Vitamins for Chronic Disease Prevention in Adults
Clinical Applications

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In the absence of specific predisposing conditions, a usual North American diet is sufficient to prevent overt vitamin deficiency diseases such as scurvy, pellagra, and beriberi. However, insufficient vitamin intake is apparently a cause of chronic diseases. Recent evidence has shown that suboptimal levels of vitamins, even well above those causing deficiency syndromes, are risk factors for chronic diseases such as cardiovascular disease, cancer, and osteoporosis. A large proportion of the general population is apparently at increased risk for this reason.

Suboptimal Amounts of Vitamins
Suboptimal levels of a vitamin can be defined as those associated with abnormalities of metabolism that can be corrected by supplementation with that vitamin. For example, many people in the general population have serum homocysteine levels from 1.62 to 2.03 mg/L (12-15 µmol/L),\(^1\) which fall to baseline levels of 1.08 to 1.35 mg/L (8-10 µmol/L) after a few weeks of supplementation with folate, along with vitamins B\(_6\) and B\(_{12}\).\(^2\) Similarly, in many elderly people, methylmalonic acid levels fall with vitamin B\(_{12}\) supplementation,\(^2\) and elevated levels of parathyroid hormone fall with vitamin D supplementation.\(^3\) Measurements of vitamin levels in blood, serum, or red blood cells, at least with current reference points for abnormality, are not a reliable guide to this form of deficiency; in one study,\(^2\) supplementation substantially reduced serum homocysteine levels in elderly patients with normal serum folate concentrations.

For some vitamins, the concept of suboptimal levels is also supported by randomized trial evidence that supplementation reduces the rate of clinical

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events. The research evidence is conclusive that folate during the first trimester of pregnancy reduces the risk of neural tube defects in women at increased risk. Similarly, vitamin D supplementation, along with calcium, reduces the risk of fractures in elderly women with osteoporosis.

The high prevalence of suboptimal vitamin levels implies that the usual US diet provides an insufficient amount of these vitamins. Fruits and vegetables are the main dietary source of many vitamins, and health experts have long recommended at least 5 daily servings. A recent survey showed that only 20% to 30% of the population actually meet this goal. Although vitamin D is added to milk, many people (especially the elderly) do not consume enough dairy products to get a sufficient amount of vitamin D.

Folate supplementation of cereal products is sufficient to raise folate intake only by about 100 µg, so many people do not meet the goal of 400 µg/d. Food preparation may decrease the activity for some vitamins; for example, keeping food hot longer than 2 hours results in a more than 10% loss of vitamin C, folate, and vitamin B₆. Vitamins are also lost during chilling, storage, and reheating, including more than 30% of vitamin C and folate. Alcohol consumption increases folate requirements, and aging is associated with decreased absorption of some vitamins such as B₁₂.

Correcting Suboptimal Vitamin Levels

Three options exist for correcting suboptimal vitamin intake. First, physicians could counsel patients to improve their diet. This approach would be relatively inefficient if the only goal were to increase vitamin consumption because patients would have to be counseled individually, and it is difficult to get individual patients to change their diets. Nevertheless, dietary change is a central component of an overall program of preventive care. Foods contain thousands of compounds that may be biologically active, including hundreds of natural antioxidants, carotenoids, and flavonoids. For these reasons, vitamin supplementation is not an adequate substitute for a good diet.

A second option is to add vitamins to generally consumed foods. The United States has been adding vitamin D to milk and some other dairy products since the 1930s because of the high prevalence of rickets and osteomalacia in northern climates at that time. Beginning in 1996, folate has been added to cereals to reduce the rate of neural tube defects. However, this approach is limited by popular mistrust of adding chemicals to food.

A third option is for individuals to take vitamin supplements. All major pharmacies carry their own brands of multivitamins as well as a variety of other brand name and generic multivitamins. The contents of basic multivitamins are remarkably similar across brands, with each having at least 100% of the daily value for nearly all vitamins (with the exception of vitamin K). In addition to vitamins, so-called multivitamins often contain other food supplements such as minerals and herbs. The amount of calcium in multivitamins is typically between 40 and 160 mg, well below the generally recommended dose of 1000 to 1500 mg/d, so one cannot depend on multivitamins for meeting calcium needs. Most multivitamins contain iron, whose supplementation may not be advisable for men and nonmenstruating women, given the high prevalence of the gene for hemochromatosis.

The cost for brand-name multivitamins may be around $20 to $30 annually, and some special formulations may cost a great deal more. However, one can easily buy large quantities (eg, 250-500 pills) of generic multivitamins for around $10 annually. We are aware of no evidence that the various multivitamins differ in bioavailability because of the way they are formulated. Patients can buy individual vitamins at an even lower price, which may make sense for women in the childbearing years, for whom folate supplementation might cost only $5 to $10 annually.

Special multivitamins are sold for subgroups of the population such as active men, perimenopausal women, and the elderly. The Internet and health-food stores are filled with promotions for these special-purpose multivitamins, which are often costly. The only evidence-based arguments for taking more than a common multivitamin once a day pertain to the elderly and women who might become pregnant. The recommended intake for vitamins B₁₂ and D in the elderly is closer to 2 times the dietary reference intake. For women who might become pregnant, folate at 800 µg/d is appropriate.

Some vitamins, such as thiamin, riboflavin, and niacin, have received little mention in this review. Although by definition severe deficiency of these vitamins is associated with disease, they have so far not been associated with chronic diseases. The absence of evidence that these vitamins are associated with chronic diseases might be because those associations do not exist, ordinary diets provide sufficient amounts to prevent chronic disease, or the research has not yet been done to discover these relationships.

Testing

Tests for vitamin levels in blood, serum, or red blood cells are now offered by commercial laboratories, as are tests for substances such as homocysteine that mark abnormal vitamin-related metabolism. The availability of these tests raises these questions: Would this additional information lead to better preventive or therapeutic interventions than might be offered without the test? If so, what kind of patients would benefit?

It is certainly possible that some individuals, because of their diets or genetic polymorphisms, have unusual vitamin needs. Many of these people can be detected by a simple review of their medical problems, including alcoholism. The MTHFR polymorphism, which is associated with low folate levels and perhaps increased rates of cardiovascular disease, is the best studied. The abnormal MTHFR gene occurs in 5% to 15% of the population and might have effects on diseases related to folate deficiency. The MTHFR gene would be detected only by specific testing not yet
commercially available. However, re-
search into the metabolic and clinical ef-
teffects of these disorders is in its infancy
and not strong enough to confidently
guide tailored supplementation pro-
grams. Therefore, we believe that test-
ing individuals who do not have a well-
recognized indication is premature.

Recommendations
We recommend that all adults take one
multivitamin daily. This practice is jus-
tified mainly by the known and sus-
pected benefits of supplemental folate
and vitamins B₉, B₁₂, and D in prevent-
ing cardiovascular disease, cancer, and
osteoporosis and because multivi-
tamins at that dose are safe and inexpen-
sive. It is reasonable to consider a dose
of 2 ordinary multivitamins daily in the
elderly, specifically because of the high
prevalence of suboptimal vitamin B₁₂ and
D intake. However, it might be safer to
supplement 1 multivitamin with addi-
tional vitamins B₁₂ and D, taken sepa-
rately, given the possibility that in-
creased vitamin A intake might increase
the risk of hip fracture and that the iron
in most multivitamins may increase the
risk of hemochromatosis in some people.

The increased folate requirement in
people with high alcohol intake can be
met with 1 multivitamin daily or folic
acid supplementation alone. For women
attempting to conceive, a multivitamin
plus folate at 400 µg/d is appropriate,
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