

Editorial

The Finnish Antioxidant and Lung Cancer Study

The recent report¹ of the study in Finland of vitamin E and beta carotene on the incidence of cancer in male smokers is important, not because of its scientific value, but for the way it was treated in the national press. The news media headlines carried the grim message — vitamins may increase cancer.² This is the message that many of my patients received, and for the next few days I received anxious calls even though my patients are much more sophisticated about vitamins than are the average individuals. They wanted reassurance that it was safe to continue with their vitamin C, or vitamin E and beta carotene. The media did not distinguish between the vitamins. There is a tendency in the public (including physicians) to have a global view of vitamins. If there is bad news about one, it means it is bad for them all. The vitamin critics were given one more opportunity to blast the use of vitamins, and to return to their ancient position that only food was safe and no one needed added vitamins.

But this is not what the dozens of authors of this study concluded. They found that these two antioxidants did not decrease the incidence of lung cancer, and because" there was an increase in risk in the treated group suggested the possibility that it might increase it. It is therefore very important to know exactly what this study did. They used a large population of male smokers ages 50 to 69. One group was given the synthetic d-alpha tocopherol³ equivalent to 50 mg of d-alpha tocopherol. There is 12.5 percent d-alpha tocopherol in the synthetic mixture of eight tocopherols. This means that the total amount of tocopherols includes the levo form which the body cannot use and other isomers not nearly as active as d-alpha. What is the effect of giving this mixture? For many years Orthomolecular physicians have recognized that trans fatty acids are harmful. These are present in hydrogenated fats like margarine. The question is whether levo tocopherols, present in four times greater amounts, are also harmful. Another group was given 20 mg of beta carotene, a third group was on placebo, and the fourth group received both antioxidants. All the subjects smoked five or more

cigarettes daily, mean 20 for over 35 years. They were followed for five to eight years. But the beta carotene group smoked one year more than the no beta carotene group, a difference of three percent. How significant is one year more of heavy smoking in increasing the number of advanced lung cancers? The authors do not discuss this. Smokers have lower vitamin C blood levels. Their vitamin E blood levels are within the normal range but washings from their lungs show they also are 30% lower in vitamin E. What is the effect on beta carotene?

At the end of the study the men in the placebo group with the highest blood levels of these two antioxidants had the lowest incidence of lung cancer. In the d-alpha tocopherol group there was an insignificant 2% reduction in incidence of lung cancer ($P = 0.8$). We do not know what the effect would have been if all the tocopherol had been d-alpha tocopherol, the natural form. In the beta carotene group there was an 18% increase in incidence. Out of 14,560 men on beta carotene, 474 developed cancer, while out of 14,573 men not on beta carotene 402 did. The incidence increased from 2.76% for the control group to 3.26% for the treated group. I suggest that this minor difference is surely not of clinical significance, even though it is statistically significant. In this statistically sophisticated study dividing 3.26 by 2.76, yields the much larger number of 18%, which appears enormous and will be the only figure the unwary reader will remember, and probably the only figure which will be used by the popular press. With large sample sizes such as these, a minor variation becomes fully blown up to a major finding.

There must have been something very odd about that Finnish group of men. For one thing, the authors reported that 34% of the men on beta carotene developed yellow skin. This is totally foreign to my experience. I have started at least 500 subjects on this amount of beta carotene and more, and have never seen any yellowing of the skin with this dose but have seen some with higher doses. Does this mean that these heavy smokers had so compromised their livers that they could not deal even with normal doses of beta carotene?

I will not say much about the minor doses of the synthetic alpha tocopherol. I consider the 50 mg dose equivalent to d-alpha tocopherol given by the much larger total dose of tocopherols almost homeopathic when it comes to preventing and treating cancer.

The authors do point out the many possible factors which might have given them these results, and in an editorial in the same issue the commentators also refer to them. These authors write, "Finally, study findings regarded as showing supplementation to be beneficial or harmful may occur by chance" when referring to the literature. But both in the original paper and in the commentary they still draw the hasty conclusion that these antioxidants might increase the incidence of cancer. There is one comment they did not make, which is simply that if you run statistical trials you can expect that every now and then they will yield spurious results, as did the original double blind controlled studies which showed that l-dopa did not help patients with Parkinsonism, and more recently a large scale study which showed that folic acid did not prevent spina bifida. These last two studies were properly dismissed as anomalous.

Finally, I wish to make clear the significance of the words "may" or "might". For example, one person claims that vitamin C may cause kidney stones. He never has written that it will, nor has he given any probability statistics. Since there are no reported cases proving an association between consumption of vitamin C and kidney stones from the millions of people routinely taking large doses of this vitamin for decades, the probability is infinitesimally small. One can say with complete accuracy that vitamin C may cause kidney stones, but that the probability that it will do so is zero or close to it. However, those who claim that vitamin C may cause stones always leave out the second part of the statement, and by so doing perpetrate lies and misinform the public.

I consider that this study simply proved nothing, except that if you give tiny doses of vitamin E nothing will happen, and if you give heavy chronic smokers 20 mg of beta carotene their incidence of lung cancer will not change. I suspect that the authors of this study were disappointed with the negative results they eventually saw and tried to salvage something so that the paper could be published. Or else it might have made it easier to have it published by the

New England Journal of Medicine, which traditionally finds it easier to publish negative reports when large doses of vitamins are used.

Cancer is probably present and undetectable in patients for a long time, perhaps several years, before it is finally discovered. The truly preventive study should therefore start long before any tumors have formed, which could mean many years. With this group of heavy smokers it is certain that a large fraction already had the cancer. This was therefore a mixed study: (1) treatment for those already with cancer, (2) prevention for those who did not have any. Unfortunately, it will never be possible to say how much each group contributed.

I would suggest that future studies start with a much younger population in whom there is much less chance of already having cancer.

Notes

1. Heinonen OP & the Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group: The Effect of Vitamin E and Beta Carotene on the Incidence of Lung Cancer and Other Cancers in Male Smokers. *New England J. of Med.* 330:1029-1035, 1994.
2. "Vitamin Supplements are Seen as No Guard Against Diseases" and later "Study Sees No Benefit in Vitamins on Cancer or Heart Disease". *New York Times*, April 14, 1994.
3. Dl-alpha tocopherol is a mixture of eight isomers in equal proportions containing only 12.5% of d-alpha tocopherol. One mg of the natural form is equal to 1.49 IU while one mg of the dl form is only equivalent to 1.0 IU One mg of dl-alpha tocopherol has the lowest vitamin E equivalence of any of the common vitamin E preparations.

Nova Scotia - First Canadian Province to Recognize Freedom of Choice in Health Care

In this Journal (Vol. 8, number 2, pp. 67-68, 1993), I discussed the action of USA in providing their citizens with freedom of choice in selecting and working with physicians. In Alaska, the first state, it is illegal for any professional body controlling the practise of medicine to prevent a physician from practising medicine, unless those practices are harmful to the patient. I know two excellent Orthomolecular physicians who have moved or will move to Alaska, because of the

freedom this gives them to practise good medicine. This is a great gain for Alaska and a tremendous loss to the states which have driven them out.

In Canada, Nova Scotia is the first province to take similar action. Last year Drs. William LaValley and David Baker were charged with practising homeopathy and electro-acupuncture. Dr. LaValley fought back and helped organize the Citizens for Choice in Health Care. This group demanded that the Minister of Health investigate the actions and procedures of the paying body, the MSI. The minister stated that his department would not be involved in decisions as to whether a particular procedure or type of therapy was appropriate. The MSI apologized. With this decision there was a change of attitude toward alternative medicine. Seventeen physicians appeared before the Board of the Medical Society. After that the board by a vote of 28 to 4 passed a resolution that alternative practitioners be granted a subsection in the provincial Medical Society Act. Said Dr. LaValley, "Alternative practitioners are now recognized by law in Nova Scotia. Ratification to change the Medical Act will happen in May."

Symposium¹ Sponsored by the Linus Pauling Institute of Science and Medicine, September 29 to October 1, 1994

Professor Linus Pauling and many years later the Linus Pauling Institute of Science and Medicine, have been in the forefront of modern medicine. With his discovery of the structure of the hemoglobin molecule in sickle cell anemia, he opened up what he called molecular medicine. Flat, two-dimensional molecules became living three dimensional molecules. These have become one of the bases of modern medicine. Only within the past five years has medicine begun to recognize the importance of working with molecules familiar in nature, which can react with the living molecules that compose nature. Pauling's work with molecules made him sensitive to the use of large doses of nutrients for diseases not considered to be nutrient deficiency diseases. Of these, the first was vitamin C.

Fortunately Linus Pauling does not work by consensus, although consensus does come about many years after. In the preface to

"Molecules in Natural Science and Medicine. An Enconium for Linus Pauling", Maksic, Z.B. and Eckert-Maksic, M.² write, "Some of his predictions were controversial; but as somebody nicely put it, it is generally true that 'the mainstream converges with Pauling's opinion twenty years later'." In 1968 Pauling³ shared with the scientific world his conclusions why large doses of certain nutrients would be therapeutic for some diseases. This report inevitably altered the science and practice of medicine, even though it required twenty years before this became apparent. Over the past five years there have been many symposia and meetings to which scientists interested in Orthomolecular medicine have made major contributions. These meetings have dealt with topics as diverse as the treatment of schizophrenia to the treatment of cancers.

Today, physicians, biochemists, and nutritionists are caught in a major paradigm shift, which had its first beginning in 1955 when it was reported that niacin in 3 gram doses lowered cholesterol levels. Until then the vitamin deficiency paradigm was the only one acceptable. Vitamins were needed only to prevent vitamin deficiency diseases such as scurvy and pellagra. The present paradigm, rapidly gaining strength, holds that for many people and for many diseases, these nutrients must be used in optimum doses, which may have to be very large or mega doses.

The single major impetus in this shift from one paradigm to the other was the work of Linus Pauling. He really became involved at around age 65 when most workers are thinking of retiring. But Pauling was impressed by the importance of his conclusions and the vast importance to science of his work. With great courage, charisma, and his dedication to hard work, he has forced science and medicine to pay attention. The fact that vitamin C is becoming one of the major factors in the treatment of the cancers is due almost entirely to Linus Pauling and the support he gave to physicians such as Ewan Cameron.

This symposium recognizes the work of Dr. Linus Pauling and of his Institute, which is in the forefront in the examination of the utility of vitamins in modern medicine. Vitamin C is the major water soluble antioxidant in the body but there are other antioxidants such as vitamin E, glutathione, selenium. It is there-

fore logical to broaden the field of inquiry to include the whole field of free radicals, their role in the cause of disease, and the use of the antioxidants in the prevention and treatment of a large variety of conditions ranging from schizophrenia, to cancer, to the ravages of aging.

The discussions will cover the mechanisms of free radical formation, their biological role and the antioxidants and their function. The major part of the symposium will consider the health benefits of the antioxidants with special attention to cardiovascular disease, to HIV/ AIDS and to cancer. A distinguished group of scientists will make these presentations. Physicians, medical scientists will find this meeting extraordinarily helpful, not only for their present practice of medical science but also in learning the future of medicine, for what they will hear at this meeting will issue from our medical schools many years later. Dr. Aleksandra Niedzwiecki, Chair of the Symposium Committee writes, "Both epidemiological data and scientific evidence increasingly support the significance of antioxidants in health and disease. The purpose of our meeting is to emphasize molecular and

mechanistic aspects of free radical and antioxidant production and action in biological systems, with practical implications for human health."

References

1. Tiburon Lodge, California (on San Francisco Bay). For more information contact A. Niedzwiecki, Ph.D., Chair, Symposium Planning Committee, Linus Pauling Institute, 400 Page Mill Road, Palo Alto, CA 94306-2025. Tel. (415) 327-4064; Fax (415) 327-8564.
2. Maksic, Z.B. and Eckert-Maksic, M. *Molecules in Natural Science and Medicine. An Enconium for Linus Pauling.* Ellis Horwood Ltd., Market Cross House, Cooper Street, Chichester, West Sussex, England, 1991.
3. Pauling L. *Orthomolecular Psychiatry. Science* 160: 265-271, 1968.

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