed findings. Four meta-analyses of randomized controlled trials and observational studies show that intravenous vitamin C does not have a significant effect on the length of hospital stay, mortality at 1 month, ICU mortality, use of invasive ventilation, use of renal replacement therapy, organ function, or incidence of kidney injury when compared with placebo or standard care. The meta-analyses reach conflicting conclusions on whether intravenous

vitamin C reduces the risk of in-hospital mortality, 30-day mortality, and the duration of ICU stay. When only data from low risk-of-bias clinical trials are considered, the effects of intravenous vitamin C on mortality at any point are no longer significant (106933,106934,109957,113663). However, a subgroup analysis in one of these analyses suggests that intravenous vitamin C as monotherapy, or in doses of at least 10 grams daily, may improve overall mortality (106934).

Vitamin C also does not appear to benefit complications from sepsis, such as vasoplegic shock. A small clinical study in adults in the ICU with vasoplegic shock mostly secondary to sepsis and requiring moderate vasopressor support shows that administering intravenous vitamin C as sodium ascorbate 1.5 grams every 6 hours for 5 days or until cessation of vasoactive therapy does not reduce the duration of vasopressors, vasopressor dose, hospital or ICU length of stay, or mortality outcomes when compared with placebo (112475).

INSUFFICIENT RELIABLE EVIDENCE to RATE

Atrophic acne scars. It is unclear if applying topical vitamin C after microblading improves atrophic acne scars.
^ Details: A clinical study in adults with mild to severe atrophic acne scarring shows that applying a serum containing vitamin C 17% to the face after a once-monthly home microblade treatment for 4 months improves the appearance of acne scars at month 5 when compared with baseline (108086). Although this study enrolled a control group that used topical insulin in place of vitamin C, no between-group statistical comparisons were conducted, limiting the validity of this study.

Age-related macular degeneration (AMD). It is unclear if dietary vitamin C or oral vitamin C taken in combination with other ingredients prevents AMD.
^ Details: An umbrella review of meta-analyses shows that increased dietary intake of vitamin C is associated with 21% higher odds of developing AMD (112095). A population study suggests that vitamin C intake is associated with increased odds of developing age-related maculopathy (9823). However, other population studies have found no association between dietary or supplemental vitamin C intake and the risk of developing AMD (14007,14257).

When taken in combination with other ingredients, most clinical and population research shows that taking vitamin C 500 mg along with other antioxidants such as vitamin E 400 IU, beta-carotene 15 mg, and/or elemental zinc 80 mg reduces the risk of visual acuity loss by 23% to 27%, progression to advanced AMD at 5 years by 25% to 32%, and AMD overall (7303,7304,11326,14257,90069). The antioxidant plus zinc combination seems to reduce the risk of progression to advanced AMD in these patients more than taking the antioxidants without zinc (7303,90069).

More evidence is needed to determine what role, if any, vitamin C intake has on the risk of developing AMD.

Aging skin. Topical vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
^ Details: Clinical research in females aged 30-65 years shows that applying a specific liquid (Antioxidant and Collagen Booster Serum, Max Biocare Pty Ltd.) containing vitamin C 20%, red raspberry leaf cell culture extract 0.0005%, and vitamin E 1% to the face nightly for 8 weeks, in addition to regular facial skin products, improves skin color, elasticity, radiance, smoothness, and appearance of wrinkles when compared with regular facial skin products alone (102355).

Albuminuria. Oral vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
^ Details: A small clinical study shows that taking vitamin C 1250 mg plus vitamin E 680 IU daily for 4 weeks can reduce the excretion of albumin by about 19% when compared with placebo in patients with type 2 diabetes (10434).

Allergic rhinitis (hay fever). It is unclear if oral vitamin C is beneficial in patients with hay fever.
^ Details: Epidemiological research has found that higher vitamin C plasma levels are not associated with a decreased risk of allergic rhinitis (15200). However, clinical research shows that some forms of vitamin C might help. In one small clinical study, intranasal vitamin C administered three times daily for 2 weeks reduces nasal secretions, nasal blockage, and edema in up to 74% of patients with perennial allergic rhinitis (15201). Another small clinical study in patients with seasonal allergic rhinitis shows that taking a single oral dose of vitamin C 2 grams reduces bronchial responsiveness to histamine at one hour after ingestion (15202). However, in another small study in patients with seasonal allergic rhinitis taking vitamin C orally in doses up to 4 grams daily for 3 days does not appear to suppress cutaneous or nasal response to histamine when compared to placebo (15203).

Alzheimer disease. It is unclear if dietary vitamin C helps to prevent this condition.
^ Details: Most epidemiological research has found that dietary intake of vitamin C is associated with a 17% reduced risk of developing Alzheimer disease (4636,9824,10131,13165,90082).

Amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease). It is unclear if oral vitamin C helps to prevent ALS.
^ Details: Observational research has found that increased dietary or supplemental intake of vitamin C is not associated with risk of developing ALS (90412).

Anthracycline cardiotoxicity. Although there is interest in using oral vitamin C for anthracycline-induced cardiac toxicity, there is insufficient reliable information about the clinical effects of vitamin C for this condition.

Aspirin-associated gastric damage. It is unclear if oral vitamin C helps to prevent gastric damage caused by aspirin.
^ Details: Some clinical research shows that vitamin C 480 mg might prevent gastric damage associated with taking aspirin 400 mg by decreasing blood loss and preventing decreased gastric blood flow (10357). However, a small clinical study in healthy patients shows that taking vitamin C 500 mg as ascorbic acid with aspirin 600 mg actually increases gastrointestinal permeability to a greater extent than either ingredient taken alone (98781).

Athletic performance. It is unclear if oral vitamin C improves athletic performance.
^ Details: Although some small preliminary clinical studies suggest that vitamin C might improve certain biomarkers during exercise (82922), a meta-analysis of small clinical trials in older and younger adults shows that taking vitamin C 500-1000 mg daily, with or without vitamin E, does not improve endurance, lean mass, or muscle strength when compared with placebo (102973). A more recent, small clinical study in recreationally trained males shows that taking vitamin C 1000 mg and vitamin E (as alpha-tocopherol) 235 mg daily for 10 weeks while participating in a resistance training program does not improve measures of muscle strength when compared with placebo (109959).

Atopic disease. It is unclear if dietary vitamin C helps to prevent atopic disease.
^ Details: Population research has found that higher intake of vitamin C is not associated with a reduced risk of eczema, wheeze, IgE-mediated food allergy, or allergic sensitization (90098).

Attention deficit-hyperactivity disorder (ADHD). Small clinical studies suggest that high-dose oral vitamin C may not improve symptoms in patients with ADHD.
^ Details: Some research suggests that taking megadose vitamins, including vitamin C, does not improve ADHD symptoms (9957,9958,9959). However, other preliminary clinical research shows that taking 25 mg of vitamin C 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 when compared with baseline (14443). It is not clear if these effects are due to vitamin C, flaxseed oil, or the combination.

Autism spectrum disorder. It is unclear if oral vitamin C is beneficial in patients with autism spectrum disorder.
^ Details: One small clinical study shows that taking vitamin C 8 grams per 70 kg daily for 10 weeks modestly reduces autism symptom severity in school children when compared with placebo (83604).

Bleeding. It is unclear if intravenous vitamin C can reduce bleeding after total abdominal hysterectomy.
^ Details: A small clinical study in patients undergoing total abdominal hysterectomy shows that administration of intravenous vitamin C 1 gram the night before surgery and 1 gram during surgery reduces postoperative hemorrhage volume by around 40 mL when compared with placebo (109465).

Brain tumor. It is unclear if oral vitamin C helps to prevent brain tumors.
^ Details: Population research has found that vitamin C intake is associated with a 14% reduced risk of glioma. This risk reduction was more prevalent in America compared to other geographic locations (98782).

Breast cancer. It is unclear if oral vitamin C helps to prevent breast cancer, its recurrence, or breast cancer-related mortality.
^ Details: Some epidemiological research has found that dietary vitamin C is associated with a reduced risk of breast cancer (1444,10823,10824). However, other epidemiological research has found no association with dietary or supplemental vitamin C (10825,10826,108080). One cohort study found no association between breast cancer risk and total, dietary, or supplemental vitamin C, regardless of dose, treatment duration, or formulation (single ingredient or combination product). Additionally, hormone and menopausal status did not appear to impact risk. Vitamin C intake might be associated with a reduced risk in individuals with a family history of breast cancer in first-degree relatives (108080).

In patients with breast cancer, supplemental or dietary intake of vitamin C might be associated with a reduced risk of mortality. A meta-analysis of results from population research shows that vitamin C supplementation following breast cancer diagnosis is associated with a 15% lower risk of breast cancer-related mortality when compared with no supplementation (90416). A large, observational study in patients with breast cancer undergoing radiation therapy has found that vitamin C supplementation does not reduce the risk of breast cancer recurrence over a period of 5 years when compared with no supplementation. Although the vitamin C group had notably less aggressive tumor types, recurrence-free survival was similar in both vitamin C and control groups (108082). The validity of these findings is limited due to unknown doses of vitamin C and the inclusion of various breast cancer subtypes.

Burns. Small studies suggest that intravenous vitamin C may modestly improve symptoms in patients with severe burns.
^ Details: A small clinical study in patients with severe burns shows that administering vitamin C intravenously (IV) 66 mg/kg hourly over 24 hours, as part of fluid resuscitation using lactated ringer solution, reduces wound edema and the volume of fluid needed when compared with fluid resuscitation alone (83145). A retrospective review of adults hospitalized with severe burns has found that those who receive a continuous IV infusion of at least 10 grams of vitamin C within 2 days of admission have an in-hospital mortality rate of 46%, compared with 58% for those who do not receive vitamin C (102128).

Cancer. It is unclear if oral or intravenous vitamin C helps to prevent cancer or cancer-related mortality.
^ Details: Some population research has found that DIETARY intake of vitamin C is linked with a lower risk of cancer and cancer-related mortality (3910,5878,10819,109779). However, clinical research shows that taking vitamin C SUPPLEMENTS does not reduce the risk for cancer (10819,14109,34580,90097). In people with cancer, although some clinical research has shown that taking high-dose vitamin C supplements can improve survival rates (9809,96704), other clinical research has not shown this benefit (4842,4843). In 2003, the US Food and Drug Administration (FDA) determined that it would allow a qualified health claim stating that some scientific evidence suggests that antioxidant vitamins, such as vitamin C, may reduce the risk of certain forms of cancer. However, the FDA has determined that there is little scientific evidence supporting this claim (102334).

Preliminary clinical research has also evaluated vitamin C supplements in patients with cancer. High-dose oral vitamin C, 10 grams daily, in patients with advanced cancer does not seem to improve survival or decrease disease progression (4842,4843,106617). However, preliminary clinical research suggests high doses of vitamin C, given intravenously, might have a beneficial effect on some outcomes, including survival rate in some patients with cancer (9809,96704,106617). However, there is no benefit to other patients studied in the case reports and this has not been tested in well-designed clinical trials (9809,96704).

Cardiac arrest. It is unclear if intravenous vitamin C is beneficial for patients after cardiac arrest.
^ Details: A small clinical study conducted in Slovenia in adult survivors of out-of-hospital cardiac arrest shows that administering intravenous vitamin C 1.5 grams every 12 hours for 8 consecutive doses, with the first dose administered within 6 hours of resuscitation, in addition to standard care protects against arrhythmias and reduces the length of intensive care unit (ICU) stay when compared with placebo and standard care. However, intravenous vitamin C does not appear to protect against neurological or myocardial injury, reduce the need for mechanical ventilation, reduce the duration of hospital stay, or increase survival when compared with placebo (113667).

Carpal tunnel syndrome. Vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
^ Details: A clinical study in adults with mild to moderate carpal tunnel syndrome shows that taking a combination product containing vitamins C, E, B1, B2, B6, and B12, alpha-lipoic acid, acetyl-L-carnitine, phosphatidylserine, and turmeric twice daily for 60 days reduces symptom severity and pain but does not improve measures of hand and wrist function when compared with control (111702). The validity of these effects is limited by a lack of blinding. The study may also be inadequately powered to detect a difference between groups. Additionally, it is unclear if the effects are due to vitamin C, other ingredients, or the combination.

Cervical cancer. It is unclear if oral vitamin C helps to prevent cervical cancer.
^ Details: Observational research has found that higher vitamin C intake is associated with a 33% to 42% reduced odds of cervical neoplasm. Increasing vitamin C intake by 50 mg daily is associated with an 8% reduced odds of cervical neoplasm (34609,98771).

Child growth. Some clinical research in pregnant smokers suggests that taking vitamin C during pregnancy may improve pulmonary function in the offspring from birth to 6 years of age.
^ Details: A meta-analysis of 4 data sets from one large clinical study in pregnant adults who smoke at least one cigarette daily shows that taking supplemental vitamin C 500 mg daily during pregnancy reduces lower airway resistance and improves lung capacity of the offspring at 0, 3, 12, and 60 months of age, but does not improve airway obstruction, when compared with control (113670). Additionally, one of the clinical studies included the meta-analysis shows that taking vitamin C during pregnancy lowers the occurrence of wheezing in offspring at 4-6 years of age (114496,114497).

Chronic fatigue syndrome (CFS). Although there is interest in using oral vitamin C for CFS, there is insufficient reliable information about the clinical effects of vitamin C for this condition.

Colistin-induced nephrotoxicity. It is unclear if intravenous vitamin C helps to prevent nephrotoxicity from colistin.
^ Details: A small clinical study shows that intravenous administration of vitamin C 2 grams every 12 hours along with colistin for around 9-10 days does not prevent nephrotoxicity when compared with colistin therapy alone (99839). However, this study was limited by a lack of statistical power to detect differences between the study groups.

Contrast induced nephropathy. It is unclear if oral vitamin C helps to prevent contrast-induced nephropathy (CIN).
^ Details: Some clinical research shows that taking vitamin C before and after coronary angiography reduces the risk of developing CIN by 33% to 55% when compared with placebo in patients with renal dysfunction (12234,90421). However, other clinical evidence published since 2012 suggests that vitamin C given orally and/or intravenously before and after angiography does not reduce the risk of CIN compared with control in high-risk patients with chronic renal insufficiency or diabetes (91232,91236,90410,90425). Reasons for the discrepancies are not entirely clear. However, it is possible that the lack of significant benefit from vitamin C in the latter studies results from the fact that incidences of CIN have become less common than in the past due to avoidance of dehydration, use of smaller catheters, and use of contrast agents with reduced nephrotoxicity (90429).

Coronary artery bypass graft (CABG) surgery. It is unclear if intravenous vitamin C helps to improve patient outcomes after CABG surgery.
^ Details: A small clinical study shows that giving vitamin C 5 grams intravenously (IV) before anesthesia induction and 5 grams in the cardioplegia solution used during surgery shortens the length of stay in the intensive care unit (ICU) by about 8 hours (102127). However, some limited research suggests that IV vitamin C does not resolve cardiac surgery complications. A small clinical study in patients with vasoplegia after receiving CABG and other cardiac surgeries shows that receiving IV vitamin C 1.5 grams every 6 hours after being admitted to the ICU does not improve vasoplegia when compared with control (102981).

Delirium. Oral vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
^ Details: Observational research in adults with septic shock has found that receiving intravenous thiamine 400 mg daily with vitamin C 6 grams daily, both in divided doses, is not associated with reduced delirium when compared with control (103001).

Dental plaque. It is unclear if vitamin C in a chewing gum helps to reduce dental plaque formation.
^ Details: A small clinical study in patients with calculus shows that chewing 10 pieces of gum, each containing 60 mg of vitamin C, daily for 3 months reduces the formation of dental calculus, visible plaque, and the number of bleeding sites when compared not chewing gum (83303). The validity of this finding is limited by a lack of placebo group.

Depression. It is unclear if oral vitamin C is beneficial for the treatment or prevention of depression.
^ Details: A small clinical study in children and adolescents shows that taking vitamin C 500 mg orally twice daily in combination with fluoxetine 10-20 mg daily for 6 months reduces most symptoms of major depressive disorder when compared with taking fluoxetine alone (90404).

However, a small clinical study in adults shows that taking vitamin C up to 1000 mg daily for 2 months does not improve the response rate or decrease symptoms of depression in adults also taking citalopram when compared with citalopram alone (96708). Reasons for these conflicting results may relate to the age of the patients, study duration, or differences in antidepressant medication being taken. One clinical guideline also provisionally recommends against the use of oral vitamin C to treat patients with depression based on low-quality evidence (110318).

Some research has also evaluated vitamin C intake for the prevention of depression. A secondary analysis of pre- and peri-menopausal adults enrolled in the Study of Women's Health Across the Nation (SWAN) program suggests that vitamin C intake is inversely associated with depressive symptoms. This association persisted regardless of age, race, physical activity, body mass index, antidepressant use or menopausal status (108083). The validity of these findings is limited due to the secondary nature of this study; additionally, follow-up time is unclear.

Diabetes. It is unclear if oral vitamin C prevents diabetes. Some low-quality research suggests that vitamin C might improve glycemic control in patients with diabetes.
^ Details: Population research has not found a link between dietary vitamin C and the risk of developing type 2 diabetes (14004). However, low certainty clinical research has found some benefit of taking vitamin C supplements for glycemic control. Two meta-analyses of several small, heterogeneous clinical studies in patients with type 2 diabetes show that taking vitamin C 200-3000 mg daily for 2-48 weeks reduces fasting blood glucose by approximately 11 mg/dL (112478) and glycated hemoglobin (HbA1c) by an average of 0.5% when compared with placebo, standard treatment, or no treatment (105461,112478). Subgroup analyses suggest that durations of supplementation longer than 12 weeks show greater glycemic benefit, and although one meta-analysis suggests there is no dose-response relationship (105461), another meta-analysis suggests that doses of vitamin C 1000 mg and higher are most beneficial for improving glycemic indices (112478).

Some research has evaluated the effects of vitamin C supplementation on the lipid profile in patients with diabetes, with mixed findings. One meta-analysis of 17 small clinical studies shows that taking vitamin C 200-3000 mg daily for 2 to 48 weeks improves levels of triglycerides and total cholesterol, but not low-density lipoprotein (LDL) or high-density lipoprotein (HDL) cholesterol. Subgroup analysis suggests that study durations of at least 12 weeks show greater benefit (106621). However, two other meta-analyses in patients with diabetes, one of 16 small heterogenous clinical studies and one of 11 small clinical studies, show no clinically important improvement in lipid levels after vitamin C supplementation (105461,105464).

Dry mouth. Oral vitamin C has only been evaluated in combination with vitamin E; its effect when used alone is unclear.
^ Details: A small clinical trial in patients receiving radiotherapy for head and neck cancer shows that taking vitamin E 100 IU and vitamin C 500 mg twice daily for an average of 3 months improves dry mouth when compared to baseline (99080). The validity of these results is limited by the lack of comparison with a control group.

Endometrial cancer. Increased dietary vitamin C has been linked to reduced risk of endometrial cancer.

^ Details: Population research has found that intake of vitamin C from dietary sources is associated with a slightly decreased risk of endometrial cancer when compared with control. However, this benefit is not observed when results from a prospective cohort study are assessed (34578).

Endometriosis. Oral vitamin C has only been evaluated in combination with vitamin E; its effect when used alone is unclear.
^ Details: A small clinical study in patients with endometriosis and pelvic pain shows that taking vitamin C 1000 mg and vitamin E 800 IU daily for 8 weeks improves dysmenorrhea, dyspareunia, and chronic pelvic pain scores when compared with placebo. Vitamin C and vitamin E supplementation also reduces some biochemical markers of oxidative stress when compared with placebo (106622). Additionally, a meta-analysis of 4 other, mostly small clinical studies in patients with endometriosis shows that taking vitamin C 1000 mg and vitamin E 800-1200 IU daily for 6-8 weeks reduces chronic pelvic pain and improves dysmenorrhea and dyspareunia when compared with placebo (114491).

Endoscopy-associated adverse effects. It is unclear if a topical vitamin C spray reduces mucosal irritation in patients undergoing Lugol chromoendoscopy.
^ Details: A small clinical trial in patients receiving a Lugol chromoendoscopy shows that spraying a vitamin C 2% solution after the application of the Lugol iodine 2% solution reduces the severity of mucosal irritation, heartburn, and pain when compared with using a normal saline spray after the Lugol iodine 2% solution (104030).

Esophageal cancer. Oral vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
^ Details: Population research has found that higher dietary intake of vitamin C is associated with reduced odds of esophageal adenocarcinoma. A 50 gram increase in dietary vitamin C intake is associated with a 13% reduced odds of esophageal cancer (34551,98770). However, a meta-analysis of clinical research shows that taking a vitamin C supplement in combination with beta-carotene and vitamin E does not reduce the risk of esophageal cancer (34581).

Exercise-induced asthma. Small clinical studies suggest that oral vitamin C may modestly improve symptoms in patients with exercise-induced asthma.
^ Details: A meta-analysis of the available clinical research shows that vitamin C supplementation might reduce exercise-induced breathlessness when compared with placebo or control. However, the available research is of poor quality, and no clear conclusions can be drawn regarding its benefits for exercise-induced asthma (90409).

Exercise-induced muscle damage. It is unclear if oral vitamin C is beneficial in exercise-induced muscle damage.
^ Details: A small clinical study in healthy females shows that taking vitamin C 1000 mg before moderate intensity cycling does not prevent muscle damage when compared with placebo (99837). Another small clinical study in endurance-trained runners shows that taking vitamin C 1000 mg and vitamin E (as alpha-tocopherol) 235 mg 2 hours prior to an exercise protocol does not reduce delayed onset muscle soreness or improve other markers of exercise-induced muscle damage when compared with placebo (109961).

Gallbladder disease. It is unclear if oral vitamin C reduces the risk of gallbladder disease.
^ Details: Cross-sectional epidemiological evidence has found that vitamin C supplementation and increased vitamin C serum levels are associated with a decreased risk of developing gallbladder disease in females, but not males (5877).

Gastric cancer. It is unclear if dietary or supplemental vitamin C reduces the risk of gastric cancer.
^ Details: Most population research has not found an association between DIETARY intake of vitamin C and gastric cancer risk (9194,10822,10819,90083). Also, clinical research shows that taking vitamin C supplements in combination with other antioxidants does not reduce the risk of gastric cancer or precancerous gastric lesions (14447,34581,90085). However, some research suggests that it might be associated with a reduced risk for specific forms of gastric cancer (9838,90083). One clinical study shows that taking vitamin C orally 500 mg daily for 6 months after eradication of Helicobacter pylori infection decreases the incidence of precancerous changes in stomach tissue when compared with no treatment (10359). Also, other clinical research shows that taking vitamin C orally 1 gram daily helps promote the regression of precancerous gastric lesions in people at high risk for gastric cancer (2579). In 2009, the US Food and Drug Administration (FDA) determined that it would allow a qualified health claim stating that vitamin C supplements may reduce the risk of gastric cancer. However, the FDA has concluded that it is highly uncertain that vitamin C supplements actually reduce the risk of gastric cancer (102332).

Gastritis. There is limited evidence on the oral use of vitamin C in omeprazole-induced corpus gastritis.
^ Details: A small clinical study shows that taking vitamin C orally 1200 mg daily along with omeprazole decreases corpus gastritis associated with omeprazole therapy in patients with H. pylori infection (10360).

Gout. It is unclear if oral vitamin C helps to prevent or manage gout.
^ Details: Population research in men has found that taking vitamin C 500-1500 mg daily from the diet and/or supplements is associated with up to a 34% reduced risk of gout when compared with less than 250 mg daily (16755). Also, men who ingest over 500 mg of vitamin C daily from the diet and supplements have serum uric acid levels that are slightly lower than men who consume less than 90 mg daily (16820). However, taking supplemental vitamin C 500 mg daily for 8 weeks does not seem to lower serum uric acid levels in patients who already have gout (90423).

Hearing loss. There is limited evidence on the intravenous use of vitamin C in idiopathic sudden sensorineural hearing loss. It is unclear if dietary vitamin C intake can affect the risk of hearing loss.
^ Details: A small clinical study in patients with idiopathic sudden sensorineural hearing loss shows that receiving intravenous high-dose vitamin C 200 mg/kg daily in combination with steroid therapy for 10 days, followed by oral vitamin C 2000 mg daily for 30 days, increases recovery rate two-fold and modestly improves hearing threshold levels when compared with receiving steroid therapy only (90417).

In addition, population research in females has found that high dietary intake of vitamin C is associated with a 22% increased risk of developing self-reported hearing loss over a 22-year period when compared with low intake (109807).

Heart transplant complications. Oral vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
^ Details: A small clinical trial shows that a combination of vitamin C 500 mg and vitamin E 400 IU, taken twice daily for 1 year starting within the first 2 years after cardiac transplant, reduced the progression of vasculopathy as measured by intravascular ultrasonography (IVUS) when compared with placebo. This suggests that the combination may help slow the progression of CAV (82826).

Hepatitis C. It is unclear if oral vitamin C is beneficial in patients with hepatitis C.

Details: A small clinical study in patients with confirmed hepatitis C shows that taking vitamin C 1000 mg daily with conventional therapy (sofosbuvir plus daclatasvir) for 4 weeks improves serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, and albumin when compared with conventional therapy alone (109463).

HIV/AIDS. Oral vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
Details: A small, low-quality study in men with HIV shows that taking vitamin C 250 mg daily in combination with vitamin A, beta-carotene, vitamin E, selenium, and coenzyme Q10 does not improve viral load, although it seems to improve markers of oxidative stress when compared to baseline. However, a 1000 mg dose of vitamin C, as well as higher doses of the other antioxidants, do not seem to provide any additional effect (9830).

HIV transmission. Oral vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
Details: A clinical study in HIV-positive mothers shows that taking vitamin B, vitamin C, and vitamin E daily during pregnancy and while breast-feeding for 20 weeks seems to reduce child mortality and HIV transmission through breast milk when compared with taking vitamin A (9801).

Hyperphosphatemia. Intravenous vitamin C might be beneficial for reducing phosphate levels in patients with end-stage renal disease.
Details: A small clinical study in hemodialysis patients with elevated phosphorus levels suggests that administering vitamin C 500 mg intravenously three times weekly for 8 weeks reduces phosphorus levels about seven-fold when compared with placebo (90414).

Idiopathic interstitial pneumonia. Oral vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
Details: A small clinical study in patients with idiopathic pulmonary fibrosis, a form of idiopathic interstitial pneumonia, shows that taking a combination of vitamin C 250 mg every other day, vitamin D 50,000 IU daily, and vitamin E 200 IU daily for 12 weeks improves some, but not all, measures of lung function and reduces markers of inflammation and oxidative stress when compared to baseline (109464). The validity of these findings is limited by a lack of placebo control group.

Infertility. It is unclear if oral vitamin C is beneficial in anovulatory females.
Details: A very small clinical study suggests that taking vitamin C 400-1000 mg daily might improve fertility, resulting in ovulation and pregnancy in some anovulatory females, when compared to baseline (14018). The validity of these findings is limited by the small study size and lack of a comparator group. However, a very large observational study suggests that there is no association between dietary vitamin C intake and in-vitro fertilization (IVF) outcomes including good oocyte quality, embryo transfer success rates, clinical pregnancy rates, and successful term pregnancy rates in subfertile couples who are candidates for IVF (112097).

Male infertility. It is unclear if oral or intravenous vitamin C is beneficial in males with infertility.
Details: A meta-analysis of three small, low-quality clinical trials in males with infertility shows that taking vitamin C up to 1000 mg daily for up to 12 weeks can improve sperm count, motility, and vitality, but does not seem to increase semen volume or sperm concentration, when compared with control (109461). It is unclear if vitamin C can increase pregnancy rates, as these studies did not assess this outcome.

A retrospective study in males with or without varicocele-related infertility has found that taking a specific combination product containing vitamin C 90 mg, zinc 10 mg, L-carnitine fumarate 1725 mg, acetyl-L-carnitine 500 mg, coenzyme Q10 20 mg, folic acid 0.2 mg, selenium 0.05 mg, and vitamin B12 0.015 mg (Proxeed Plus, Sigma-Tau) orally twice daily for 6 months improves sperm count, sperm concentration, and sperm motility when compared with baseline. Improvement in semen parameters were greatest in subjects with more severe varicoceles. The validity of this study is limited by the lack of a comparator group (111296).

Mastalgia. Oral vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
Details: A small clinical trial in patients with mastalgia shows that taking a combination of vitamin C 100 mg, vitamin B12, and gamma-linolenic acid daily for 12 weeks does not improve the proportion of patients with minimal or no pain when compared with placebo (111059).

Melasma. It is unclear if topical vitamin C is beneficial in patients with melasma.
Details: A small clinical study in patients with bilateral symmetrically distributed facial melasma shows that topical application of 0.5 mL of vitamin C (Cosmotech, Alpha Medical Cosmotech) following dermapen microneedling every 2 weeks for 6 weeks is similarly effective to tranexamic acid for improving melasma severity and pigmented, but not vascular, findings on dermoscopic examination (106939).

Nonalcoholic fatty liver disease (NAFLD). It is unclear if oral vitamin C is beneficial in patients with NAFLD.
Details: A clinical study in patients with NAFLD shows that taking vitamin C 250 mg, 1000 mg, or 2000 mg daily for 12 weeks improves some biochemical markers of liver health and glucose metabolism when compared with baseline. However, the improvement from baseline was similar between groups (106942).

Nonalcoholic steatohepatitis (NASH). Oral vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
Details: Preliminary clinical 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).

Non-Hodgkin lymphoma. It is unclear if oral vitamin C reduces the risk of developing diffuse large B-cell lymphoma.
Details: In one population study, higher dietary or supplemental intake of vitamin C was associated with a reduced risk of diffuse large B-cell lymphoma, a type of non-Hodgkin lymphoma, when compared with lower intake in postmenopausal adults (90945).

Oral cancer. It is unclear if oral vitamin C reduces the risk of developing oral cancer.
Details: Population research has found that higher dietary intake of vitamin C is associated with a reduced risk of oral cancer (10821). However, clinical research has not shown benefit with oral vitamin C supplements. A small clinical trial in Japanese adults with oral leukoplakia shows that taking vitamin C 500 mg and beta-carotene 10 mg daily for 12 months does not reduce the development of oral cancer over 5 years when compared with vitamin C 50 mg daily (91384).

Oral leukoplakia. Oral vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear.

^ Details: A small clinical trial in Japanese adults with oral leukoplakia shows that taking vitamin C 500 mg and beta-carotene 10 mg daily for 12 months does not improve leukoplakia symptoms or reduce the development of oral cancer over 5 years when compared with vitamin C 50 mg daily (91384).

Osteoarthritis. It is unclear if dietary vitamin C reduces the risk of developing osteoarthritis.
^ Details: Observational research has found that increased vitamin C from dietary sources is associated with a reduced risk of cartilage loss and disease progression in people with osteoarthritis (5881).

Osteoporosis. It is unclear if dietary vitamin C improves bone density or reduces fracture risk in patients at risk for osteoporosis.
^ Details: Some cross-sectional observational research in postmenopausal patients without a history of smoking or estrogen use has found that higher serum vitamin C levels are associated with lower bone mineral density (9828). However, other observational research in a larger population of adults at risk for osteoporosis has found that higher dietary vitamin C intake is not associated with fracture risk (104415).

Ovarian cancer. Dietary vitamin C might not affect the risk of ovarian cancer.
^ Details: Epidemiological research has found that dietary vitamin C intake is not linked with ovarian cancer risk (9193,102977).

Pancreatitis. It is unclear if intravenous vitamin C is beneficial in patients with acute pancreatitis.
^ Details: A small meta-analysis of clinical studies in patients with acute pancreatitis shows that intravenous vitamin C does not improve the odds of developing organ failure when compared with placebo or no intervention. Intravenous vitamin C seems to reduce hospital stay, but not in-hospital mortality (106941).

Parkinson disease. Dietary vitamin C might not affect the risk of developing this condition.
^ Details: Observational research has found that moderate or high dietary intake of vitamin C is not associated with a reduced risk of Parkinson disease (83316).

Periodontitis. Oral vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear. It is also unclear if dietary vitamin C reduces the risk of periodontitis.
^ Details: A small clinical study in patients with moderate or advanced periodontitis shows that taking a supplement containing vitamin C 100 mg, alpha-lipoic acid, coenzyme Q10, cranberry extract, grapeseed extract, selenium, vitamin E, and zinc twice daily for 8 weeks in addition to standard nonsurgical therapy does not improve periodontal indices including bleeding on probing, gingival recession, plaque index, or inflammation, among others, when compared with placebo (111708). It is unclear if these effects are due to vitamin C, other ingredients, or the combination.

There is also interest in whether dietary vitamin C intake impacts the risk of periodontitis. Observational research in US adults has found that individuals with dietary intake of vitamin C in the third quartile, but not the second or fourth quartiles, have lower odds of periodontitis when compared with vitamin C intake in the lowest quartile. Furthermore, the investigators identified a non-linear relationship between vitamin C intake and periodontitis risk, suggesting that individuals with intakes either much lower or much higher than 158 mg daily are at increased risk of developing periodontitis (109958).

Peripheral arterial disease (PAD). It is unclear if dietary vitamin C helps to reduce the risk of developing PAD.
^ Details: In females, epidemiological evidence has found that dietary intake of vitamin C of 142 mg daily or greater is associated with a 36% reduced risk of PAD when compared with lower intake levels of less than 80 mg daily (10130).

Physical performance. It is unclear if oral vitamin C helps to improve physical performance and muscle strength in older people.
^ Details: Population research has found that higher intake of dietary vitamin C is associated with improved physical performance and muscle strength in elderly people (14006). In contrast, a small clinical study in elderly men undergoing strength training shows that taking vitamin C 1000 mg and vitamin E 258IU daily for 12 weeks does not increase strength, and might even attenuate increases in muscle mass, when compared with strength training alone (96701).

Pneumonia. It is unclear if oral or intravenous vitamin C helps to prevent or treat pneumonia.
^ Details: A meta-analysis of 6 clinical studies in adults with community-acquired pneumonia shows that oral or intravenous vitamin C does not reduce overall mortality, hospital or intensive care unit length of stay, or the risk of mechanical ventilation when compared with control (114490). The interpretation of these results is limited by significant heterogeneity of the included studies. An earlier meta-analysis of two small, low-quality clinical studies in children shows that vitamin C does not seem to reduce the risk of pneumonia when compared with a control (104033).

Postoperative recovery. It is unclear if oral or intravenous vitamin C improves postoperative recovery.
^ Details: Meta-analyses of clinical research show that oral or intravenous vitamin C can shorten the duration of hospitalization after cardiac surgery when compared with control (91233,96703). However, other research shows no decrease in intensive care unit (ICU) or hospital stay with vitamin C supplementation (96705), while another clinical study in patients undergoing cardiac surgery with extracorporeal circulation shows that intravenous vitamin C administered during surgery and 48 hours after surgery reduces ICU stay and re-admission rates, wound infection, and hospital mortality, but not length of hospital stay, when compared with control (114492). A meta-analysis of 37 clinical trials in adults undergoing low- to high-risk noncardiac surgery (i.e., orthopedic, abdominal, gynecologic, or kidney transplantation), shows that receiving perioperative vitamin C, either orally or intravenously, does not improve duration of hospitalization or overall mortality when compared with control (108087).

Postoperative pulmonary complications. It is unclear if intravenous vitamin C improves postoperative pulmonary complications.
^ Details: A large, single-blind clinical study in patients with recent cardiac surgery with extracorporeal circulation shows that parenteral administration of vitamin C 50 mg/kg intraoperatively and 50 mg/kg every 6 hours for the next 48 hours, followed by oral vitamin C 2000 mg daily until 1-week post-discharge, reduces the incidence of postoperative pulmonary complications (PPC) by 22% and improves PPC severity scores when compared with control. Specifically, vitamin C reduces the incidence of pneumothorax, pleural effusion, pneumonia, and re-intubation and may ameliorate lung damage as suggested by higher Horowitz index when compared with control (114492). A small clinical trial in patients undergoing low-risk cardiac surgery shows that receiving intravenous vitamin C 1 gram 10 minutes after anesthesia might slightly reduce the rate of postoperative pulmonary complications when compared with receiving a saline injection (104034).

Postoperative swelling. It is unclear if vitamin C reduces postoperative swelling after dental surgery.
^ Details: A small observational study in adults undergoing surgery for wisdom tooth extraction shows that taking vitamin C 500 mg three times daily for 7 days in addition to standard treatment reduces swelling 7 days after surgery when compared

with control. However, vitamin C does not seem to reduce swelling 3 days after surgery when compared with control, suggesting that longer durations are needed for anti-inflammatory effects (113664).

Premature rupture of membranes (PROM). Oral vitamin C seems to reduce the risk of PROM in some patients; however, the addition of oral vitamin E seems to negate any benefit.
^ Details: A meta-analysis of clinical research shows that taking vitamin C alone decreases the risk of both term and preterm PROM by 45% and 34%, respectively, when compared with placebo or control (96707). Another meta-analysis of clinical research shows that taking vitamin C during pregnancy decreases the risk of PROM by 43% and preterm PROM by 33%, but does not decrease the risk of term PROM, when compared with a control. While vitamin C was studied in doses of 100, 500, and 1000 mg daily, the decreased risk of PROM was only observed in studies of 100 mg daily (114493). A moderate-sized clinical study in patients with a history of PROM shows that taking vitamin C 100 mg daily, starting at 14 weeks' gestation, increases the gestational age at recurrent PROM by around 1 week and increases the gestational age at birth by around 1.3 weeks when compared with placebo (109960). Additionally, a meta-analysis of observational studies suggests that vitamin C levels in the blood tend to be lower in patients with PROM, particularly preterm PROM (114493).

Taking vitamin C in combination with vitamin E, however, does not seem to reduce the risk of term or preterm PROM; some research suggests that it might even increase the risk of non-preterm PROM (83472,96707). However, other research shows that taking vitamin C 1000 mg plus vitamin E 400 IU daily, beginning at 24 to 34 weeks gestation and continuing until delivery, may help increase the latency period until delivery by 5 days and increase gestational age at delivery by almost 1 week when compared with placebo in patients with preterm PROM (90078).

Pressure ulcers. It is unclear if oral vitamin C, when used alone or in combination with other ingredients, can improve the healing of pressure ulcers.
^ Details: A small clinical study in institutionalized patients with pressure ulcers shows that taking vitamin C 500 mg twice daily for 12 weeks does not improve wound closure or increase healing rates when compared with vitamin C 10 mg twice daily (83617).

Oral vitamin C has also been evaluated in combination with other ingredients for the treatment of grade II-IV pressure ulcers. Two small clinical studies in hospitalized patients with pressure ulcers shows that administering an oral nutritional supplement enriched with vitamin C, L-arginine, and zinc improves ulcer healing when compared with a standard diet (31953,87173). Also, clinical research in patients living in long-term care facilities shows that taking an oral nutritional supplement enriched in protein, vitamin C, L-arginine, and zinc daily for 9 weeks reduces ulcer area and decreases oozing when compared to baseline (32045). The validity of this finding is limited by the lack of a comparator group.

Radiation proctopathy. Oral vitamin C has only been evaluated in combination with vitamin E; its effect when used alone is unclear.
^ Details: A small clinical study in patients with chronic radiation proctitis shows that vitamin C 500 mg plus vitamin E 400 IU three times daily might improve symptoms when compared with baseline (9825). The validity of these findings is limited by the lack of a comparator group.

Renal cell carcinoma. It is unclear if increased dietary intake of vitamin C helps to reduce the risk of renal cell carcinoma.
^ Details: Population research has found that increased dietary intake of vitamin C is associated with a 12% reduced risk of renal cell carcinoma (98779).

Respiratory tract infections. It is unclear if oral vitamin C is beneficial for preventing respiratory tract infections or reducing the duration of these infections.
^ Details: A meta-analysis of clinical research in children and adults shows that, when compared with placebo, oral vitamin C supplementation reduces the average number of symptomatic days per individual, but does not reduce the average symptom days per respiratory episode. Also, vitamin C intake does not reduce the incidence or severity of respiratory disease or improve recovery in hospitalized patients with respiratory tract infections (108077). The validity of this trial is limited by the high heterogeneity of included studies, which evaluated various vitamin C regimens, ranging from 100 mg to 8 grams daily, as preventive therapy or as an adjuvant to active treatment.

A clinical study in children aged 3-10 years shows that taking vitamin C 50 mg in combination with a specific product (Lab4) containing Lactobacillus acidophilus, Bifidobacterium bifidum, and Bifidobacterium animalis subsp. lactis daily for 6 months reduces the incidence of cough and sore throat by 16% and 20%, respectively, when compared with placebo. However, it did not improve total symptoms, nasal congestion, nasal discharge, or sneezing. Also, aside from a 33% reduction in the average number of days with a sore throat, daily supplementation does not reduce the duration of individual symptoms or total symptoms (106943). It is unclear if these effects are due to vitamin C, the probiotics, or the combination.

Restless legs syndrome (RLS). It is unclear if oral vitamin C helps to reduce symptoms of stress.
^ Details: A small clinical study in hemodialysis patients with RLS shows that taking vitamin C 200 mg daily, alone or in combination with vitamin E 400 mg, for 8 weeks reduces the severity of RLS when compared with placebo (90093). More research is needed to determine if vitamin C is beneficial in treating RLS that is not associated with hemodialysis.

Sunburn. Topical and oral vitamin C has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
^ Details: 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 UV radiation (4715). Also, applying topical vitamin C in combination with topical vitamin E and melatonin seems to provide modest photoprotective effects when used prior to UV exposure. However, it has no effect when used during or after UV exposure (4713,4714).

Stress. It is unclear if oral vitamin C helps to reduce symptoms of stress.
^ Details: A small clinical study in healthy adults shows that taking vitamin C 3000 mg daily for 14 days modestly reduces blood pressure and subjective stress response to psychological stress when compared with placebo (10353).

Stroke. Observational research has found that although taking vitamin C supplements does not seem to be beneficial, eating more vitamin C-rich food is linked with reduced risk of stroke.
^ Details: Lower plasma levels of vitamin C have been associated with increased stroke risk (90408). Additionally, population research has found that higher dietary intake of vitamin C is associated with a 8% to 19% reduction in stroke risk when compared to lower intake (90408,109779). This reduction appears to be dose-dependent, with each 100 mg/day increase in

dietary vitamin C intake associated with about a 17% reduction (90408). However, taking vitamin C supplements has not been found to be associated with reduced stroke risk (1449,90408).

Tetanus. It is unclear if intravenous vitamin C helps to reduce symptoms of tetanus.
^ Details: A low quality clinical trial in children and young adults with tetanus shows that intravenous vitamin C 1 gram daily along with conventional treatment reduces fatality when compared to control (21539).

Tooth extraction. It is unclear if oral vitamin C is beneficial for reducing pain or improving healing after tooth extraction.
^ Details: A small clinical study in healthy patients aged 14-41 years who are undergoing bilateral premolar extraction shows that taking vitamin C 200 mg three times daily, beginning immediately after extraction and continued for 10 days, improves pain on days 1-3, and may reduce mesio-distal wound size between days 1 and 7, when compared with placebo, but not when compared with vitamin C 500 mg three times daily. A dose of 500 mg three times daily did not improve pain scores or extraction wound healing when compared with placebo (108084). The validity of this trial is limited by the short duration of treatment; additionally, this study did not report baseline vitamin C levels.

Urinary tract infections (UTIs). Although there is interest in using oral vitamin C for UTIs, there is insufficient reliable information about the clinical effects of vitamin C for this condition.

Vascular dementia. It is unclear if oral vitamin C reduces the risk of vascular dementia.
^ Details: Population research has found that supplemental intake of vitamin C and vitamin E is associated with a reduced risk of vascular dementia in Japanese-American men (4636). However, when cases in which dementia was diagnosed prior to the study are excluded from data analysis, intake of vitamin C and vitamin E is not associated with a reduced risk of vascular dementia in these patients (9824).

Wound healing. It is unclear if oral vitamin C improves the healing of chronic foot ulcers. It is also unclear if intravenous vitamin C improves healing of surgical wounds after total abdominal hysterectomy.
^ Details: A very small clinical study in adults with chronic foot ulcers shows that taking slow-release vitamin C 500 mg daily for 8 weeks seems to result in a median of 100% ulcer healing, compared with a median of 14% ulcer healing in patients taking glucosamine 1000 mg daily (105456). This finding is limited due to the small and heterogeneous patient population, which included patients with diabetes, vascular disease, and/or vitamin C deficiency.

Another small clinical study in patients undergoing total abdominal hysterectomy shows that administration of intravenous vitamin C 1 gram the night before surgery and 1 gram during surgery does not reduce the rate of surgical site infection or wound dehiscence when compared with placebo (109465). However, this study may not have been adequately powered to detect differences between groups.

More evidence is needed to rate vitamin C for these uses.

Dosing & Administration

- **Adult**

  Oral:

  The daily recommended dietary allowances (RDAs) for vitamin C are 90 mg for males and 75 mg for females aged 19 years and older. During pregnancy the RDA is 85 mg daily for 19-50 years of age and 80 mg daily for 14-18 years of age. During lactation, the RDA is 120 mg daily for 19-50 years of age and 115 mg daily for ages 14-18 years of age. People who use tobacco should take an additional 35 mg per day (4844).

  Vitamin C supplements have been used in doses of up to 2000 mg daily, which is the tolerable upper intake level (UL) for adults aged 19 years and older. Vitamin C has been used most often in doses of 400-1000 mg daily for up to 6 months (1959,4713,4714,4844). See Effectiveness section for condition-specific information.

  Intravenous:

  Vitamin C 50 mg/kg, or 2-3 grams, daily has been used. See Effectiveness section for condition-specific information.

  Topical:

  Vitamin C has been used in various topical formulations, including as a liquid, lotion, serum, spray, and patch. See Effectiveness section for condition-specific information.

- **Children**

  Oral:

  The Adequate Intake (AI) of vitamin C for infants 0-6 months is 40 mg daily and for infants 7-12 months is 50 mg daily. The daily recommended dietary allowances (RDAs) of vitamin C are as follows:; 1-3 years, 15 mg; 4-8 years, 25 mg; 9-13 years, 45 mg; 14-18 years, 75 mg for males and 65 mg for females. The ULs for vitamin C are as follows: 1-3 years, 400 mg daily; 4-8 years, 650 mg; 9-13 years, 1200 mg; and 14-18 years, including during pregnancy and lactation, 1800 mg (4844).

- **Standardization & Formulation**

  In some trials, vitamin C has been administered as a slow-release formulation (1918,89234). The slow-release formulation has been shown to decrease fluctuations in plasma concentrations of vitamin C following oral intake compared to plain formulations (90935).

Interactions with Drugs

ACETAMINOPHEN (Tylenol, others)
Interaction Rating = **Minor** Be watchful with this combination.

Severity = Insignificant • Occurrence = Probable • Level of Evidence = **B**

High-dose vitamin C might slightly prolong the clearance of acetaminophen.

Details

A small pharmacokinetic study in healthy volunteers shows that taking high-dose vitamin C (3 grams) 1.5 hours after taking acetaminophen 1 gram slightly increases the apparent half-life of acetaminophen from around 2.3 hours to 3.1 hours. Ascorbic acid competitively inhibits sulfate conjugation of acetaminophen. However, to compensate, elimination of acetaminophen glucuronide and unconjugated acetaminophen increases (6451). This effect is not likely to be clinically significant.

ALKYLATING AGENTS

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = High • Occurrence = Possible • Level of Evidence = **D**

Theoretically, antioxidant effects of vitamin C might reduce the effectiveness of alkylating agents.

Details

The use of antioxidants like vitamin C during chemotherapy is controversial. There is concern that antioxidants could reduce the activity of chemotherapy drugs that generate free radicals, such as cyclophosphamide, chlorambucil, carmustine, busulfan, and thiotepa (391). 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 effect, if any, antioxidants such as vitamin C have on chemotherapy.

ALUMINUM

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = Mild • Occurrence = Probable • Level of Evidence = **B**

Vitamin C can increase the amount of aluminum absorbed from aluminum compounds.

Details

Research in animals and humans shows that vitamin C increases aluminum absorption, theoretically by chelating aluminum and keeping it in solution where it is available for absorption (10549,10550,10551,21556). In people with normal renal function, urinary excretion of aluminum will likely increase, making aluminum retention and toxicity unlikely (10549). Patients with renal failure who take aluminum-containing compounds such as phosphate binders should avoid vitamin C supplements in doses above the recommended dietary allowances.

ANTITUMOR ANTIBIOTICS

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = High • Occurrence = Possible • Level of Evidence = **D**

Theoretically, the antioxidant effects of vitamin C might reduce the effectiveness of antitumor antibiotics.

Details

The use of antioxidants like vitamin C during chemotherapy is controversial. There is concern that antioxidants could reduce the activity of chemotherapy drugs which generate free radicals, such as doxorubicin (391). 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, if any, antioxidants such as vitamin C have on chemotherapy.

ASPIRIN

Interaction Rating = **Minor** Be watchful with this combination.

Severity = Insignificant • Occurrence = Possible • Level of Evidence = **B**

Acidification of the urine by vitamin C might increase aspirin levels.

Details

It has 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 daily of vitamin C does not seem to affect urinary pH or salicylate excretion (10588,10589), suggesting this interaction is not clinically significant.

CHOLINE MAGNESIUM TRISALICYLATE (Trilisate)

Interaction Rating = **Minor** Be watchful with this combination.

Severity = Insignificant • Occurrence = Possible • Level of Evidence = **B**

Acidification of the urine by vitamin C might increase choline magnesium trisalicylate levels.

Details

It has 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 daily of vitamin C does not seem to affect urinary pH or salicylate excretion (10588,10589), suggesting this interaction probably is not clinically significant.

ESTROGENS

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = Moderate • Occurrence = Probable • Level of Evidence = **B**

Vitamin C might increase blood levels of estrogens.

Details

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 is 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 does not have any effect on estrogen levels. Increases in plasma estrogen levels may occur when patients who are deficient in vitamin C take supplements (11161). Monitor these patients for estrogen-related side effects.

FLUPHENAZINE (Prolixin)

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = Moderate • Occurrence = Possible • Level of Evidence = **D**

Theoretically, vitamin C might decrease levels of fluphenazine.

Details

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

INDINAVIR (Crixivan)

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = Mild • Occurrence = Probable • Level of Evidence = **B**

Vitamin C can modestly reduce indinavir levels.
Details
One pharmacokinetic study shows that taking vitamin C 1 gram orally once daily along with indinavir 800 mg orally three times daily reduces the area under the concentration-time curve of indinavir by 14%. The mechanism of this interaction is unknown, but it is unlikely to be clinically significant in most patients. The effect of higher doses of vitamin C on indinavir levels is unknown (11300,93578).

LEVOTHYROXINE (Synthroid, others)
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Probable • Level of Evidence = **B**
Vitamin C can increase levothyroxine absorption.
Details
Two clinical studies in adults with poorly controlled hypothyroidism show that swallowing levothyroxine with a glass of water containing vitamin C 500-1000 mg in solution reduces thyroid stimulating hormone (TSH) levels and increases thyroxine (T4) levels when compared with taking levothyroxine alone. This suggests that vitamin C increases the oral absorption of levothyroxine, possibly due to a reduction in pH (102978).

NIACIN
Interaction Rating = **Minor** Be watchful with this combination.
Severity = Mild • Occurrence = Possible • Level of Evidence = **A**
Vitamin C might decrease the beneficial effects of niacin on high-density lipoprotein (HDL) cholesterol levels.
Details
A combination of niacin and simvastatin (Zocor) effectively raises HDL cholesterol levels in patients with coronary disease and low HDL levels. Clinical research shows that taking a combination of antioxidants (vitamin C, vitamin E, beta-carotene, and selenium) along with niacin and simvastatin (Zocor) attenuates this rise in HDL, specifically the HDL-2 and apolipoprotein A1 fractions, by more than 50% in patients with coronary disease (7388,11537). It is not known whether this adverse effect is due to a single antioxidant such as vitamin C, or to the combination. It also is not known whether it will occur in other patient populations.

SALSALATE (Disalcid)
Interaction Rating = **Minor** Be watchful with this combination.
Severity = Insignificant • Occurrence = Possible • Level of Evidence = **B**
Acidification of the urine by vitamin C might increase salsalate levels.
Details
It has 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 does not seem to affect urinary pH or salicylate excretion (10588,10589), suggesting this interaction probably is not clinically significant.

WARFARIN (Coumadin)
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Possible • Level of Evidence = **D**
High-dose vitamin C might reduce the levels and effectiveness of warfarin.
Details
Vitamin C in high doses may cause diarrhea and possibly reduce warfarin absorption (11566). There are reports of two people who took up to 16 grams daily of vitamin C and had a reduction in prothrombin time (9804,9806). Lower doses of 5-10 grams daily can also reduce warfarin absorption. In many cases, this does not seem to be clinically significant (9805,9806,11566,11567). However, a case of warfarin resistance has been reported for a patient who took vitamin C 500 mg twice daily. Cessation of vitamin C supplementation resulted in a rapid increase in international normalized ratio (INR) (90942). Tell patients taking warfarin to avoid taking vitamin C in excessively high doses (greater than 10 grams daily). Lower doses may be safe, but the anticoagulation activity of warfarin should be monitored. Patients who are stabilized on warfarin while taking vitamin C should avoid adjusting vitamin C dosage to prevent the possibility of warfarin resistance.

Interactions with Supplements

ACEROLA: Acerola contains high concentrations of vitamin C.
Details
Acerola contains an average of 2000 mg of vitamin C per 100 grams of fruit (30260). Concomitant use of acerola with vitamin C supplements might exceed the tolerable upper intake level (UL) of 2000 mg vitamin C per day for adults (4844,12651,21557). This could increase the risk for adverse effects.

CHROMIUM: Limited data suggests that vitamin C increases chromium absorption.
Details
The amount of chromium absorbed from a 1000 mcg dose approximately doubled when taken along with vitamin C 100 mg (10600). Advise people to avoid taking large doses of chromium and vitamin C together. It is not known whether separating the doses by several hours avoids this interaction.

COPPER: High doses of vitamin C might interfere with copper absorption.
Details
Low doses of vitamin C do not seem to affect copper absorption or retention (21562); however, 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 is also suggested that vitamin C can stimulate tissue copper utilization (710,11538). It is unlikely that this interaction is clinically significant unless dietary copper intake is low (710).

GRAPE: Vitamin C taken with grape seed polyphenols might increase blood pressure.
Details
One small clinical study shows that taking vitamin C 500 mg/day in combination with grape seed polyphenols 1000 mg/day significantly increases systolic and diastolic blood pressure in adults with hypertension (13162). The potential mechanism of this interaction is not known.

IRON: Supplemental and dietary vitamin C can increase the absorption of iron.
Details
Supplemental or dietary vitamin C improves absorption of dietary non-heme iron when ingested at the same time (9518,9571,9586,11571,21563,83168,83661). Also, 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 dietary substances which inhibit iron absorption, such as phytates, polyphenols, and tannins, possibly by chemically reducing iron and preventing the formation of less soluble ferric compounds (9518,9573,9586,11571). The effect of vitamin C on iron status seems to be greater in individuals with iron deficiency compared to those with sufficient iron levels (21502). However, some clinical research in patients with iron deficiency shows that taking iron with vitamin C is no better for improving hemoglobin levels when compared with taking iron alone (104680,112477). Taking a vitamin C supplement to improve absorption of iron is probably not necessary for most people, especially if their diet contains plenty of vitamin C (9571).

ROSE HIP: Rose hips contain high concentrations of vitamin C.
Details
Concomitant use of rose hip with vitamin C supplements might exceed the tolerable upper intake level (UL) of 2000 mg vitamin C per day for adults (12652). This could increase the risk for adverse effects.

VITAMIN B12: Despite claims to the contrary, vitamin C does not seem to reduce levels of vitamin B12 in the body.
Details
High-dose vitamin C seems to degrade certain forms of vitamin B12 in solution and in test tubes. Although early clinical research suggested that vitamin C might also reduce serum vitamin B12 levels, this was later disproven. There appears to be no clinically significant change in serum vitamin B12 levels in patients taking as much as 4 grams of vitamin C daily (9511,104078). Overall, it seems that high-dose vitamin C does not affect serum levels of vitamin B12.

Interactions with Conditions

ALCOHOL USE DISORDER

Alcohol intake can increase urinary excretion of vitamin C by almost 50% (90941). In healthy patients, this increased excretion does not appear to significantly affect vitamin C status (90939). However, with chronic alcohol use, particularly in those who are acutely unwell or critically ill, vitamin C deficiency is common. In such patients, conventional intravenous supplementation with vitamin C (two to three times daily for 3 days) might be insufficient to restore vitamin C levels. Prolonged supplementation may be needed (90940).

CANCER

Cancerous cells accumulate high concentrations of vitamin C. Cancer cells take up 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 supplemental vitamin C benefits the growth of cancer cells or has any detrimental effect on cancer treatments. Until more is known, patients with cancer should only use supplemental vitamin C under the direction of their oncologist.

CHRONIC KIDNEY DISEASE (CKD)

CKD might lead to vitamin C deficiency. Kidney disease can also decrease the excretion of oxalate and increase the risk of oxalate nephropathy. Theoretically, supplemental vitamin C could increase the risk for hyperoxaluria. One observational study in children with CKD found that vitamin C supplementation did not affect oxalate levels (104026). However, in one case report, a bariatric surgery patient with CKD experienced acute kidney failure from secondary oxalosis that was attributed to intake of supplemental vitamin C 1000 mg daily (96710). Theoretically, intake of vitamin C supplements might increase the risk of hyperoxaluria in patients with concomitant kidney dysfunction, especially those who have undergone bariatric surgery.

GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY

Large amounts of vitamin C can cause hemolysis in individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency (15). In one case, a 9-month-old infant with G6PD deficiency presented with acute hemolytic anemia after being treated with intravenous vitamin C 2000 mg every 4 hours for two days (90937). In another case, a 3-year-old child presented with acute hemolytic anemia and acute kidney injury following accidental ingestion of vitamin C 300 mg (106944).

KIDNEY STONES (Nephrolithiasis)

Larger amounts of vitamin C can increase the risk of oxalate kidney stones, especially in those prone to oxalate stone formation. Vitamin C is metabolized to oxalic acid, so increased consumption increases the urinary concentration of oxalic acid and the formation of oxalate kidney stones (10356). People who have a history of oxalate stones seem to be more sensitive to supplemental vitamin C than non-stone formers. In those 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). In males, daily supplemental vitamin C doses as low as 250 mg have been associated with a higher risk of kidney stones (104029). Tell patients prone to kidney stone formation to avoid higher doses of vitamin C.

NICOTINE AND SMOKING

Smokers have lower plasma levels of vitamin C than nonsmokers with similar dietary intake of vitamin C (5875,11501). The reason for these lower levels is unclear. There does not seem to be an effect of nicotine on vitamin C levels, and depletion has not been reported with nicotine replacement products (e.g., patches, gum, etc). Advise smokers to consume a diet rich in vitamin C, or recommend a supplement if this is not possible. Smokers may need between 124-200 mg daily to maintain normal plasma levels (11546).

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 the risk of precancerous oral lesions (11502). Advise tobacco users to consume a diet rich in vitamin C.

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 vitamin C can cause falsely elevated results of serum tests relying on color reactions (Redox reactions) and Technicon SMA 12/60 (275).

BILIRUBIN

Large amounts of vitamin C can cause falsely elevated serum test results measured by Technicon SMA 12/60 or colorimetric methods (275).

CARBAMAZEPINE (Tegretol)

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

CREATININE

Vitamin C can cause falsely elevated 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). Also, large amounts of vitamin C can cause a falsely elevated blood glucose result when measured using a self-monitoring blood glucose device. In one case, a patient with type 2 diabetes who had been taking vitamin C 10 grams daily for 10 days presented with a falsely elevated blood glucose level (90938). In another case report, a patient with lymphoma received intravenous vitamin C 1 gram/kg in nine separate injections over 19 days, which resulted in falsely elevated glucometer measurements (104031).

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 vitamin C in doses of 250 mg or more daily (3042). Patients should avoid dietary or supplemental vitamin C for 3 days prior to guaiac fecal occult blood testing (21566,21567).

THEOPHYLLINE

Large amounts of vitamin C can cause a falsely low theophylline serum level when measured by the ARIS system or Ames Seralyzer photometer (275).

VITAMIN B12

Large amounts of vitamin C can interfere with vitamin B12 assay, resulting in falsely low vitamin B12 levels (1965).

Nutrient Depletion

SOME DRUGS CAN AFFECT VITAMIN C LEVELS:

ALCOHOL

Depletion Rating = **Insignificant Depletion** A supplement is not needed for most patients.

Alcohol increases vitamin C excretion in the urine.

Details

Preliminary clinical evidence suggests that alcohol intake increases urinary excretion of vitamin C by 47% (90941). In healthy patients, this increased excretion does not appear to significantly affect vitamin C status (90939). However, in chronic alcohol abusers, particularly those who are acutely unwell or critically ill, vitamin C deficiency is common and scurvy can occur (90940).

ASPIRIN

Depletion Rating = **Insignificant Depletion** A supplement is not needed for most patients.

Aspirin might reduce levels of vitamin C.

Details

Aspirin reduces tissue and leukocyte uptake of vitamin C, leaving more in the plasma to be filtered into the urine and increasing elimination (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 long-term (10591). Supplements aren't needed with the low doses of aspirin used for cardiovascular indications.

CALCIUM CHANNEL BLOCKERS

Depletion Rating = **Insufficient Evidence to Rate** Clinical significance is not known.

Dihydropyridine calcium channel blockers (DCCBs) might decrease vitamin C absorption.

Details

DCCBs inhibit uptake of vitamin C by intestinal cells in vitro (9808). Whether this causes a clinically significant reduction in vitamin C absorption in humans is not known.

DIURETIC DRUGS

Depletion Rating = **Insignificant Depletion** A supplement is not needed for most patients.

Diuretics might reduce levels of vitamin C.

Details

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 long-term oral use of furosemide or other diuretics.

ESTROGENS

Depletion Rating = **Insignificant Depletion** A supplement is not needed for most patients.

Estrogens might reduce levels of vitamin C.

Details

Evidence on 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 tissue (10548,10583,10587,11161,11875). This may only be clinically relevant in patients with very low intake of vitamin C (10548,11161,11528). Supplements aren't necessary for people on estrogens who have an adequate dietary intake of vitamin C.

PROTON PUMP INHIBITORS (PPIs)

Depletion Rating = **Insufficient Evidence to Rate** Clinical significance is not known.

PPIs might reduce vitamin C levels.

Details

Preliminary research suggests omeprazole reduces vitamin C levels, possibly due to increased destruction of vitamin C at higher gastric pH levels (10572). It is not known if this interaction results in clinically significant reductions in vitamin C levels.

Overdose

There is insufficient reliable information available about the presentation or treatment of overdose with vitamin C.

Commercial Products Containing: Vitamin C

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Pharmacokinetics

Absorption: 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 (9809). This is due to the fact that vitamin C is transported from the intestines into the blood by the sodium-dependent vitamin C transporter (SVCT1), which is saturable (83482). The decreased bioavailability of vitamin C with increased dosages, as increased renal excretion, limits the plasma levels attainable with oral vitamin C supplementation (9809).

Excretion: Most vitamin C that is absorbed is excreted in the urine (9809).

Mechanism of Action

General: Vitamin C is a commonly used water-soluble vitamin and essential nutrient. Although many mammals can produce vitamin C, humans must obtain vitamin C from foods and other sources (1964,4844). 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).

Antiallergic effects: 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).

Antihypertensive effects: Taking vitamin C orally, in combination with antihypertensive drugs, seems to decrease systolic blood pressure in some patients (2044,13162,83444,83483). Animal research suggests that vitamin C reduces blood pressure by increasing levels of the antioxidant glutathione, as well as improving insulin-stimulated glucose metabolism (30859).

Anti-inflammatory effects: C-reactive protein (CRP) is an acute-phase protein that is produced by the liver in response to inflammation. Some research suggests that taking vitamin C 515-2000 mg daily can reduce CRP levels in people who are actively or passively exposed to cigarette smoke or air pollution (14010,109466). Vitamin C also seems to reduce other markers of inflammation such as tumor necrosis factor alpha (TNF-alpha) and interleukin-6 (IL-6) in individuals exposed to air pollution (109466). However, vitamin C 50 or 500 mg daily for up to 5 years does not appear to reduce CRP levels in patients with atrophic gastritis (90405), though vitamin C administered intravenously during and 48 hours after cardiac surgery with extracorporeal circulation does reduce CRP and sedimentation rate (114492).

Antioxidant effects: 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, decreases lipid peroxidation, and decreases oxidative DNA and protein damage (3042,83215). Damage by reactive oxygen species is thought to be a contributing factor to a number of diseases including dementia, asthma, hypertension, osteoarthritis, and cancer. However, in a rat model of exercise under polluted conditions, administration of vitamin C only very modestly improved markers of oxidative stress (106940). Researchers theorize 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 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). Free oxygen radicals are also produced during cardiopulmonary bypass procedures, causing plasma vitamin C to drop by 70% within 24 hours of surgery (102127).

Anti-sepsis effects: There is interest in using vitamin C to improve outcomes in patients with sepsis. Observational research suggests that patients with septic shock are more likely to have low plasma levels of vitamin C and higher C-reactive protein (CRP) levels than critically ill, non-septic patients (100317). Exploratory clinical research in patients with severe sepsis shows that intravenous administration of vitamin C reduces CRP and procalcitonin levels, indicating an anti-inflammatory effect. It also attenuates an increase in thrombomodulin levels, possibly indicating a reduction in vascular endothelial injury (100318). Clinical research in patients with septic shock also suggests that intravenous vitamin C may increase levels of norepinephrine and precursors to endogenous norepinephrine synthesis such as tyrosine hydroxylase, tetrahydrobiopterin, and dopamine-beta-hydroxylase. As a result, this might lower the dose of norepinephrine required during sepsis treatment (114489). Preclinical research also shows that vitamin C can prevent the cytokine surges in early sepsis that activate and sequester neutrophils in the lung and contribute to acute respiratory distress syndrome (ARDS) (102130). Laboratory research also suggests that vitamin C might alter cell membrane permeability in sepsis. The lipopolysaccharides (LPS) found in gram negative bacteria can cause cell membrane hyperpermeability. In vitro research shows that vitamin C with hydrocortisone reduces cell membrane permeability in LPS-treated human lung microvascular endothelial cells; however, this effect was not seen with either vitamin C or hydrocortisone alone (100314). Furthermore, animal research shows that administering intravenous vitamin C reduces oxidative stress, attenuates a reduction in heart rate, and improves survival in septic mice that are predicted to have worsened outcomes based on physiological measurements. This effect was not seen in mice that were predicted to have better outcomes prior to vitamin C administration, suggesting that benefits of vitamin C might be limited to more severe cases of sepsis (100313).

Cardiovascular effects: 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 nitric oxide (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 (14014,14017,83222).

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). There is some evidence that vitamin C reduces LDL cholesterol levels in patients with hypercholesterolemia (83445). 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).

Anti-fibrillatory effects of vitamin C are possibly related to the prevention of oxidative byproducts in atrial tissue. Benefits do not seem to be directly electrophysiological (96705).

A meta-analysis of cardiac and noncardiac patients, most of whom have normal cardiac function, shows that vitamin C may improve left ventricular ejection fraction (LVEF), with an average increase of 12% and 5% in cardiac and non-cardiac patients, respectively, when compared with either placebo or no treatment. It is unclear if route of administration may affect outcomes. Greater benefit was observed in patients with lower baseline LVEF levels (108074).

Chemotherapy-modulating effects: 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).

Dermatologic effects: 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). Topical application of vitamin C has been shown to increase collagen production and improve collagen organization (83421).

Ergogenic effects: 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).

Gastrointestinal effects: A small clinical study in healthy adults shows that supplementation with vitamin C 1000 mg daily for 2 weeks can modulate the gut microbiota, leading to beneficial shifts in bacterial populations (106623).

Immunostimulant effects: 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 (1963,1965,83560). 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 (83214). 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). 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).

Musculoskeletal effects: Since vitamin C is a cofactor in the synthesis of collagen, there is interest in its effects for tendon healing. A preliminary clinical study in adults after arthroscopic rotator cuff repair shows that taking vitamin C 500 mg daily for 45 days does not improve postoperative outcomes when compared with no supplementation. However, there was a non-significant trend to an increased healing rate (radiographically measured) in the vitamin C group (105460). This study was limited by a lack of placebo control and inappropriate randomization.

Radiotherapy effects: 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).

However, there is some concern that vitamin C might reduce the efficacy of radiotherapy. In vitro research suggests that pretreatment with vitamin C prior to irradiation might enhance breast cancer proliferation and reduce radiosensitivity, although these effects appear to depend on cancer type. Human epidermal growth factor 2-positive cells appeared to be more sensitive to vitamin C when compared with triple-negative or estrogen receptor-positive cells. An observational study in patients with breast cancer undergoing radiotherapy did not find an association between vitamin C supplementation and risk of breast cancer recurrence over a period of 5 years. However, even though the vitamin C group had notably less aggressive tumor types, recurrence-free survival was similar in both vitamin C and control groups (108082).

Uricosuric effect: 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). A meta-analysis in a heterogenous population shows that oral vitamin C supplementation at doses of 200-2000 mg daily for 14 days to 6 months is associated with reduced serum levels of uric acid. The effect of oral vitamin C supplementation on serum levels of uric acid is greater in patients younger than 65 years, at durations less than 1 month, and when used alone (106619).

Classifications

Immunomodulators, Water-Soluble Vitamins

References

See Monograph References

Monographs are reviewed on a regular schedule. See our Editorial Principles and Process for details. The literature evaluated in this monograph is current through 12/17/2024. This monograph was last modified on 12/16/2024. If you have comments or suggestions, please tell the editors.