

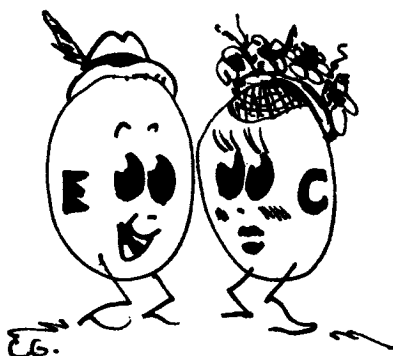
II. A VITAMIN E SCARE

In Part I of the vitamin E story (*Felix Letter* #9), I examined Dr. Hyman Roberts' speculation that, besides a whole spectrum of unpleasant side-effects, self-administration of large doses of the vitamin may have "caused or aggravated" 80 cases of thrombophlebitis (blood clots and inflammation in deep veins of the legs) that he had personally observed in patients over a span of about 12 years. A number had also developed pulmonary embolism (blood clots in arteries of the lungs), and both ailments can be serious indeed. The *Journal of the American Medical Association (JAMA)* had seen fit to give his views special prominence in its "Commentary" section July 10, 1981.

As noted in the August *Felix Letter*, a leading researcher had told me that "in almost hundreds of clinical trials" over the years using megadoses of vitamin E, they had never seen thrombophlebitis, pulmonary embolism, or any serious ailment develop. As to the long list of side effects tallied by Dr. Roberts, he said, "If you look at enough people, you're going to get things like headaches, muscular fatigue, and so on, but the numbers we have seen are no different from a control [placebo or untreated] population." Dr. Marvin Bierenbaum, a cardiologist, was also quoted as being "mystified" by Dr. Roberts' experiences, because two recent studies he conducted using megadoses of vitamin E for three months in one group, and for 8 months together with megadoses of vitamin C in another, showed none of the adverse effects described by Dr. Roberts. In the 3-month experiment (on 25 diabetic subjects), 2000 IU (International Units) per day brought about helpful reductions in both blood sugar and blood pressure levels. The 8-month study in a different group showed improvement in peripheral circulation (blood flow to legs, feet, hands, etc.). Both researchers felt strongly that evidence presented by Dr. Roberts was

very fragile and in no sense represented results of controlled trials.

To date, the major experimenters using large amounts of E on human subjects have found nothing to warrant Dr. Roberts' warning regarding thrombophlebitis and pulmonary embolism. Some have noted a lowering of thyroid hormone levels, but others have seen no depression of thyroid function or any other serious abnormalities from long-term use of high doses. The only clear caution is that in heart patients given medication to decrease blood clot formation, megadoses of vitamin E can exaggerate the effect to such an extent that small hemorrhages may occur. This, of course, is related to the vitamin's effectiveness in *preventing* abnormal blood clots, not, as Dr. Roberts suggests, causing them.



Some Caution Needed

The observation was made in the August *Letter* and bears repeating that in cases of rheumatic heart disease or high blood pressure, vitamin E supplementation has to be instituted very slowly to prevent an initial rise in blood pressure. Persons suffering from diabetes and heart diseases should take the vitamin under medical supervision. BUT . . . the potential benefit to such patients may be considerable and it is hoped their physicians are of the grow-

ing number who find vitamin E (and other nutritional adjuncts) a useful therapeutic tool.

Dr. Roberts, an internist and angiologist, author of textbooks and many professional papers, is one of the medical fraternity who is not amused by the growing practise of self-help with vitamins guided largely by popular literature or word of mouth, and he has an undeniable right to sound off.

Mountains from Molehills

No, the *real* significance of Dr. Roberts' observations is the pre-eminence they were given by *JAMA*. One of the most prestigious and widely read medical journals in the world chose to present his tenuous anecdotal material as if it were gospel. Two tables listed a staggering number of clinical disorders and "laboratory abnormalities induced by vitamin E." When I chased down the references, the ominous picture shriveled to peanut size, and the dangers shrank to the few that I have noted in both issues of the *Letter*. Vitamin E is potent stuff when taken in huge amounts and it behooves all of us, health workers and laymen alike, to use it with respect and caution. However, Dr. Roberts' case for a connection with thrombophlebitis is a frail one, since he himself indicated in both his 1978 letter to *Lancet* and his 1979 paper published in *Angiology* that the majority of the 80 patients had the kinds of serious disorders that would predispose them to small-vessel disease and thrombosis. The danger would increase, he noted, if estrogens were being taken, and about 26% had received estrogen prior to presenting themselves to him with symptoms of thrombophlebitis.

I noted wryly that the 1981 *JAMA* "Commentary" by Dr. Roberts made no mention of this essential extenuating information from his earlier articles.

Gospel According to AMA

We simply cannot underestimate the power of journals like *JAMA* to affect the therapeutic climate. A number of science publications soon picked up on *JAMA*'s warnings without, of course, examining the references; and the long list of anecdotal ailments quickly became clinical "facts." Six months ago, a nurse friend told me seriously about the "new dangers" of vitamin E. The word has spread and continues to do so.

Although many of its members do not concur, the A.M.A. continues its policy of ignoring, minimizing, or maligning the value of therapeutic nutrient supplementation (except in rare ailments where absorption is known to be severely impaired, as in cystic fibrosis). In the same vein, because its priorities lie elsewhere, medical orthodoxy has lagged far behind the exploding knowledge in nutrition. Because of long hours in medical libraries, I regularly ate in the cafeterias of two major medical schools during my recent years as a reentry student. When you've seen a huge dining-roomful of doctors, nurses, interns, dietitians, and medical students, day after day, placidly eating without protest the gray-gravied, vulcanized slop on their plates — in communities where outstanding advances have taken place in other public eating facilities — you will have witnessed something of the vast detachment that medicine has towards the whole subject of nutrition, let alone towards nutrition as a preventive and healing force. It helps also to explain why hospital food is often indistinguishable from prison fare.

Nevertheless, work on vitamin E continues, generating international conferences and a great volume of scientific papers. It also has created a cautious optimism in the field. The chances of getting it in the professional neck for intemperate manifestations of enthusiasm are well known, but a lot of the researchers have become sub rosa poppers of vitamin E pills. Some of them are sore that *JAMA* and other journals, while continuing to assert that scores of controlled trials do not constitute convincing evidence for the vitamin's worth, nevertheless find Dr. Roberts' loosely-based warnings on its dangers sufficiently sound to warrant a "Stop the presses" approach. "I know

of at least four or five investigators who wrote responses criticizing the *JAMA* article," a researcher told me, "but the other journals decided they didn't want to get involved in the controversy and refused to publish them."



Protecting the Cell

As molecules go, vitamin E is a fairly small and simple one to have stirred up the stormy disputes in its wake. Most vitamins function solely as catalysts ("coenzymes"), allowing metabolic processes to take place. Vitamin E has no known coenzyme function. It appears instead to be involved in cell structure as part of membranes that envelop each cell of the body and each of the tiny functioning units within the cell called "organelles." One hypothesis with which many researchers are comfortable is that molecules of vitamin E exist in a certain ratio to the molecules of unsaturated fatty acid that are the major component of all cell and organelle membranes. The vitamin is there to protect its neighboring molecules from the rancidity and oxidation to which unsaturated fatty acids are especially prone, in or out of the body.

This protection permits the integrity of the membranes to be maintained and therefore that of the cell as a whole.

When vitamins are not involved in structure, deficiencies are more readily produced. For example, depletion of vitamin B₁ (thiamin) in laboratory animals causes severe, predictable symptoms and finally death unless the

vitamin is supplied. Tragic circumstances of deprivation — not experimental conditions — showed that the corollary in man is a terrible disease called beri-beri. With vitamin E, a deficiency in human beings — with or without dramatic symptoms — is difficult to demonstrate.

In contrast to humans, deficiency of the vitamin in both experimental and farm animals leads to a great number of unequivocal symptoms, including a form of muscular dystrophy (white muscle disease) in calves, lambs, and pigs. In a variety of animals, extensive damage to heart muscles takes place and small blood vessels become so fragile that plasma leaks out into the tissues. A fatal condition of the brain in baby chicks (encephalomalacia) happens after only three weeks of vitamin E deprivation. Izaak Molenaar, M.D., and coworkers from the Netherlands, in the excellent compilation *Vitamin E, A Comprehensive Treatise*, edited by Lawrence J. Machlin, Ph.D. (1980), state:

The specific changes in membrane structure and function will be dependent upon the kind of membrane which is affected most. We think that this is probably the reason why in vitamin E deficiency there is such a large variety of macroscopical and microscopical lesions in different organs of the same animal and in the different species — not because of intricate molecular events but because tocopherol [vitamin E] is located in all, or nearly all cellular membranes, all of which differ in composition and function, leading to unspecific or at least nonvitamin E-specific pathological manifestations . . . It is known that among the very susceptible tissues are testis, liver, and adrenal cortex.



The short life span of experimental animals permits a visible acceleration of the destructive processes initiated by the vitamin lack, but it is not illogical to infer that, at a slower pace, parallel forms of damage may be taking place in vitamin E-deprived human beings.

Human Deficiency: Yes or No?

Much of the rancor and contention in the scientific community arises at this point. One group maintains that, except in certain premature infants and in diseases of malabsorption, vitamin E deficiency simply does not exist in man; hence attributing to it a wide spectrum of ailments is untenable. This is the more widely held view among nutrition and medical policy setters. The "hard" evidence that they demand of vitamin E's effectiveness in ameliorating various conditions appears to be never hard enough to satisfy them. A substantial group of researchers and clinicians, on the other hand, believes that human deficiencies of the vitamin are not only plausible but widespread, and that the degree and extent of the symptoms depend on the kinds of tissues whose membranes have suffered the most damage.

Below are some of vitamin E's major therapeutic roles.

Benefits of supplementation well accepted by conservative medicine:

- Preventing and curing hemolytic anemia in premature babies.
- Treatment of deficiencies caused by malabsorption of fats, as in cystic fibrosis and liver cirrhosis.
- Improvement in peripheral vascular disease with intermittent claudication (pain in calf of the leg when walking caused by insufficient oxygen due to plaque and narrowing in the arteries). Believed similar to chest pains upon exertion when there is insufficient O₂ to the heart (angina pectoris).
- Prevention of chronic lung disease (pulmonary dysplasia) in newborn babies treated with oxygen via mechanical ventilation for severe respiratory distress.
- Prevention of retrolental fibroplasia: damage by high O₂ atmosphere to the eyes of premature infants often leading to blindness.
- Use in burn units of some hospitals because of anti-inflammatory effect and reduction of scar tissue.

Some additional benefits of supplementation. Indicated by experimental trials but needing further verifying studies:

- Reduced platelet aggregation. (Abnormal clumping of blood platelets is a factor in blood clots leading to thrombophlebitis, stroke, or heart attack.)

- Prevention of embolisms (obstructive blood clots) after surgery.
- Improvement in chronic cystic mastitis ("lumpy breast" disease).
- Decrease by over 40% in damaged (sickled) red blood cells in sickle cell anemia patients.
- In animal studies, stimulates antibody formation and resistance to bacteria.
- In humans, ninety percent reduction in mutagenic activity in feces — an indication that vitamin E by reducing harmful nitrosamine formation may help to prevent cancer of the bowel.
- May help women who habitually miscarry to maintain full term pregnancy. Recent evidence that some miscarriages and stillbirths are associated with unexpected decreases in blood levels of the vitamin late in gestation.
- Enhancement of activity of enzyme systems which detoxify harmful substances in our liver.
- Animal and cell studies showing supplementation makes animals less susceptible to tissue damage from smog, radiation, and cigarette smoke.
- Possibility that vitamin E may increase HDL-cholesterol carriers in blood, a strong protective factor against heart disease.
- Indications that vitamin E is needed for normal prostacyclin production in arteries. Prostacyclin is a natural hormonelike substance that dilates arteries and keeps blood platelets from clumping.
- In a new study presented by Fitzgerald and Brash at the latest N.Y. Academy of Sciences conference on vitamin E, huge doses given to normal subjects suppressed production of a substance (thromboxane) that causes blood platelets to clump and arteries to constrict, but not of prostacyclin. Too much thromboxane and not enough prostacyclin are thought to be a factor in heart attacks and strokes. Aspirin suppresses both thromboxane and prostacyclin.

Vitamin E's relationship to prostacyclin synthesis may be a long sought key to the vitamin's reputed usefulness in preventing or ameliorating heart and artery disease. I spoke by telephone with one of the major researchers in the field, Dr. Lawrence J. Machlin, who said:

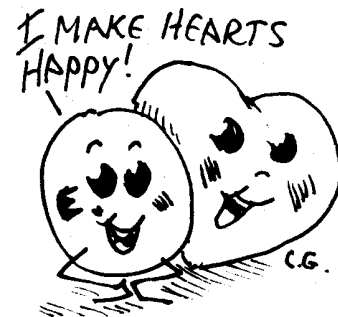
The prostacyclin hypothesis is a very attractive one. There is a reasonable body of animal work supporting the idea that in the absence of vitamin E you would get a decrease in prostacyclin production. Unfortunately, the only way you can get the clinical data that you need [on humans] is to run trials that run for ten years and cost five million dollars.

This, of course, is how it is in the world of nutrition research — why clearcut answers to our questions are so slow in forthcoming and controversies so seldom resolved. A number of

reasonable scientists feel, for example, that longterm supplementation with vitamin E will protect against cancer and aging. Yet without taking a whole lifetime, how can they come up with the "hard" data needed to verify such subtle and pervasive benefits?

A Little Quackery, Folks!

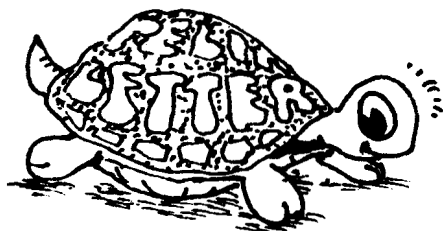
At this point, common sense must take over. A vitamin that keeps our cell membranes intact is going to do a lot to protect us overall. My own subjective observations on the effects of supplementation for over 20 years in family, friends, and myself are these: I've seen very little heart disease and cancer, even in the older folks; vitamin E also appears to provide protection against formation of varicose veins, including hemorrhoids which are varicose veins in the rectal area. I've noticed that it sometimes makes hair grow more thickly — not eliminating male baldness, but filling in thinned areas common in women after pregnancy; and it definitely slows down wrinkling. We could do worse!



Scientists no longer argue about vitamin E's essentiality, only about the amounts needed for health. Dr. Roberts says that anything over 100 to 300 IU is a megadose that may pose dangers. Therapeutic and popular self-help use ranges from 200 to 2000 IU/day. The recommended dietary allowances (RDA's) set by the National Academy of Sciences in 1980 are in milligrams of alpha-tocopherol instead of IU's: 10 mg for men and 8 for women, based on the adequacy of "average" diets. Judging by the modern rise of cancer, diabetes, and heart disease, maybe a not so average diet is needed. Here are two approaches to the business of nourishing ourselves:

AN "AVERAGE" DIET		A PROTECTIVE DIET	
	Milligrams of Vitamin E		MILLIGRAMS OF VITAMIN E CALORIES
Breakfast		Breakfast:	
Cornflakes, 100 grams (g)	0.2	Oatmeal, 100 grams	2. 390
100 grams = 3.5 ounces		Blackberries (wild), 200 g	25 115
Milk, 200 g	0.2	Wheat germ, 4 Tbsp, 24 g	7 90
2 slices white bread, 50 g	1	Whole milk, 1/2 cup, 122 g	0.1 80
Jam	0	Tsp sunflower oil, 4.5 g	3 40
Tbsp butter, 14 g	0.3		
Sugar	0	Lunch	
Bacon, 50 g	0.3	Shrimp, 100 g	3 95
Lunch		Peas, 100 g	3 85
Hamburger:		Spinach, 100 g	3 20
Bun, ground beef, mayonnaise, lettuce and tomato	4.9	Sweet corn, 100 g	5 80
Coca Cola	0	Butter, 1 Tbsp, 14 g	0.3 100
French fried potatoes, 200 g	0.4	3 Apricots, 100 g	0.9 50
Cupcakes, 100 g	2		
Dinner:		Supper:	
Wine, beer, or soft drink	0	Sweet potato, 200 g	9 165
Frozen dinners:		Salad with Avocado, 50 g	1 75
Beef and vegetables, 200 g	1	Parsley, 25 g	0.6 -
Macaroni and cheese, 200 g	0.2	Tomato, 100 g	0.5 20
Apple	0.7	Asparagus, 50 g	1 10
Ice cream	0.3	Cabbage, green outer leaves, 50 g	4 10
TOTAL	11.5	Peanut butter, 2 Tbsp, 32 g	6.4 200
		Whole rye crackers, 13 g	0.8 45
		Mango, 200 g	2 130
		Snacks:	
		Tomato juice, 8 oz., 243 g	1.7 45
		Almonds, 2 oz., 57 g	14 340
		Sunflower seeds, 100 g	52 560
		TOTAL	145.3 2,745 calories

I've stacked the decks by choosing foods loaded with vitamin E. They happen to contain large amounts of the most active form, alpha tocopherol. The best sources are nuts, seeds, and dark green leaves — foods our evolutionary cousins, the primates, enjoy abundantly, and I don't doubt that our early primitive ancestors enjoyed them as well. The great forests covering the continent where man evolved provided for an intake far above the RDA's 10 mg. How much is too much? The last word from science may never arrive. In the interim (our own lifetimes!) a diet



generous in natural amounts plus a protective supplement makes sense. How much a physician or a person chooses will depend on which current literature is the most convincing. I'm hoping that any excess will help to keep dangerous nitrosamines from forming in our colons.

Dr. Max Horwitt, an eminent researcher writing in Dr. Machlin's book, believes that because of vitamin E's protective anti-oxidant function, . . . larger amounts of an antioxidant should protect tissues susceptible to oxidative stress more efficiently than would smaller amounts . . . The kinds of pollutants now found in our atmosphere represent a relatively new phenomenon in human experience. Perhaps it will be necessary to take what most

nutritionists would consider unorthodox action to protect ourselves from this threat to our health — much more work in this field is indicated. ■



Illustrations are by Clay Geerdes.