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Intravenous Vitamin C Gaining More Attention for Its Cancer Fighting Benefits

Thirty years ago, Nobel laureate Linus Pauling advocated high-dose vitamin C as part of the treatment of cancer. His recommendations were based on a small number of patients who had been given either oral or intravenous (IV) vitamin C. Subsequent clinical trials at the Mayo Clinic failed to demonstrate any benefits from oral vitamin C, and the therapy was rejected by conventional medicine.

Recent experimental studies, however, have found that IV vitamin C can raise blood levels of vitamin C 25 to 70 times higher than those achievable through oral supplements. That's significant because such high doses are toxic to cancer cells, but not normal cells.

To explain, large amounts of oral vitamin C increase blood levels up to 70 to 220 $\mu\text{mol/L}$ – far less than the 1,000 $\mu\text{mol/L}$ needed to destroy many types of cancer cells. With IV vitamin C, blood concentrations can be increased up to 14,000 $\mu\text{mol/L}$ of blood.

In a report in the *Canadian Medical Association Journal*, Mark Levine, MD, PhD, of the U.S. National Institutes of Health, and his colleagues described three people treated with IV vitamin C and other supplements. Two of the patients are still alive, and the third (a long-standing cigarette smoker) lived much longer than expected.

One of the cases was a 49-year-old man diagnosed in 1996 with a primary bladder cancer that was starting to metastasize. The tumors were removed surgically, and the patient declined chemo and radiation therapy. The patient decided to receive IV vitamin C at the Bright Spot for Health, a nutritional medicine clinic in Wichita, Kansas. He received two 30-gram IVs weekly for three months, followed by 30 grams once every month or so for four years. "Now, nine years after diagnosis, the patient is in good health with no symptoms of recurrence or metastasis," wrote Levine and his coauthors.

In a separate report published in the *Puerto Rico Health Sciences Journal*, doctors described the safety of high-dose IV vitamin C in 24 late-stage terminal

cancer patients. The patients were given 10,000 to 50,000 mg of IV vitamin C daily. Most had been deficient in vitamin C before treatment, and side effects were infrequent and mild.

Levine and his colleagues believe that vitamin C produces large amounts of hydrogen peroxide, a potent generator of free radicals, inside tumors. The mechanism is similar to conventional chemotherapy, but without the side effects.

However, a recent report in the journal *Nature* suggests another mechanism to vitamin C's benefits. Cancer cells produce large amounts of the enzyme lysyl oxidase, which promotes metastasis. However, an earlier study found that vitamin C inhibited the activity of lysyl oxidase.

References: Padayatty SJ, Riordan HD, Hewitt SM, et al. Intravenously administered vitamin C as cancer therapy: three cases. *CMAJ*, 2006;174:937-942. Riordan HD, Casciari JJ, Gonzalez MJ, et al. A pilot clinical study of continuous intravenous ascorbate in terminal cancer patients. *Puerto Rico Health Sciences Journal*, 2005;24:269-276. Erler JT, Bennewith KL, Nicolau M, et al. Lysyl oxidase is essential for hypoxia-induced metastasis. *Nature*, 2006;440:1222-1226. Kuroyanagi M, Shimamura E, Kim M, et al. Effects of L-ascorbic acid on lysyl oxidase in the formation of collagen cross-links. *Bioscience, Biotechnology, and Biochemistry*, 2002;66:2077-2082. □

Perspectives...

Are We Awash in a Sea of Pills?

Too often, health magazines and alternative medical journals read a little too much like conventional medical journals. The parallel is odd, even uncomfortable.

Most medical journals publish drug ads for a variety of ills, along with articles describing the benefits of various drugs. The ads are doctor-oriented versions of the commercials you frequently see on television – ads to help you sleep better, have less

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heartburn, lower cholesterol, improve your mood, be less shy, and have better erections.

The pitch is not just for the seriously ill. The underlying message is often based on arousing your fear of disease, discomfort, or, as the case may be, a soft penis. Take a lot of pills and all your problems will disappear, assuming that the side effects don't produce new problems.

Health magazines and alternative medical journals often follow a similar tack. An ad in a recent consumer health magazine pitched products for blood sugar, eye health, sports injuries, hormone replacement, bone health, immunity, and prostate health – on a single page!

Articles in some of the alternative medical journals aren't much better. They commonly include long lists of vitamins, minerals, and herbs – a natural polypharmacy for preventing and reversing the same health problems described in conventional journals. Granted, I think there's research behind these supplements, and they're safer than drugs. But when both conventional and alternative recommendations point only to pills, something is seriously wrong.

We live in a pill-oriented society. We've been bred to believe that a pill, whether natural or synthetic, is the solution for our health problems. It's easy to forget that the foods we eat – wholesome versus junk – is of fundamental importance. After all, a dinner of fish and veggies provides a diversity of nutrients not found in any supplement. Similarly, physical activity and stress reduction foster good physical and mental health.

I'm a firm believer in the health benefits of nutritional supplements. The scientific evidence behind their use is sound. But let's be careful to not use supplements only as a natural way of mimicking drugs. Fostering good health demands that we eat, not just swallow. —JC

Browning of Foods During Cooking Reduces Protein Quality and Absorption

The Maillard, or "browning," reaction occurs during the cooking of food, when heat irreversibly binds proteins and sugars. On the positive side, browning reactions account for the aroma, color, and flavors of cooked foods, including the crust of bread and roasted meats. On the negative side, they reduce the nutritional value of protein.

In a recent series of experiments, Spanish researchers described how diets with large amounts of "Maillard reaction products," or MRPs, significantly reduced the available protein in foods.

Isabel Seiquer, PhD, of the High Spanish Council for Scientific Research, Grenada, fed 18 boys, ages 11 to 14 years, two diets for two weeks, separated by

a 40-day "washout" period. One diet contained large amounts of MRPs and the other had relatively low amounts of MRPs.

Seiquer noted that fast-food diets, with their preponderance of fried foods, are high in MRPs. So are foods that are broiled and roasted.

She and her colleagues found that two MRP markers, hydroxymethylfurfural and fluorescence intensity, were higher when the boys consumed the MRP-rich diet.

The diets high in MRPs also led to less digestible protein. "The Maillard reaction causes serious reductions in the availability of several amino acids, mainly lysine, that may become as much as 50 percent blocked," Seiquer wrote.

She also noted that hydroxymethylfurfural inhibits the activity of an important digestive enzyme, carboxypeptidase A, interfering with the breakdown of protein.

Maillard reactions also generate large amounts of advanced glycation end products, or AGEs, which are known to damage DNA and cells. Other research has found that AGE-related damage is related to the amount of AGEs consumed in the diet.

Reference: Seiquer I, Diaz-Alguacil J, Delgado-Andrade C, et al. Diets rich in Maillard reaction products affect protein digestibility in adolescent males aged 11-14y. *American Journal of Clinical Nutrition*, 2006;83:1082-1088. □

Vitamin D Increases the Activity of a Potent Germ-Killing Peptide

A century ago, cod-liver oil and sunshine were the chief treatments for tuberculosis. Cod-liver oil is rich in vitamin D, and sunshine prompts the body's manufacture of vitamin D from cholesterol in the skin.

But it has taken until now for scientists to identify exactly how vitamin D fights tuberculosis and other infections.

Philip T. Liu, PhD, of the University of California, Los Angeles, and his colleagues investigated how "toll-like receptors" on immune cells trigger a response against disease-causing bacteria, such as *Mycobacterium tuberculosis*. Toll-like receptors are sensors that identify the presence of disease-causing bacteria.

It turns out that the immune system's follow-up response to identifying bacteria depends on vitamin D. The vitamin stimulates the production of a powerful antimicrobial peptide known as LL-37.

Liu and his fellow researchers found that activated monocytes, a type of immune cell, had higher activity in two genes. One gene programmed an enzyme that converts vitamin D to a more active

form, and the other gene programmed a cell receptor needed to use vitamin D.

High levels of vitamin D boosted levels of the germ-killing peptide LL-37 in monocytes and macrophages, another type of immune cell. With high levels of LL-37, the immune cells were able to capture and kill the bacteria that cause tuberculosis.

In a related review article, Michael Zasloff, MD, of the Georgetown University School of Medicine, Washington, D.C., wrote: "We currently base vitamin D requirements on amounts required to sustain optimal health of our skeleton...optimal functioning of our innate immune system might require more vitamin D."

Reference: Liu PT, Stenger S, Li H, et al. Toll-like receptor triggering of a vitamin D-mediated human antimicrobial response. *Science*, 2006;311:1770-1773. Zasloff M. Fighting infections with vitamin D. *Nature Medicine*, 2006;12:388-390. □

Vitamin D and Calcium Supplements Seem to Protect Against Diabetes

High intake of vitamin D and calcium, particularly from supplements, may reduce the risk of type 2 diabetes in women.

Anastassios G. Pittas, MD, of the Tufts-New England Medical Center, and his colleagues tracked the health and eating habits of almost 84,000 women participating in the Nurses' Health Study. When the study began in 1980, none of the women had a history of diabetes, cancer, or heart disease.

During 20 years of follow up, women with the highest intake of vitamin D from supplements alone had a modest 13 percent lower risk of diabetes, and those who had the greatest intake of calcium from supplements and foods were 18 percent less likely to develop the disease.

Women who consumed a combination of more than 800 IU of vitamin D and 1,200 mg of calcium daily, mostly from supplements, had a 33 percent lower risk of diabetes.

Pittas wrote that "the beneficial of the two nutrients appears to be additive." However, he noted that the benefits of dietary vitamin D and calcium were not as great.

He cited other research showing that low vitamin D increases the risk of insulin resistance and impaired pancreatic beta-cell function. Beta-cells manufacture insulin. Low vitamin D levels are also associated with impaired glucose tolerance and diabetes, and high calcium intake has been inversely associated with overweight.

Reference: Pittas AG, Dawson-Hughes B, Li T, et al. Vitamin D and calcium intake in relation to type 2 diabetes in women. *Diabetes Care*, 2006;29:650-656. □

High Intake of Some Nutrients May Lower the Risk of ALS

Diets high in vitamin E and omega-3 polyunsaturated fatty acids (PUFAs) appear to greatly reduce the risk of amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease.

Jan H. Veldink, MD, of the University Medical Center, Utricht, The Netherlands, and his colleagues compared the dietary habits of 132 patients with ALS (without a family history of the disease) and 220 healthy subjects. They found that high daily intake of PUFAs reduced the risk of ALS by 60 percent and that high intake of vitamin E lowered the risk by 50 percent.

The nutrients appeared to have a synergistic benefit. People who consumed a lot of both PUFAs and vitamin E had about a 70 percent lower risk of ALS.

Veldink wrote that omega-3 fatty acids, one family of PUFAs, have an anti-inflammatory effect that might protect brain cells. The omega-3s might have a direct neuroprotective effect by reducing toxicity from high levels of glutamate, a stimulating neurotransmitter.

Reference: Veldink JH, Kalmijn S, Groeneveld GJ, et al. Intake of polyunsaturated fatty acids and vitamin E reduces the risk of developing amyotrophic lateral sclerosis. *Journal of Neurology, Neurosurgery, and Psychiatry*, 2006: epub ahead of print. □

Lycopene and Vitamin E Combination May Slow Growth of Prostate Cancers

Clinical trials with men have shown that vitamin E supplements can lower the risk of prostate cancer, and that lycopene supplements are capable of shrinking active prostate cancers. A study with laboratory mice suggests that combining the two nutrients might yield exceptional treatment benefits.

Wytske M. van Weerden, PhD, of the Erasmus Medical Center, Rotterdam, The Netherlands, and colleagues injected human cancer cells into the prostates of mice. They then tested the effects of high- and low-dose lycopene and vitamin E, as well as a combination of the two nutrients.

The combination of lycopene and vitamin E – equivalent to about 350 mg each for a 150-pound man – led to a significant suppression of tumor growth. Forty-two days after implanting the cancer, cancer size was 73 percent lower in the mice given lycopene and vitamin E, compared with those not receiving any supplemental nutrients. In addition, the survival time of the mice increased by 40 percent, from 47 to 66 days.

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Quick Reviews of Recent Research

• High-glycemic foods boost risk of eye disease

A study of 526 Boston-area nurses found that consumption of a high-glycemic diet – typified by such foods as sugars, refined carbohydrates, and potatoes – increased the risk of developing age-related macular degeneration by almost three times. High-glycemic diets are known to cause diabetes, and the risk of serious eye disorders increases in people with diabetes.

Chiu CJ, et al. *American Journal of Clinical Nutrition*, 2006;83:880-886.

• Fish oils lower resting heart rate

A relatively low resting heart rate is usually considered a healthy sign. Conversely, high resting heart rate increases the risk of sudden cardiac death. In a crossover study of 18 men, supplements of omega-3 fish oils (585 mg DHA and 225 mg of EPA daily) for two months reduced resting heart rate from 73 to 68 beats per minute. The fish oils also improved heart rate after exercise.

O'keefe JH, et al. *American Journal of Cardiology*, 2006;97:1127-1130.

• Bariatric surgery leads to nutrient deficiencies

Bariatric surgery entails stapling the stomach or removing part of the digestive tract to reduce the digestion of food, calorie absorption, and weight. Although such surgery is becoming more popular as a way of treating extreme obesity, it has undesirable nutritional consequences. The surgery can result in protein malnutrition and malabsorption of essential dietary fats. The most common micronutrient deficiencies resulting from bariatric surgery are of vitamin B12, iron, calcium, and vitamin D. Other

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Vitamin E alone did not affect tumor growth. However low-dose lycopene did slow tumor growth by 53 percent 42 days after tumor implantation and also increased average survival by 19 percent.

Levels of prostate-specific antigen (PSA) reflected tumor size, and the mice treated with a combination of lycopene and vitamin E had the lowest PSA levels.

Human studies have found that 30 mg of lycopene daily can reduce tumor size and likelihood of metastasis.

Reference: Limpens J, Schroder FH, de Ridder CMA, et al. Combined lycopene and vitamin E treatment suppresses the growth of PC-346C human prostate cancer cells in nude mice. *Journal of Nutrition*, 2006;136:1287-1293. □

nutritional deficiencies that can result in serious complications include vitamin B1, folic acid, vitamin A, and vitamin E. According to this review article, supplementation is "essential" for preventing and treating the nutritional complications of bariatric surgery.

Malinowski SS. *American Journal of the Medical Sciences*, 2006;331:219-225.

• Low folic acid linked to low bone density

In a study of more than 5,000 middle-age and elderly men and women, researchers found that low blood levels of folic acid and elevated homocysteine levels were associated with twice the risk of low bone density. Elevated homocysteine is a marker of impaired metabolism.

Gjesdal CG, et al. *Archives of Internal Medicine*, 2006;166:88-94.

• Fish oils improve blood vessel tone

Flexible blood vessels, with their rhythmic movement, aid the heart's ability to circulate blood throughout the body. Seven healthy subjects were given omega-3 fish oil supplements (2 grams DHA and 3 grams EPA daily) for six weeks. Compared with placebos, the fish oils significantly improved blood flow during exercise.

Walser B, et al. *European Journal of Applied Physiology*, 2006: epublication ahead of print.

• High magnesium, low copper better for health

In an analysis of 4,035 middle-age men in the Paris Prospective Study 2, researchers found that high blood levels of magnesium were associated with a 40 percent decrease in deaths from cardiovascular disease and all causes, as well as a 50 percent reduction in deaths from cancer. In contrast, high blood levels of copper were associated with a 50 percent increase in all-cause deaths, a 40 percent increase in cardiovascular deaths, and a 30 percent increase in cancer deaths.

Leone N, et al. *Epidemiology*, 2006;17:308-314.

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