

Conversation with the Experts

Toward Optimal Health: Meir Stampfer, M.D., Dr.P.H., Discusses Multivitamin and Mineral Supplementation for Women

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MULTIVITAMIN AND MINERAL SUPPLEMENTATION has grown so rapidly that more than half of the adult population in the United States is believed to be taking some form of dietary supplement. The typical multivitamin and mineral supplement user tends to follow a healthier lifestyle, which makes observational studies of the relationship between supplement use and disease outcomes difficult to interpret. Also complicating the picture is the increasing reliance on nutrient fortification of foods. Historically, fortification of foods has led to the remediation of vitamin and mineral deficits, but the cumulative effects of supplementation and fortification have also raised safety concerns about exceeding upper limits. Despite the uncertainty of health benefits from multivitamin use, millions of Americans believe supplements reduce their disease risks. However, experts have come to different conclusions about the value of such routine use of vitamin supplementation.

In 2006, the National Institutes of Health (NIH) convened a consensus panel to examine the efficacy and safety of multivitamin/mineral supple-

ment use in primary prevention of cancer and chronic disease in the general population. The State-of-the-Science Statement attempted to respond to two issues: Has efficacy of use been proven in clinical trials of multivitamin and mineral supplements for the primary prevention of cancer and chronic diseases? What is known about the safety of multivitamin and mineral supplement use in the general population of adults? The report passed on drawing definitive conclusions, yet in the most recent study on vitamin supplementation, heavy use of vitamins—taking more than 7 vitamin pills/week—doubled the risk of dying from prostate cancer. This should give women's health practitioners pause because the findings suggest a potential risk from excessive micronutrient supplementation.

Many physicians may be unaware of common dietary sources of vitamins and minerals and may be uncertain about which nutrients should be recommended or discouraged. As one of the foremost authorities on nutrition and health, Dr. Meir Stampfer agreed to interpret the current evidence on vitamin and mineral supple-

mentation to promote health and reduce chronic disease risk.

Multivitamins can easily supply needed nutrients, but a recent report from the NIH concluded that not enough evidence exists to make a firm recommendation for or against the use of multivitamins for disease prevention. What does that mean in terms of the clinician's role in advising individual patients?

This conclusion is inadequate, as clinicians and individual patients would like some guidance based on available data, even if the data are incomplete. The conference panel took a purist view that unless and until there are supporting data, from randomized trials, we cannot and should not make any recommendations for use of supplemental vitamins and minerals. This is a narrow, impractical view. After all, government recommendations, specifically Dietary Reference Intakes, exist for individual nutrients based on the best available research compiled by the Food and Nutrition Board of the Institute of Medicine and is supported by findings from consumption data, such as the NHANES survey. What the collective data tell is that the majority of Americans are not meeting the recommended intake levels for most vitamins. Thus, a more useful conclusion from this NIH panel would have been that Americans still need to eat better, but unless or until they do, they may benefit from a basic multivitamin/mineral supplement. Although this concept may go against the traditional axiom that everyone is best off getting what they need from food, that advice ignores the reality, in that most diets fall short in some essential vitamins and minerals.

Can a multivitamin supplement meet the needs for most women, or are there specific micronutrients that may be needed to supplement the diet in the face of particular conditions such as anemia and osteoporosis?

There are some exceptions. Certain women may have specific (single source) nutrient needs at different life stages (premenopausal vs. postmenopausal), namely, calcium, vitamin D, folic acid, iron, and vitamin B₁₂. These micronutrients sometimes cannot be consumed in adequate amounts even in a well-balanced diet, necessitating supplementation. Women of childbearing age

should take the supplemental folate. Many elderly women absorb vitamin B₁₂ poorly, because of decreased stomach acid, but acid is not required for absorption from a supplement. The best bet is to suggest a multivitamin supplement to be sure that all these nutrients are sufficiently available. Many premenopausal women have subclinical iron deficiency. Here again, any shortfall can be addressed with a multivitamin and mineral supplement that contains iron.

The issue of osteoporosis becomes a clinical issue in many postmenopausal women. However, the evidence for benefit from calcium supplementation remains weak. Certainly, women who do not drink milk or consume any dairy products, as well those who consume a lot of cola, may benefit from supplemental calcium. Clinicians may want to advise these women of the inconclusive information about calcium supplementation so they do not have unrealistic expectations for improved bone health based only on calcium supplementation. These women should be advised of the known benefits from regular walking and weight training as well as mounting data that support the need for supplemental vitamin D. Even a good diet is unlikely to provide enough vitamin D, and this is one nutrient that clinicians should consider recommending to women as a single supplement, particularly if they live in the northern United States, where exposure to sunlight prevents adequate formation of vitamin D, or if they are African American.

How do the results from the NIH consensus conference compare with findings from the Nurses Health Study?

In terms of multivitamin and mineral supplementation to reduce cancer risk, the strongest evidence seems to support a relationship between folic acid (being more critical before broad food fortification began) and reduced risk of colon cancer. Also, cereal fortification has improved folate levels, often addressing the issue of deficiency, but intakes are still not optimal. Therefore, the existing data support the value of recommending a daily multivitamin that contains the recommended dietary intake for folate, especially for women of childbearing potential. Every individual may not benefit from the added folate in a multivitamin supplement, but as there is no way to determine those who need it most and given

that no harm will come to those for whom there is no benefit, clinicians can comfortably extend the recommendation to all. Exceptions would include patients who are undergoing chemotherapy and those who are taking certain medications with known vitamin interactions. For otherwise healthy individuals, however, taking a multivitamin and mineral supplement is a reasonable option.

There has been significant attention to the role of diet as a potentially modifiable risk factor for breast cancer. Dietary factors that have been studied include fat intake, fruit and vegetable consumption, antioxidant vitamins (vitamins A, C, E, and beta-carotene), serum antioxidants, carbohydrate intake, glycemic index and glycemic load, dairy consumption (including vitamin D), consumption of soy products and isoflavones, green tea, heterocyclic amines, and red meat. The only dietary factors that appear to increase risk are alcohol intake, overweight, and red meat. There is no apparent association between single vitamins and breast cancer. Also, suggestive evidence points to folate as lessening the risk associated with alcohol intake.

Conflicting reports persist about primary prevention from multivitamin vs. single nutrients for chronic disease prevention. What does the best available evidence suggest with regard to such women's health issues as cancer, Alzheimer's disease, and other chronic conditions?

The data are not conclusive in regard to prevention of Alzheimer's disease. There is some evidence suggesting that low folate levels may be a problem and that antioxidants may have some benefit, making these associations worth studying. However, the strength of the evidence does not support a likely benefit from supplementation with a multivitamin. Because folate and antioxidant vitamins have no evidence for material toxicity, there is not a safety issue in taking a folate supplement or one containing antioxidant vitamins, provided the upper limits for recommended levels are heeded and with the recognition that the data are meager.

There are always stories arising about the protective benefit against cancer of certain dietary nutrients. However, there are data to suggest that a multivitamin and mineral supplement or

high dose single supplements may stimulate growth of a tumor that is already present. Regarding cancer, clinicians are cautioned to avoid automatically recommending multivitamin supplementation because the result may be more harmful than helpful, as cancer cells also need nutrients.

The benefit of omega-3 supplementation seems to have taken center stage in promising a protective effect against the progression of atherosclerosis. Is there a similar benefit gained by taking supplemental vitamins and minerals?

The data on vitamin E are ambiguous. There may be some evidence in favor of folate and vitamin B₆, but other approaches are more strongly beneficial. Because there are proven and effective therapeutic approaches ranging from type and amount of dietary fat and beneficial effects from moderate alcohol consumption, physical activity, and weight management, there is really no strong evidence for micronutrient supplementation to affect disease risk for cardiovascular disease and diabetes.

Calcium and vitamin D have long been touted as necessary for bone health. What can you tell us about the newest vitamin, vitamin K, to enter the discussion?

There is pretty good evidence to support the need for adequate vitamin K in addition to the solid data on vitamin D, but women are still advised to eat green leafy vegetables and to supplement their diet with a multivitamin.

Is there sufficient evidence to recommend micronutrient supplementation to reduce risk for or progression of eye-related disease, such as macular degeneration and cataracts?

A randomized trial was conducted with antioxidant vitamins and zinc that indicated a potential beneficial effect in slowing progression of macular degeneration. At present, women with intermediate macular degeneration may consider supplementing their diet with antioxidant vitamins (C and E). B vitamins and selenium have been linked to a reduced risk of cataract, and vitamin C appears to play a protective role in cataract prevention. There is no evidence to date,

however, that earlier use provides substantial benefit.

There has been a particular interest in the use of multivitamin supplementation in women who are HIV-positive. Are the results favorable enough to warrant a public health recommendation in favor of a multivitamin supplementation in this vulnerable population?

A recently published African study showed a delayed need for medication/retroviral therapy in HIV-positive women who took a multivitamin supplement. Vitamin supplementation given during pregnancy and postpartum caused significant improvements in the hematological status among HIV-infected women and their children, providing further support for the value of multivitamin supplementation.

In what ways might cigarette smoking or oral contraceptives affect supplement needs?

Women who smoke and take beta carotene were shown to have a higher risk of lung cancer. In women who smoke, it is clear that clinicians should focus on getting the patient to quit before any other health intervention is considered. The serum levels of B vitamins tend to be lower in women taking oral contraceptives; hence, a multivitamin supplement would be advisable for these women.

Another antioxidant, selenium, has been shown to reduce some forms of cancer—lung, colorectal, and nonmelanoma skin—as well as to lower the mortality rate in a small, randomized trial. In addition, observational studies suggest that heart disease, Crohn's disease, bariatric surgery patients, and thyroid disease are lowest among those women with the highest intakes of selenium, although it is premature to recommend selenium supplementation.

REFERENCES

Dwyer J, Picciano M, Raiten D, Members of the Steering Committee. National Health and Nutrition Examination Survey. Collection of food and dietary supplement

intake data: What we eat in America—NHANES. *J Nutr* 2003;133:590S.

- Fairfield K, Fletcher R. Vitamins for chronic disease prevention in adults: Scientific review. *JAMA* 2002;287:3116.
- Fawzi W, Msamanga G, Kupka R, et al. Multivitamin supplementation improves hematologic status in HIV-infected women and their children in Tanzania. *Am J Clin Nutr* 2007;85:1335.
- Goggs R, Vaughan-Thomas A, Clegg P, et al. Nutritional therapies for degenerative joint diseases: A critical review *Crit Rev Food Sci Nutr* 2005;45:145.
- Huang HBC, Chang S, Alberg A, Semba R. NIH State-of-the-Science Panel. National Institutes of Health State-of-the-Science Conference Statement: Multivitamin/mineral supplements and chronic disease prevention. *Ann Intern Med* 2006;145:372.
- Juhasz-Pocsine K, Rudnicki SA, Archer RL, Harik SI. Neurologic complications of gastric bypass surgery for morbid obesity. *Neurology* 2007;68:1843.
- McBee W, Lindblad A, Ferris FR. Who should receive oral supplement treatment for age-related macular degeneration? *Curr Opin Ophthalmol* 2003;14:159.
- Moreira PI, Zhu X, Nunomura A, Smith MA, Perry G. Therapeutic options in Alzheimer's disease. *Expert Rev Neurother* 2006;6:897.
- Neuman MI, Willett WC, Curhan GC. Vitamin and micronutrient intake and the risk of community-acquired pneumonia in U.S. women. *Am J Med* 2007;120:330.
- Nieves J. Osteoporosis: The role of micronutrients. *Am J Clin Nutr* 2005;81:1232S.
- Otten JJ, Hellwig JP, Meyers LD, eds. Dietary reference intakes: The essential guide to nutrient requirements. Washington, DC: National Academies Press, 2006.
- Reichrath J, Lehmann B, Carlberg C, Varani J, Zouboulis CC. Vitamins as hormones. *Horm Metab Res* 2007;39:71.
- Schachter M, Raziell A, Strassburger D, Rotem C, Ron-El R, Friedler S. Prospective, randomized trial of metformin and vitamins for the reduction of plasma homocysteine in insulin-resistant polycystic ovary syndrome. *Fertil Steril* [Epub ahead of print], March 3, 2007.
- Young A, Johnson S, Steffens D, Doraiswamy P. Coenzyme Q10: A review of its promise as a neuroprotectant. *CNS Spectr* 2007;12:62.

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