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Deficiencies of Selenium and Vitamin E Create Dangerous Form of Common Virus

In what may be one of the most significant discoveries in the fields of nutrition and virology, researchers have discovered that a common virus mutates into a deadly strain when it infects a person or animal deficient in selenium and vitamin E.

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Traditionally, infectious disease specialists have considered nutritional deficiencies only in terms of host defenses—that is, whether a poor diet or a lack of vitamins or minerals might interfere with immunity. The new research has the potential to dramatically change the way physicians and researchers view the origin, evolution, and spread of diseases, including influenza (flu), hepatitis, and acquired immunodeficiency syndrome (AIDS).

Melinda Beck, PhD, a virologist at the University of North Carolina at Chapel Hill, and Orville Levander, PhD, a nutritional chemist at the USDA's Agricultural Research Service, Beltsville, Md., have described how a "host" deficiency of either selenium or vitamin E permanently turn a relatively benign strain of the coxsackievirus into a deadly, rapidly reproducing form of the virus. (See Beck MA, Journal of Medical Virology, 1994;43:66-70 and Journal of Nutrition, 1994;124:345-58.)

Some 20 million people in the United States are infected each year by coxsackieviruses. Only two million of these infections actually result in illness, usually no more serious than a common cold, sore throat, or diarrhea. The coxsackievirus mutation, however, inflames heart muscle, leading to cardiomyopathy and heart failure.

From a scientific standpoint, Beck and Levander's most recent study is especially significant because it describes the specific genetic changes that occur when the virus changes from benign to virulent in a seleniumdeficient host.

According to their report in Nature Medicine (May 1995;1:433-6), a recent spinoff of the prestigious British journal Nature, the researchers fed mice either selenium-deficient or selenium-adequate diets. Four weeks later, they injected all of the mice with the coxsackievirus. After another week, they began studying the mice and the descendants of the original coxsackievirus strain.

The mice on selenium-deficient diets displayed clear signs of heart inflammation, the most deadly consequence of a coxsakievirus infection. Beck and Levander found that the virus in all of the seleniumdeficient mice had become virulent, whereas the virus in all of the other mice had remained benign and caused no serious effects.

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By comparing the genetic structure of the benign "parent" coxsackievirus to that of its virulent descendants, Beck and Levander pinpointed six specific changes in the nucleotides, or genetic structure, of the virulent coxsackievirus. Although it's not yet clear whether one or all of these genetic changes triggered the more aggressive virus, the genetic evidence provides the proof needed to unequivocally link a host's selenium deficiency with a more dangerous form of the coxsackievirus.

Furthermore, even though the study was conducted on coxsackievirus infections of mice, the findings have direct implications in Continued on page 4

Vitamin E, Zinc Protect Against Melanoma

This being the peak of summer, it's worthwhile reporting a Washington state epidemiological study on the relationship between diet and melanoma. While most skin cancers, if detected early, are easily treatable through conventional means, melanomas can be deadly.

Constance S. Kirkpatrick, PhD, an epidemiologist at the University of Washington, analyzed 16 nutrients from the diets of 234 melanoma patients and 248 patients without the disease. Only vitamin E in the diet was inversely related to the risk of melanoma, according to Kirkpatrick's report in the American Journal of Epidemiology (1994;139:869-80). When she combined nutrient intake from both diet and supplements, zinc emerged as the single nutrient most associated with a low risk of melanoma.

In addition, obese people were more likely to develop melanomas than thin people.

"These results provide limited support for the hypothesis that antioxidants such as vitamin E or cofactors in protection from oxidative damage such as zinc may be protective for melanoma, and they suggest that obesity should be measured in future studies of melanoma," Kirkpatrick wrote.

Another Vitamin C Analysis: It Eases Symptoms and Shortens the Length of Common Colds

Much of the skepticism surrounding the use of vitamin C in treating common colds derives from a 20-year-old meta-analysis of seven vitamin studies. This analysis by Thomas Chalmers, MD, reported that supplemental vitamin C had few if any benefits. (See Chalmers, T., American Journal of Medicine, 1975;58:532-6). Many physicians have assumed that Chalmers' study contradicted the benefits Nobel laureate Linus Pauling, PhD, reported in an earlier meta analysis, and Chalmers' study has been cited twice as often as Pauling's in the medical literature.

Even though almost 21 studies since 1971 have confirmed the benefits of high-dose vitamin C in the common cold, medicine has been less than enthusiastic in recommending it. So Harri Hemilä, PhD, of the University of Helsinki, Finland, re-analyzed Chalmers' original data. He found that Chalmers' analysis contained serious errors and omissions of data. And using all the original data Chalmers had, Hemilä calculated that large doses of vitamin C did reduce the severity of symptoms and the length of common cold infections.

"Chalmers' review of vitamin C and the common cold has been a cornerstone for the belief that the vitamin has no significant effects in reducing the severity of the common cold. The review has been used in several monographs as the basis for the conclusion that vitamin C is worthless for the treatment of the common cold," Hemilä wrote in the *Journal of the American College of Nutrition* (April 1995;14:116-123.)

Hemilä found numerous "erroneous and misleading numerical values" in Chalmers' analysis. But, points out Hemilä, Chalmers did not take into account what may be the most important variable: the amount of vitamin C given to subjects. Whereas Pauling had looked at studies in which people were given at least 1 gram (1,000 mg) of vitamin C daily, Chalmers included studies in which as little as 250 mg were given. "Studies using at least 1 gram/day of vitamin C show quite a consistent benefit, whereas studies with smaller doses show less consistent results."

The greatest amelioration of common cold symptoms occurred in people taking 2 to 6 grams of vitamin C daily, and the majority of studies on vitamin C and the common cold "consistently and persuasively support the conclusion that vitamin C supplementation alleviates the symptoms of the common cold," Hemilä added. It's an easy and inexpensive way, he observed, to reduce the most common cause of absenteeism from work and school.

In the same issue of the *Journal of the American College of Nutrition* (April 1995,14:124-136), Adrianne Bendich, PhD, FACN, a researcher at Hoffman La-Roche Inc., reviewed the medical literature describing the health benefits of vitamin C with respect to the prevention of cancer, cardiovascular disease, and cataracts. The evidence overwhelmingly points to the value of vitamin C in maintaining health and preventing these diseases. "The associations between high intake of vitamin C (and other antioxidant vitamins) and lowered disease risk are at least as strong as associations with established risk factors such as dietary fat intake," Bendich wrote.

She noted that the most recent survey of nutrient intake in the United States "found that the median vitamin C intakes were 73 mg/day for men and 66 mg/day for women." The median number, of course, is the midpoint, meaning that half the people consumed more and half consumed less. (The RDA for vitamin C is 60 mg.) In fact, 25 percent of the people surveyed ate only 39 mg/dayand 10 percent consumed only 25 mg/day. In addition, only 17 percent of Americans take multivitamin supplements on a daily basis, and only 7.6 percent take vitamin C supplements.

Also in this issue (pp 112-3), Victor Herbert, MD, JD, of the Bronx Veterans Affairs Medical Center, criticized both Hemilä and Bendich's Continued on page 4

Vitamin B6 Safeguards Immune Response

If you're a sun worshipper, you've no doubt heard all the warnings about wrinkles and skin cancer. Here's one more: excessive exposure to the ultraviolet rays in sunlight also suppresses your immune system.

Reserchers have long known that ultraviolet radiation suppresses Tcell activity in both humans and animals. A team of researchers from the University of Sydney, Australia, reported a likely mechanism: sunlight converts *trans*-urocanic acid, normally found in the skin, into *cis*- urocanic acid. Cis-urocanic acid suppresses T-cells, which play a key role in immunity.

Vivienne E. Reeve, PhD, noted in the American Journal of Clinical Nutrition (March 1995)61:571-6) that a component of ammonia caramel, a food coloring, also suppresses T-cell immunity and that vitamin B6 prevents this suppression. Similarly, B6 inhibits the production of cisurocanic acid.

Comment: Always take large doses of a single B vitamin with a B-complex supplement.

TaurineReducesBloodClotsinDiabetics

Taurine supplements can reduce the risk of dangerous blood clots in insulin-dependent diabetics, who as a group are more likely than nondiabetics to suffer from cardiovascular diseases.

Flavia Franconi, MD, of the University of Sassari, Italy, compared the effects of taurine on 39 diabetics and 34 people without the disease. At the start of the study Franconi noted that diabetics had lower levels of taurine in blood, blood plasma, and blood platelet cells than did healthy subjects.

When Franconi gave taurine supplements to the diabetics, it reduced their tendency toward platelet aggregation. The supplements had no such effect on healthy people.

"In conclusion, our data suggest that taurine may have direct cytoprotective effects in diabetes, although the mechanism of the taurine-induced decrease in platelet aggregation is still unknown. Its antioxidant behavior would undoub-

Why Might Homeopathy Work?

Conventional physicians have long criticized homeopathy for its methods and its perceived lack of reproducibility, a cornerstone of the scientific method. Indeed, homeopathy's tenet of using *less* of a medicinal substance instead of more flies in the face of modern pharmacology. While physicians increase the dose of a drug for greater effect, homeopathic practitioners use less—sometimes dilutions that may be virtually impossible to measure.

David T. Reilly, FRCP, of the Glasgow Royal Infirmary, explained in *Lancet* (Dec 10, 1994;344:1601-6), how he successfully used a homeopathic dilution in the treatment of asthma. This study, the third of a series in the treatment of inhalent allergy (hayfever or asthma), found that homeopathy worked better than the placebo—and that the results could be repeated.

A meta-analysis of the three studies confirmed that homeopathy worked better than a placebo. The results reflected an earlier analysis demonstrating that homeopathy was beneficial in 77 percent of more than 100 controlled studies. (See Kleijnen, F., *British Medical Journal*, 1991;302:316-323.)

Why might homeopathy work? In his conclusion, Reilly speculated that the mechanisms might be (1) similar to those in oral immunotherapy or (2) the result of biochemical encoding from the trace amounts of the medicinal substance. Oral immunotherapy is used in allergy treatments, and, according to Reilly, theoretical physicists seem more comfortable than pharmacologists with the latter idea.

Whatever the mechanism, Reilly concluded, "Our results lead us to conclude that homeopathy differs from placebo in an inexplicable but reproducibile way."

Magnesium Reduces Risk of Cerebral Palsy

Pregnant women preparing for hospital delivery are sometimes given magnesium sulfate intravenously to prevent convulsions in pre-eclampsia and contractions in preterm labor. It turns out that the inexpensive procedure reduces the risk of cerebral palsy (CP), a congenital central nervous system defect, in very low birth weight infants.

Karin B. Nelson, MD, and Judith Grether, PhD, found that mothers given magnesium sulfate before delivery were less likely to deliver children with CP. Only 7.1 percent of the mothers of 42 children born with CP had received magnesium before delivery, compared to 36 percent of 75 mothers who delivered tedly impart protection to cell membranes as well as to other cellular components," Franconi wrote in the *American Journal of Clinical Nutrition* (May 1995;51:1115-9).

"Furthermore, the oral administration of taurine brings about a decrease in platelet aggregation," she added. "This may lead to a reduction in diabetic complications such as micro- and macroangiopathies, the pathogenesis of which is associated with an increase in platelet aggregaion. In this context it is important to point out that a taurine deficiency or a decrease in taurine concentrations could lead to the emergence of retinopathy."

Vitamin E Supplements Protect Cyclists

A study of vitamin E supplementation among racing cyclists found that supplements of 330 IU daily for five months protected against oxidative stress caused by exercise, but it did not increase physical performance, according to an article in the *International Journal* of Sports Nutrition (Rokitzki, L.,1994;4:253-64.)

healthy children.

Mothers of children with CP also tended to deliver soon after hospital admission. "Since magnesium sulfate is commonly administered by continuous infusion, longer time from hospital entry to delivery might have permitted a larger dose of magnesium sulfate and transfer of more magnesium to the fetus," Nelson and Grether wrote in *Pediatrics* (Feb 1995;95:263-9).

Maternal magnesium crosses the placenta and reaches the fetus. In fact, 32-week-old neonates had higher blood levels of magnesium than infants, suggesting that magnesium has a role in brain development, the researchers stated.

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the health of people. Researchers have long known that Keshan disease, a form of heart failure, is associated with selenium deficiency in China. Because of the seasonal nature of Keshan disease, researchers looked for an associated microorganism and turned up the coxsackievirus.

In earlier studies, Beck and Levander demonstrated that selenium deficiency predisposed mice to the virulent form of coxsackievirus that caused Keshan disease. They also discovered that, once created, the virulent form of the virus could infect and cause disease in those animals eating diets with adequate selenium.

According to Beck, this situation might explain the steady emergence of new influenza strains from China, where selenium-deficient soils are common. The flu virus originates in Chinese ducks, jumps to pigs, and then infects people. Similarly, the AIDS virus emerged from a region in Africa with poor soil levels of selenium. (For research on selenium and AIDS, see THE NUTRITION REPORTER, NOV 1994.)

"The importance of this finding is not limited to nutritionally deprived populations," the researchers said in a statement released by the USDA Agricultural Research Service. "In theory, it would take only one selenium-deficient person or animal to produce a new family of virus mutants"—which could cross species and spread across a nation or the world.

Researchers describe the coxsackie, influenza, hepatitis, and AIDS viruses as "RNA viruses," because their genetic material is based on ribonucleic acid, not deoxyribonucleicacid (DNA). DNA viruses tend to be more stable because they contain an enzyme system that proofreads and corrects genetic errors. In contrast, RNA viruses reproduce rapidly with a high rate of mutation because they lack the ability to correct genetic errors.

The fact that selenium and vitamin E are powerful antioxidants and involved in immunity did not escape Beck and Levander. They believe that the deficiency of either nutrient has two consequences. One, the nutrients protect cells, DNA, and RNA against oxidative damage from free radicals. The absence of a critical antioxidant would leave genes, including viral genes, more vulnerable to oxidation-induced mutation. In addition, deficiencies of either selenium or vitamin E weaken the host's immunity, leaving the virus unchallenged and permitting it to reproduce faster. This rapid reproduction, combined with oxidation, increases the likelihood of still more mutations.

In an editorial in *Nature Medicine* (May 1995, 1;5:405-6), Charles Gauntt, PhD, of the University of Texas Health Sciences Center, Austin and Steven Tracy, PhD, of the University of Nebraska Medical Center, Omaha, asked whether "it is now prudent to determine whether viral infections could, in fact be exacerbated by periodic or chronic additional minor nutritive deficiencies such that the course of the viral disease might be worse under deficient conditions?

"If the rapid emergence of a more virulent viral quasi-species occurs in the host during minor dietary deficiencies, this might suggest a mechanism by which adequate diets are linked to better overall health...Perhaps virus evolution does depend on what we eat or what we *do not* eat."

Vitamin C and the Common Cold...

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papers, as well as the work of other vitamin C researchers. Herbert concluded, without giving a single reason for his opinion, that "Chalmers' review delineating the worthlessness of pharmacologicdose vitamin C supplements against the common cold, except as a mild antihistiminic, remains fully viable."

A much more positive assessment of vitamin C was offered in an editorial by John H. Weisburger, PhD, MD (pp 109-111). "The main emphasis of the late Linus Pauling was that the conventional RDA of 60 mg of vitamin C was far too low. Rather, Pauling developed the theme that grams of vitamin C per day were more likely to produce optimal effects health maintenance and in promotion....There is increasing support for the new concept that optimal nutrition and optimal defense systems...ward off not only infectious diseases but chronic diseases such as risk of coronary heart disease and several types of cancer...," Weisburger wrote.



