work in the area of nutrition are specialized in nutrition support of critically ill patients, or are directed to the care of a patient with a specific disease state—such as bone marrow or liver transplant, renal disease, or burns. In this case a specialty certification in nutrition support such as that being developed by the American Society for Parenteral and Enteral Nutrition might be appropriate.

Finally, until reimbursement for nutrition services provided by a registered dietitian is part of the standard coverage from third party payers, government agencies, and managed care organizations, emphasizing the importance of integrating nutrition care throughout the life cycle and disease process to these payers is more important than another certification. Incidentally, I am both a PhD and an RD.

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Alfalfa, vitamin E, and autoimmune disorders

Dear Sir:

Montanaro and Bardana (1) have reviewed the literature concerning dietary amino acid–induced systemic lupus erythematosus, and it appears that substantial dietary intake of alfalfa seeds or sprouts may produce lupus and lupus-like symptoms in humans and monkeys, respectively. A nonprotein amino acid, L-canavanine, present naturally in alfalfa seeds and sprouts at a concentration of 1.5% dry wt, is thought to be responsible for the autoimmune effects. It has been suggested that patients with autoimmune disease avoid large ingestions of alfalfa seeds and sprouts.

The connection between canavanine-containing alfalfa seeds and lupus understandably led to the question of whether alfalfa supplements, composed of alfalfa plant cuttings rather than seeds, might also be a rich source of canavanine. Indeed, two early reports in the literature suggested this was true (2, 3). However, randomly selected samples of our alfalfa plant–based tablets, sent to four different independent laboratories that routinely assay for amino acids, tested negative for canavanine in all cases, with a limit of detection of 5 ppm. A subsequent review of the pre-column derivatization HPLC method used to assay for canavanine in the original reports (2, 3) indicated that the amino acid alanine was mistakenly identified as canavanine. Cation-exchange chromatographic separation of amino acids by postcolumn derivatization affords better resolution of individual amino acids, and was used for the independent analyses. Verification of peak identity was confirmed by mass spectrometry.

In view of these facts, we were surprised by the suggestion of Victor Herbert in a recent letter to this journal (4) that alfalfa tablets might be a factor in autoimmune disease in his patients. In fact, when first contacted by Herbert on this subject, we promptly responded in writing that our product had repeatedly tested negative for canavanine in the past, and offered to test a sample of the specific products used by his patients. This analysis for canavanine also proved negative. These findings were communicated to Herbert in a letter dated August 18, 1994.

Given these events, the purpose of Herbert's letter to the editor is unclear. If alfalfa tablets were a possible factor in autoimmune disease, Herbert's case report fails to address any of the criteria normally required to establish a relation between exposure and symptoms or disease. Details such as patient medical histories and symptoms, tests conducted to establish a diagnosis, tablet intake, duration of intake and temporal association with onset of symptoms, resolution of symptoms after patients discontinued their supplements, and potentially confounding dietary, genetic, and environmental factors were not reported.

Herbert also speculated that vitamin E supplements, known to enhance immune activity, might have activated latent autoimmune disease in his patients. The only cited support for this assertion is a letter to the Journal, authored by Herbert himself (5), where he presents no data or analysis, but offers his opinion that elderly people taking megadoses of vitamin E died faster than those taking no supplements—an opinion that contradicts the conclusions of the study's authors (6).

The response of the authors to whom Herbert's letter was directed is appropriate to summarize here (7): *1*) the study of elderly vitamin takers actually found lower-than-expected mortality rates among people consuming a variety of nutrient supplements including vitamin E, *2*) autoimmune diseases are a manifestation of an uncontrolled not enhanced immune response, and *3*) the authors speculated that if the immunostimulant action of vitamin E persists over a long period, supplementation would have a beneficial effect on the health span by reducing the incidence of infectious diseases and other conditions associated with impaired immune responsiveness.

Moreover, the Journal recently published yet another report on the safety (including immune responses) of vitamin E supplementation in healthy older adults (8). Also, a recent preliminary report has shown that long-term (6 mo) administration of vitamin E supplements to young and older adults enhanced immune responsiveness with no adverse effects (9).

In conclusion, careful scrutiny of Herbert's letter, the references cited, and the facts presented indicate that there is no scientific basis for linking supplements of alfalfa tablets or supplementary vitamin E to autoimmune disorders.

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REFERENCES

1. Montanaro A, Bardana EJ Jr. Dietary amino acid-induced systemic lupus erythematosus. Rheum Dis Clin North Am 1991;17:323–32.
2. Roberts JL, Hayashi JA. Exacerbation of SLE associated with alfalfa association. N Engl J Med 1983;308:1361.
3. Weissberger LE, Armstrong MK. Canavanine analysis of alfalfa ex-

tracts by high performance liquid chromatography using pre-column derivatization. J Chromatogr Sci 1984;22:438–40.
4. Herbert V, Kasdan TS. Alfalfa, vitamin E and autoimmune disorders. Am J Clin Nutr 1994;60:639–40.
5. Herbert V. Vitamin E supplementation of elderly people. Am J Clin Nutr 1991;53:976 (letter).
6. Enstrom JE, Pauling L. Mortality among health-conscious elderly Californians. Proc Natl Acad Sci U S A 1982;79:6023–7.
7. Meydani SN, Meydani M, Miller RA, Cannon JG, Rocklin R, Blumberg JB. Reply to V Herbert. Am J Clin Nutr 1991;53:976–7.
8. Meydani SN, Meydani M, Rall LC, Morrow F, Blumberg JB. Assessment of the safety of high-dose, short-term supplementation with vitamin E in healthy older adults. Am J Clin Nutr 1994;60: 704–9.
9. Meydani M, Meydani SN, Leka L, Gong J, Blumberg JB. Effect of long-term vitamin E supplementation on lipid peroxidation and immune response of young and old subjects. FASEB J 1993;7:A415 (abstr).

Reply to J Whittam et al

Dear Sir:

The Shaklee group, Whittam et al, fault us for not providing all the criteria required to establish a causal relation between alfalfa pills, vitamin E, and autoimmune disease in the family we reported. To establish a causal relation requires rechallenge by reinstitution of daily alfalfa pills and vitamin E, which we could not ethically do. They indicate that they wrote me that their alfalfa pills "tested negative for L-canavanine;" in fact they wrote that their alfalfa pills tested "less than 3 to 4 parts per million of L-canavanine." They convey that the only potential immunomodulatory agent in alfalfa pills is L-canavanine. There are > 150 different phytochemicals in alfalfa. As we noted, if L-canavanine is not the culprit, it could be one or more of the other phytochemicals in the alfalfa pills.

They allege that Meydani et al (1) demonstrated the safety of high-dose (800 mg/d), short-term (1 mo), supplementation with vitamin E in healthy older adults. Meydani et al (1) were only able to conclude that ingestion of daily vitamin E supplements for 1 mo is safe for elderly people because they did no before-and-after delineation of prohemorrhagic or increased autoimmune antibody actions of vitamin E. Vitamin E supplements inhibit cell adhesion (2), and are prohemorrhagic via decreasing platelet adhesion (3, 4). They could be expected to harm persons predisposed to easy bleeding, producing in them anything from easy bruising to cerebral hemorrhage (3, 4). Vitamin E supplements are immunostimulatory (4–6), and have the potential, under the right circumstances, to increase autoantibodies and promote expression rather than suppression of autoimmune disorders (4–6): diabetes, thyroid disease, asthma, food allergy, rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, etc (6). Whether vitamin E induces desirable self-tolerance or undesirable increased autoimmune reactivity is a function of a variety of factors only now being explored (7). Antioxidant supplements are promoted as harmless by failing to cite published harms (8, 9). The dosage (quantity × days taken) makes the poison: 200 IU vitamin E/d over a short period of time is prohemorrhagic (10); 50 mg/d over a long time increases hemorrhagic strokes (11).

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REFERENCES

1. Meydani SN, Meydani M, Rall LC, et al. Assessment of the safety of high-dose, short-term supplementation with vitamin E in healthy older adults. Am J Clin Nutr 1994;60:704–9.
2. Martin A, Blumberg JB, Meydani M. Vitamin E (alpha-T) decreases intracellular adhesion molecule (ICAM-1) expression and monocyte adhesion to human aortic endothelial cells. FASEB J 1995;9:A726 (abstr).
3. Herbert V, Shaw S, Jayatilleke E, Stopler-Kasdan T. Most free-radical injury is iron-related: it is promoted by iron, hemin, holoferritin, and vitamin C, and inhibited by desferrioxamine and apoferritin. Stem Cells 1994;12:289–303.
4. Herbert V. The antioxidant supplement myth. Am J Clin Nutr 1994; 60:157–8.
5. Meydani SN. Micronutrients and immune function in the elderly. In: Bendich A, Chandra RK, eds. Micronutrients and immune functions. Vol 587. New York: Ann NY Acad Sci 1990:196–207.
6. Herbert V, Kasdan T. Alfalfa, vitamin E, and autoimmune disorders. Am J Clin Nutr 1994;60:157–8.
7. Dixon FJ. Current understanding of autoimmune disease. Hosp Pract 1995;30:11–2.
8. Barrett SJ, Herbert V. The vitamin pushers: how the "health food" industry is selling America a bill of goods. Amherst, NY: Prometheus Books, 1994.
9. Herbert V. Vitamin C supplements and disease: counterpoint. J Am Coll Nutr 1995;14:112–3.
10. Schalch W. Antioxidants, prooxidants, and their effects. JAMA 1994; 272:1660 (letter).
11. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study Group. The effects of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. N Engl J Med 1994; 330:1029–35.

Alfalfa pills and autoimmune diseases

Dear Sir:

Herbert and Kasdan (1) recently commented on the possible link between ingestion of alfalfa tablets and activation of autoimmune disease in humans, suggesting that the amino acid L-canavanine, known to concentrate in alfalfa seeds and sprouts, might be the culprit.

When considering the toxic potential of plants, it is extremely important to know the part of the plant that is ingested. For example, L-canavanine has been reported to exist only in the seeds of such food plants as peas (*Pisum sativum*) (2), soybeans (*Glycine max*) (2), string beans (*Phaseolus vulgaris*) (2), clover (*Trifolium pratense, P. repens*) (3, 4), and fava beans (*Vicia faba*) (2), as well as in the seeds and sprouts of alfalfa (*Medicago sativa*) and other legumes. However, in these