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Who should take them and who should not.

Vitamin Supplements

Many patients ask their physicians whether they should take vitamins. Since the last Medical Letter article on this subject,¹ more data have become available on the benefits and risks of taking vitamin supplements.

VITAMIN E — Vitamin E in food, which is mostly gamma-tocopherol, acts as an antioxidant. Vitamin E in supplements is mostly alpha-tocopherol, which may block the antioxidant activity of gamma-tocopherol and have a pro-oxidant effect *in vivo*. High doses of vitamin E may interfere with vitamin K metabolism and platelet function. A meta-analysis of clinical trials using vitamin E dosages higher than 400 IU/day found an increased risk of mortality.² A randomized controlled trial in more than 9000 patients with vascular disease or diabetes found that longer term supplementation with 400 IU of vitamin

E per day did not prevent cancer or major cardiovascular events and may have increased the risk of heart failure.³ A randomized controlled trial in almost 40,000 women ≥ 45 years old found that 600 IU of vitamin E per day provided no overall benefit for major cardiovascular events or cancer.⁴

VITAMIN A AND BETA CAROTENE — Vitamin A and beta carotene, a potent source of the vitamin, are antioxidants, but may also have pro-oxidant effects *in vivo*. A high intake of vitamin A from supplements and food has been associated with an increased risk of hip fracture in postmenopausal women⁸ and with teratogenicity when taken during early pregnancy.⁹

Multivitamin preparations usually contain 1000 to 10,000 IU (0.6 to 6 mg) of beta carotene. Beta carotene supplements usually contain 12 to 15 mg. A placebo-controlled intervention trial in Finnish smokers found that 20 mg/day of a beta carotene supplement increased the incidence of lung cancer by 18%, which was statistically significant.⁵ Another large double-blind intervention trial in smokers and asbestos-exposed workers, terminated early because no benefit was demonstrated, found that combined therapy with 30 mg of beta carotene and 25,000 IU of vitamin A daily was associated with an increase in the incidence of lung cancer, cardiovascular mortality and total mortality.^{6,7} A meta-analysis of 7 cohort studies found no association between carotenoid intakes estimated from dietary questionnaires and the incidence of lung cancer during 7-16 years of follow-up.¹⁰

VITAMIN D — Many elderly people, especially those with dark skin, receive inadequate amounts of vitamin D because of limited exposure to sunlight, decreased synthesis of vitamin D in the skin, and decreased absorption and activation of the vitamin. The latest US recommendations for daily vitamin D intake, based on amounts that have slowed the rate of bone loss, are 400 IU for men and women 51 to 70 years old, and 600 IU for men and women more than 70 years old. Elderly people who do not drink milk and do not expose themselves to sunlight will need to take supplements to achieve this level of

SOURCES OF SOME VITAMINS

Vitamin/RDA ¹	Some Food Sources
Vitamin E 15 mg (22.5 IU)	Vegetable and seed oils, nuts
Vitamin A 900 mcg (3000 IU)	Dairy products, meats, fish and fish oil; beta carotene in green or yellow fruits and vegetables
Vitamin D 5 mcg (200 IU)	Fish and fortified milk
Vitamin C 75-90 mg	Citrus fruits, tomatoes
Vitamin B ₁₂ 2.4 mcg	Meat, fish and dairy products
Folate 400 mcg	Meat and dark-green leafy vegetables
Vitamin B ₆ 1.3 mg	Meat, whole-grain breads and cereals, soybeans and vegetables

1. Recommended Dietary Allowance (RDA) is the average daily dietary intake level that is sufficient to meet the nutrient requirements of most healthy adults.

vitamin D intake. A meta-analysis of randomized controlled trials of vitamin D in patients more than 60 years old found a reduced risk of hip and other non-vertebral fractures with 700-800 IU/day, but not with 400 IU/day.¹¹ However, a randomized controlled trial in more than 3000 high risk women found no evidence that 1000 mg calcium with 800 IU vitamin D per day reduced the risk of clinical fractures.¹²

VITAMIN C — Dietary levels of about 300-400 mg/day of vitamin C maintain maximal body pools of the vitamin. One 8-oz glass of orange juice contains about 100 mg of vitamin C. No long-term intervention studies with vitamin C have been published. A meta-analysis of 3 small, relatively short trials in elderly people, found no benefit on mortality.¹³ Short-term randomized controlled trials have shown that taking vitamin C does not prevent upper respiratory infections.¹⁴ High doses of vitamin C (more than 1 gram) are poorly absorbed, cause diarrhea, and could increase urinary oxalate excretion to a level that might cause kidney stones in people with pre-existing hyperoxaluria.

VITAMIN B₁₂ — Atrophic gastritis, which affects 10% to 30% of older people, results in inability to absorb vitamin B₁₂ bound to food protein, with absorption of crystalline vitamin B₁₂ usually left intact.¹⁵ Elderly patients, therefore, should take vitamin B₁₂, either in the form of B₁₂-fortified foods such as cereals or as a daily dietary supplement containing at least the Recommended Dietary Allowance.

FOLATE — The standard US diet provides 50 to 500 mcg of absorbable folate per day, but the bioavailability of folate in mixed diets varies. Folic acid in supplements is about twice as bioavailable as folate in food.¹⁶ All enriched cereal grains sold in the US now contain 140 mcg of folic acid per 100 g of grain; estimates suggest that this fortification increases folic acid intake by about 215 to 240 mcg/day.¹⁷ Even this amount, however, may be inadequate for prevention of neural tube defects, which occur early in pregnancy before most women know that they are pregnant. Supplementing the diet of women of child-bearing age with 400 mcg of folic acid per day, the amount contained in most multivitamin preparations, has dramatically decreased the incidence of neural tube defects in their offspring.¹⁸ Low intake of absorbable folates has also been associated with high serum concentrations of homocysteine and a higher incidence of cardiovascular disease and stroke; folate supplements can reverse hyperhomocystinemia, but it is not known whether this reduces

coronary disease.¹⁹ High doses of folic acid can mask vitamin B₁₂ deficiency, permitting progression of neurologic disease.

VITAMIN B₆ (Pyridoxine) — One prospective cohort study based on dietary questionnaires found a lower risk of coronary heart disease in women who had vitamin B₆ and folate intakes above the RDA.²⁰ Prospective intervention studies are lacking, however, and the optimal dose and effectiveness of vitamin B₆ supplements remain to be determined.²¹

CONCLUSION — Supplements are necessary to assure adequate intake of folic acid in young women and possibly of vitamins D and B₁₂ in the elderly. There is no convincing evidence that taking supplements of vitamin C prevents any disease except scurvy. Women should not take vitamin A supplements during pregnancy or after menopause. No one should take high-dose beta carotene supplements. A balanced diet rich in fruits and vegetables may be safer than taking vitamin supplements. No biologically active substance taken for a long term can be assumed to be free of risk. □

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