HEALTH AND STRESS

The Newsletter of
The American Institute of Stress

October 2001

STRESS, FREE RADICALS, ANTIOXIDANTS AND AGING

KEYWORDS: Irwin Stone, Norman Cousins, oxidative stress, phytochemicals, Jonathan Swift, Sodi Pallares, polarizing solution, The School of Salerno.

A decade or so ago, "free radical" was likely to suggest some protestor who was finally released from prison or a Communist who had escaped to the U.S. Few people knew what antioxidants were and many may have thought they had something to do with depriving the body of oxygen and should be strictly avoided.

Today, all health conscious individuals know that free radicals contribute to cancer and coronary heart disease and cause the stigmata of aging, including cataracts, gray hair, wrinkled skin, and accelerated atherosclerosis.

Antioxidant is another buzzword because of the enthusiasm for nutritional supplements that is riding the crest of a tidal wave of interest in alternative medicine. Since the FDA and other regulatory agencies have relatively little control over such "natural" products, manufacturers have had a field day with extravagant claims for antioxidants that promise to prevent cancer and heart disease, delay the ravages of old age and restore youthful vigor.

Unfortunately surveys show **there is often little correlation with what is listed on the label of the product and the contents of the container. In some instances, none of the active ingredient can be detected** or the amounts are much lower or higher. Many concoctions are combinations of various vitamins and antioxidant chemicals and herbals like ginkgo biloba and ginseng that purportedly provide similar benefits. Very little is known about how all these ingredients interact with one another, and as emphasized in a previous Newsletter, some can seriously interfere with prescription and over-the-counter drugs that are also being taken.

Another problem is that nutritional supplement enthusiasts who are convinced that taking more must be better are taking megadoses of all sorts of vitamins and other products that make potential complications more likely. This fad was initiated by the late Linus Pauling, who was firmly convinced that taking enough vitamin C could cure everything from the common cold to cancer and coronary artery disease. He believed

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that adults should take a minimum of 2000 mg. daily and preferably 2 or three times this for senior citizens to prevent problems, and that much more was needed during illness and other stressful situations. I know from personal experience that Linus took a minimum of 12,000 mg. (12 grams) daily and often 50 percent more. His rationale for consuming such large amounts has an interesting history.

Linus Pauling And Vitamin C Megadoses

Pauling's opinions on anything were very highly regarded as he had received numerous scientific honors and accolades and was the only person to have ever been awarded two unshared Nobel Prizes. The 1954 Nobel Prize in Chemistry was for his seminal contributions to our understanding of molecular structures based on principles of quantum mechanics. He was the first to use X-ray diffraction technology to demonstrate magnetic effects on electron flow, to measure the heat involved in forming chemical compounds and to calculate interatomic distances and the angles between chemical bonds. His 1939 *The Nature of the Chemical Bond, and the Structure of Molecules and Crystals* is considered to be one of the most influential 20th Century scientific texts.

His interest in vitamin C stemmed from the research of Irwin Stone, a brilliant biochemist who initially described how the antioxidant properties of ascorbic acid (vitamin C) protected foods from deterioration. By 1935, Stone had obtained three patents on this application and he had become convinced that humans could also benefit from much larger amounts of Vitamin C than medical and nutritional authorities considered adequate.

In his book, *The Healing Factor*, Stone emphasized that cancers most frequently arise in organs with vitamin C levels below 4.5 mg./ml. and are seldom seen in those with higher amounts. **Since primates are the only animals incapable of manufacturing vitamin C and are also unable to store it, daily requirements were much greater than scientists suspected.**

Pauling first met Stone in 1966 when the general view was that **the maximum daily amount of vitamin C the body required was less than 100 mg.** and any amount over this would be excreted in the urine. **Pauling was taking one hundred times this amount!** When he measured the vitamin C content in a 24 hour urine specimen, it was only 1,500 not 9,900 mg. So what happened to the other 8,400 mg.?

Pauling postulated that up to a third of this was probably not absorbed and remained in the intestinal contents where it protected the lower bowel from cancer by destroying or blocking carcinogens in fecal material. Vitamin C also attracted water into the gut, which increased the volume of waste material and had a laxative effect that speeded up elimination. The remainder that reached the blood stream but was not excreted in the urine was quickly converted into various products that helped reduce the risk of cancer, heart disease, colds and other viral infections.

In 1976, Pauling and Ewen Cameron, a Scottish surgeon, reported in the prestigious *Proceedings of the National Academy of Sciences*, that **patients with advanced cancer who had received 10,000 mg. of vitamin C daily survived three to four times longer than controls** at the same hospital who had not received vitamin C supplements. All of the patients had been "treated initially in a perfectly conventional way, by operation, use of radiotherapy, and administration of hormones or cytotoxic substances." The vitamin C group not only lived an average of 300 days longer but allegedly also experienced a significant improvement in their quality of life during this terminal period, whereas the others went progressively downhill. The enthusiastic researchers reasoned that giving much more vitamin C might improve their results.

Could Megadoses Cause Cancer & CHD?

Many scientists were not impressed and raised questions about the validity, reliability, and quality of the control population. They pointed out that this was not a clinical trial in which vitamin C patients were compared to carefully matched controls chosen at random and then followed using a

standardized protocol. Instead, an attempt had been made to reconstruct what happened to the controls merely by their medical records, which could have caused bias in the selection of this group.

Pauling and Cameron tried to counter this by replacing some of the patients and controls and published another analysis in the same journal in 1978. Two Japanese researchers affiliated with the Linus Pauling Institute later claimed similar results in 130 cancer patients. Critics were still not satisfied and the controversy continued for several years. Most supporters had the attitude that "Well Linus Pauling has been right so often in the past, he's probably right about this too".

In 1982, William DeWys, chief of the clinical investigations branch of the National Cancer Institute's cancer therapy program put what appeared to be the final nail in the coffin. He complained that treated and untreated patients had not been matched equally with respect to the stage of their disease, functional ability, weight loss, or the number and sites of metastases, all of which are important for judging prognosis and the severity of the disease.

Another issue of contention was that the patients began getting vitamin C whenever Cameron had judged them to be "untreatable". The duration of their survival was compared to that of the control patients from the time he had also arbitrarily placed them in this category. DeWys argued that if the two groups had been comparable, the average time from the initial diagnosis to "untreatable" status should have been similar for both of these groups, but they were not. Many of Cameron's vitamin C patients had been deemed "untreatable" much earlier in the course of their disease and therefore would have been expected to have lived much longer. For example, more than 20 percent patients in the control group died within a few days of being labeled "untreatable". Not one of Cameron's patients succumbed so quickly, providing further proof their disease was much less advanced when he started treatment.

Several subsequent studies suggested that this megadose supplementation might not only provide few benefits but could cause a variety of problems, including cancer. Mt. Sinai Medical School's Victor Herbert showed that such high doses interfered with the assimilation and function of riboflavin, a B Complex vitamin required to make red blood cells and produce antibodies. He also warned that vitamin C supplements can convert benign ferric iron to ferrous compounds that lead to the formation of powerful free hydroxyl radicals known to damage the heart and other organs. Finnish researchers found that an elevated serum iron was a more powerful predictor of heart attacks than LDL levels and that vitamin C increased iron absorption. Iron is included in many once daily multivitamin-mineral products. If a megadose of vitamin C is taken at the same time it acts as a prooxidant to promote the production of free radicals that convert harmless cholesterol into deadly oxidized LDL.

Sloan-Kettering Cancer Center's physician-in-chief reported that cancer cells seemed to soak up large amounts of vitamin C that protected them against the radiation and chemotherapy being given to destroy them. University of Pennsylvania researchers found that adding vitamin C to test tubes containing solutions of fatty acids found in the blood triggered changes in DNA that resulted in the production of mutational agents that have been implicated in causing cancer.

UCLA investigators reported that middle-aged men who took just 500 milligrams of vitamin C daily showed a significant narrowing of the carotid arteries after only 18 months due to atherosclerosis. Although they had no symptoms, this is a risk factor for stroke and there is a strong correlation between the degree of carotid atherosclerosis and coronary artery disease.

How Much Vitamin C Should You Take?

The current recommendations are 90 mg. for men and 75 mg. for women, with an additional 35 mg. for smokers. That's an increase from the previous RDA of 60 mg. but far lower than most multivitamin products contain. Linus Pauling advocated taking the largest amount that would not cause bowel complaints, which usually occur at doses well over 10,000 mg. Most people do not realize that vitamin C is used up within a few hours so that two or three doses daily or a timed-release product is required to obtain optimal benefits.

Last year, the Institute of Medicine, an independent scientific organization that advises the Federal government, examined the **findings from over 1000 vitamin C studies and found no proof that it was effective in preventing any disease except scurvy**. While the panel found no evidence of serious side effects from large doses of vitamin C, it suggested a maximum daily dose of 2,000 mg. to minimize such problems. In addition to causing diarrhea, very high doses should be avoided by anyone with hemochromatosis (iron storage disease), thalassemia (sickle cell anemia), a history of kidney stones, kidney disease, or anyone taking estrogens or anticoagulants.

Contrary to Pauling's claims, the panel concluded that high doses of vitamin C probably won't protect you from getting a cold either, though they may shorten the duration of symptoms. With regard to his contention that heart disease and cancer would also be reduced, one panel member told reporters "I think what the data show is that vitamin C is an important antioxidant, but it's not a magic bullet. Taking more of it is not going to solve those diseases. Americans are spending around $750 million annually on vitamin C supplements that are simply not necessary."

According to a NIH study, taking more than 200 mg. a day is a waste of money. It found that the body can't absorb more than 100 mg. of vitamin C and that blood concentrations do not increase with larger amounts. Even the director of the Linus Pauling Institute conceded that "above a certain threshold, you urinate out most of what you take in."

But what is that threshold? Does it vary for each of us? Is it higher during stress and certain diseases as Pauling proposed? Norman Cousins, another good friend who also played an important role in the founding of The American Institute of Stress, was suffering from a severe and progressive form of rheumatoid arthritis. Impressed by Pauling's theories, he insisted on receiving large doses of vitamin C and his doctor acquiesced, but didn't know how much to give. Norman wanted to start at 10 grams and work up to 25 via an intravenous infusion over a few hours. He achieved this unheard of dosage in eight days, during which his pain, disability and abnormal sedimentation rate plummeted. He continued to improve on this regimen and daily doses of humor, and later found that he could take 2000 mg. of vitamin C orally before appreciable amounts were detected in his urine. But when symptoms worsened or he was under considerable stress, over twice as much was required.

Based on studies of over 9,000 patients, Robert Cathcart also reported that vitamin C requirements varied greatly and were proportional to the severity of stress or illness. Dosage was determined with his "Bowel Titration" technique by ascertaining how much vitamin C could be tolerated before the onset of diarrhea. In healthy people, this ranged from 4,000 to 20,000 mg. when divided into 4 to 6 doses over 24 hours. This could increase to 30,000 to 60,000 mg. for a mild cold, 75,000 to 100,000 for one more severe, 50,000 to 150,000 for influenza, and **up to 200 grams or 200,000 mg. might be required for patients with infectious mononucleosis or viral pneumonia!**

Patients start to improve at doses just under those that cause bowel complaints and requirements rapidly fall as they recover. Cathcart believes that vitamin C is used up as it destroys the free radicals produced by a disease process and not enough reaches the rectum to attract water and produce loose stools. He also feels that the additional amounts utilized in fighting respiratory infections and other disorders reveals a magnitude of free radical production not generally appreciated by the scientific community.

Vitamin C proponents objected vehemently to allegations that it was ineffective or could actually cause cancer and heart disease. They pointed out that much of the evidence was based on extrapolation from test tube findings that were not pertinent. In the University of Pennsylvania study, researchers tested lipid peroxidation of fatty acids and while it is possible that these by-products might damage DNA there is no proof that this causes cancer. Humans have complex biochemical mechanisms to deal with lipid peroxidation and other nutrients. For instance, vitamin E protects and augments the effect of vitamin C. Since

this and other antioxidants were not present in the test tubes, their normal synergistic effect was prevented.

There has never been any evidence of riboflavin deficiency in people taking megadoses of vitamin C for years. The Memorial Sloan-Kettering Cancer researchers transplanted human cancer cells into mice, injected the mice with vitamin C, and found that cancer cells seemed to soak up large amounts, but this hardly proved it made them more resistant to radiation or chemotherapy.

Die-hard enthusiasts emphasized that the tissues of most mammals are saturated with vitamin C and some, like squirrels, manufacture their own. Primates have to get it from foods and gorillas consume at least 1000 mg. daily from the leaves they eat. Citrus fruits are a rich source for humans but **Pauling would have had to consume 255 oranges a day to obtain the equivalent dose of vitamin C he felt he needed**. Many adherents follow his practice of ordering soluble Vitamin C in kilo quantities and adding a teaspoon (4 grams) or more to a beverage a few times a day.

As for the rest of us, one clear message emerges from all the research studies. People whose diets are rich in fruits and vegetables have lower rates of cancer, heart disease, and other chronic illnesses. **The ideal way to meet your vitamin C requirements is to eat at least five servings of fruits and vegetables a day.** You not only get plenty of vitamin C, but also reap the benefits from numerous other nutrients these foods contain.

What Form Of Vitamin E Is Best?

Vitamin E is a popular antioxidant vitamin because of evidence that it can reduce the risk of heart disease, stroke, prostate and other cancers and Alzheimer's disease and can boost immune system function. Like vitamin C, it has also been the subject of considerable controversy since many of these claims are based on blood levels from dietary sources rather than supplements. Vitamin E prevents the oxidation of unsaturated fatty acids, protein and DNA, protects biomembrane integrity and has recently been shown to play an important role in cell signal transduction.

What most people do not recognize is that the vitamin E family consists of eight different compounds, four tocopherols and four tocotrienols. These act as a team since some have different functions and are attracted to different body sites. While foods contain all eight, most vitamin E supplements consist only of synthetic or natural alpha-tocopherol. Studies have shown that vitamin E's gamma-tocopherol fraction is more potent in suppressing free radical damage and that **protection against heart disease, cancer and other diseases is best achieved with a combination of gamma-tocopherol and alpha-tocopherol**.

Unfortunately, the alpha-tocopherol most people take displaces gamma-tocopherol in tissues so that its benefits are lost. A government report recently stated that **taking high doses of alpha-tocopherol could be dangerous and recommends that vitamin E supplements should contain at least 20 percent gamma-tocopherol**. How much to take is another problem. The I.U. standard was established when it was thought that alpha-tocopherol was all you needed. This does not tell you if the product is natural, synthetic or esterified or contains other family members.

The current RDA is 15 milligrams (22 I.U.) with an upper level of 1,000 mg. (equivalent to 1,500 I.U. of natural d-alpha-tocopherol or 1,100 I.U. of the dl synthetic version). Some authorities suggest taking 200 I.U. plus 200 mg. of mixed tocopherols and tocotrienols for prophylaxis and twice this amount to obtain therapeutic benefits.

Free Radicals Are Two-edged Swords

As Albert Einstein once said, **"Everything should be made as simple as possible - but not simpler"**. A good example of dangerous oversimplification is the notion that free radicals are the bad guys that cause cancer and coronary disease and the good guys that stop their deadly activities are antioxidants. This doctrine has been promulgated by the manufacturers of these products and perpetuated by media hype to cash in on the allure of these popular buzzwords. The pseudoscientific scenario they propose goes something like this.

Free radicals make iron rust, wood become brittle or change color, rubber lose resiliency and harden, and cement crumble due to oxidative stress. Free radicals also cause acid rain, pollute water and damage hair, skin and the exterior of our body so it is quite likely they can wreak similar havoc inside, and there is little doubt that they do. Cigarette smoke, air pollution, exposure to sunlight, radiation, pesticides, certain drugs and polyunsaturated fats all generate free radicals. People living at very high altitudes and frequent flyers have to deal with larger numbers of free radicals because of higher levels of gamma-ray radiation damage.

The biggest source of free radicals by far comes from normal metabolic activities, breathing and physical exertion, particularly prolonged exercise. Many are formed when oxygen reacts with certain molecules resulting in atoms or groups of atoms that lack one or more electrons. To correct this deficit, they must immediately steal what they need from anything they can. It has been estimated that each cell in the body is bombarded by free radicals 10,000 times a day and more during stressful situations. In addition to disrupting and distorting normal functions, this blitzkrieg causes the generation of free radicals in injured tissues, setting up a self-perpetuating domino-like chain reaction of further damage. These excess free radicals can contribute to cancer, coronary disease, cataracts, Alzheimer's and Parkinson's disease. Aging is simply the accumulated result of free radical damage. **We don't age because we wear out but rather "rust out" due to oxidative stress.**

The most destructive and unstable is the hydroxyl radical that lacks an electron in its outer shell. It oxidizes everything it latches on to from cholesterol to DNA. Enter the free radical scavengers, appropriately referred to as antioxidants. They include melatonin, superoxide dismutase, glutathione, DHEA, estrogen and testosterone. These natural antioxidants effectively block hydroxyl and other free radical damage but our ability to manufacture them progressively declines after the fourth decade. Therefore, why not correct this deficiency by taking them as supplements and add some antioxidant vitamins to help out.

It's just not that simple. Free radicals are necessary for life. Without certain free radicals we could not convert air and food into chemical energy or attack harmful invaders. Immune system and white blood cells use free radicals to destroy bacteria and virus-infected cells thus preventing immediate death from infection. With the help of other free radicals, the liver's cytochrome P-450 enzymes detoxify harmful chemicals, protecting us from a quick death. Free radicals are a normal byproduct of breathing that allow us to use oxygen to generate energy in the mitochondria, a part of all cells often referred to as "the energy factory". This complex respiratory chain process depends on the availability of specific free radicals in the mitochondria.

In addition, free radicals are important regulators of vascular tone and cell signaling. One of the most important is nitric oxide, which transmits messages between nerve cells and modulates processes involved in learning, memory, sleeping, pain perception and depression. Drugs that liberate nitric oxide or enhance its actions improve impotence, lethal breathing disorders, and the list keeps growing. Some chemotherapy drugs generate free radicals that act like "magic bullets" to destroy cancer cells they have targeted.

How natural antioxidants maintain the delicate balance of free radicals needed to keep us alive and healthy is not clearly understood. Some authorities believe that **megadoses of antioxidant supplements disrupt this equilibrium and could prove harmful**.

Antioxidants Are Not Armor All

Most people are under the impression that antioxidant supplements are scientifically validated wonder pills. "They're not, although the data don't seem to make any difference to the sales of supplements", according to Richard Veech, Chief of the Unit on Metabolic Regulation and Laboratory of Membrane Biochemistry at NIH. Americans spent $31 billion on vitamin supplements in 1999, nearly $2 billion of which was for vitamins E, C,

beta-carotene and selenium. In a recent interview, Veech, who has written about the interplay of free radicals and antioxidants for over 30 years, said, "The very notion that free radicals, produced naturally, are some type of unwelcome houseguest is silly. Free radicals have been incorporated into the functioning human system over millions of years of evolution. The idea that they should be wiped out or minimized is nonsense. God is no fool."

Antioxidants have different functions and may not be harmless in the large doses that some people consume. Vitamin E can cause excessive bleeding, and **if you smoke, it's probably not wise to take beta-carotene**. In one large study that compared the effects of these two antioxidants on the incidence of lung cancer in smokers, there were no benefits from vitamin E; lung cancers were 18 percent higher in those receiving beta-carotene, and the vitamin E group had a higher frequency of hemorrhagic stroke. A trial to test a combination of beta-carotene and vitamin A was terminated after four years when it was found that supplement-takers who smoked had a 28 percent higher incidence of lung cancer and a 17 percent higher death rate. In another study to determine if vitamin E and beta-carotene could prevent a second heart attack, there were twice as many cardiac deaths in the 20 mg./day beta-carotene and 1.5 times more in the 50 mg./day of alpha-tocopherol groups.

Other reports reveal no evidence that vitamins C and E or beta-carotene prevented colorectal cancer or that these "Big Three" combined prevented arteries from re-clogging after angioplasty. Beta-carotene didn't reduce cancer or heart disease rates in over 22,000 physicians after 12 years nor did selenium supplements in another long-term study of 60,000 nurses.

It's not all bad news. A study of 30,000 male smokers found that those taking vitamin E had 32 percent fewer cases of prostate cancer and 41 percent fewer prostate cancer deaths compared to control groups taking nothing or beta-carotene. Another showed that men taking selenium had 63 percent less prostate cancer on 10-year follow-up. The government recently started a large study to examine the long-term effects of a vitamin E and selenium supplement. Tomato products have also been reported to reduce prostate cancer morbidity and mortality, presumably because of their high lycopene content. Lycopene is a powerful antioxidant but giving large doses alone has no such effect.

That's the problem. Large-scale population studies show that people whose diets are rich in vegetables and fruits have lower rates of cancer and heart disease. This protection comes from phytochemicals, natural compounds that protect plants from sunlight and other environmental threats. There are thousands of phytochemicals grouped under various classifications like carotenoids, flavonoids and polyphenols, but they affect different mechanisms and may need to be in the combinations found in foods to be effective. Carotenoids include not only beta, but also alpha-carotene, lycopene, lutein and cryptoxanthine. Giving one doesn't have the same effect as natural antioxidant mixtures and upsetting their balance could backfire.

This is currently an area of intense study and we may soon see supplements that mimic the concentrations of natural antioxidant "phyterchemicals" found in fruits, vegetables, grains, nuts, oils and seeds. **Such combinations maybe crucial since these compounds affect different enzyme systems.** Phase I enzymes convert carcinogens so they can be rendered inert by phase II enzymes. If not enough phase II enzymes are present, the products not removed can prove carcinogenic and **megadoses of antioxidants that activate only phase I can prove harmful**. We will discuss this and other effects of single supplements and useful alternatives in a future Newsletter.

"Phyterchemical" Nutraceuticals, Coenzyme Q10, ATP And Bioenergetic Medicine

As the great satirist Jonathan Swift noted some 300 years ago, **"Every man desires to live long, but none would be old"**. Longevity is largely hereditary, and while lots of things can shorten your

lifespan, there are few interventions that are guaranteed to extend it. Laboratory animals and fruit flies live longer when oxygen and caloric intake is severely restricted but are not likely to add years to life for humans. We all know that avoiding risky behaviors, regular exercise and a nutritious diet can help keep us healthy and prevent premature death but what most people seem to want is a nutritional supplement that will do this. According to some product ads, such magic potions are readily available.

They're definitely not here yet but may be on the way due to advances in bloenergetic medicine that are zeroing in on which phytochemicals are good for what. The body uses their antioxidants to make its own and knows where to send them. In contrast, fat soluble vitamin E is attracted to lipid structures and water soluble vitamin C to others but may not reach their correct destination if other substances needed to direct them are not available. The energy for all cellular activities comes from ATP (adenosine triphosphate) a remarkable molecule found in the mitochondria of all cells. Anything that increases ATP production or facilitates its activities will increase energy and promote health.

Sodi Pallares' polarizing solution rejuvenated injured cells after a heart attack because ATP production falls when cell walls are damaged and the normal pumping mechanism that keeps sodium out and potassium in is impaired. Polarizing solution forces potassium in and sodium out so that ATP increases and cells can repair themselves. He later found that pulsed electromagnetic fields could further increase ATP production to treat terminal cancer and cardiomyopathy. Bioenergetic research shows that Coenzyme Q10 also increases ATP and could be the ideal antioxidant. More on this later.

Swift also wrote, **"The best Doctors in the world are Dr. Diet, Dr. Quiet, and Dr. Merryman"**, but this did not originate with him and he had the wrong order. One thousand years ago, Salerno, a town in the south of Italy, was a famous health resort and the site of the first European medical school. Their congratulatory poem to King William The Conqueror contained the following advice: *The Salerno school doth by these lines impart, All health to England's King, and* ***doth advise From care his head to keep, from wrath his heart****, Use three Physicians still; first Doctor Quiet, Next Doctor Merry-man, and Doctor Diet.* The emphasis was quite different, since reducing stress was clearly their leading priority.

That's still good advice since stress is associated with increased free radical production. Learning how to avoid and cope with stress may help you live longer and will certainly improve your quality of life. If you want to try larger than RDA doses of antioxidant supplements, two experts who have studied this agree that 400 I.U. vitamin E (200 alpha-tocopherol and 200 mixed tocopherols), 2,000 mg. vitamin C, 100 mcg. selenium, and 30-50 mg. coenzyme Q10 daily can't hurt and might help. As for beta-carotene, one takes 25,000 I.U. every other day and the other says "no way". We will discuss this very controversial topic in a future Newsletter and try to generate more light than heat - so stay tuned!

Health and Stress
The Newsletter of
The American Institute of Stress
124 Park Avenue Yonkers, NY 10703

ANNUAL SUBSCRIPTION RATE:
E-MAIL.....$25.00

ISSN # 1089-148X

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