

Editorial

The Search For Vitamin C Toxicity

Recently *Science* carried a report concerning the action of vitamin C *in vitro* on fatty acids which led to the production of DNA damaging compounds. The lead author emphasized that this did not mean that vitamin C causes cancer and this was reported by Paul Recer, the Associated Press Science writer, and also by Reuters. I have not read this *Science* report nor do I intend to do so since I have no argument with the author's only important conclusion which is that his study had no relevance to whether vitamin C causes cancer. I am interested in how the press perceived and reported it and how it was used by critics to condemn the use of vitamin C and to come back to the ancient and long discredited idea that one can get enough vitamin C by a well balanced diet, whatever that is. This idea probably was current when our scientists were still swinging in the trees and spending the major part of the day chewing leafy green vegetation, when we might have consumed 3 to 4 grams daily. I defy any human today to get this amount of vitamin C from any modern diet without using vitamin C supplements.

It is amazing how few people get even the ridiculously low RDAs recommended for vitamin C. As I expected, the press almost ignored the only correct statement which was that this study was not relevant to human clinical studies since it was done in the laboratory, in the test tube, under conditions that do not exist in living tissue and from which one can draw no conclusions that have anything to do with real life. It would be just as appropriate to conclude that since oils will burn *in vitro* to yield heat and light that therefore no fatty acids and fatty foods can ever be consumed. I am not surprised by this report and the press reaction because it is a rehash of a similar report that appeared nearly 30 years ago. The only difference was in the public perception of the original report and the

present one. With the original report there were very few competent scientists, except like Linus Pauling, willing to stand up and criticize that badly flawed piece of research. With this report you will find many comments on the internet from workers in the field who really examined this present report and accepted it for what it could mean, ie. very little to us, those of us who wish to be healthier rather than to be a milligram away from chronic scurvy. If we accepted the conclusions drawn by the press from that *Science* report, it would appear that the optimum amount of vitamin C would be close to zero, ie. in the scorbutic range, because then there would be the least amount of fatty acid oxidized derivatives.

In 1976, in this journal, Irvine Stone and I criticized a report out of Vancouver released by scientists who had cooked vitamin C with copper, a very powerful oxidizing agent and then placed these oxidized products on cell cultures in the test tube; The cell's DNA showed breaks. Their reported suggested that vitamin C might cause cancer. This was promptly picked up by the *New York Times* with huge flaming headlines and was carried around the world. After that I received many calls from my patients very worried that the vitamin C they were taking might create cancer. In the present case, as with the earlier one, both of the reports were carried in almost all the media. They carried the authors' statement that this study was not relevant. But they then began to use their poetic license to draw all sorts of grim negative conclusions. The *Science* reporters are only partially to blame since they followed the implied conclusions from the original paper and by talking to critics. These were written into the report by the lead author who declaimed that his work was not relevant to vitamin C and cancer. Thus he said people can get all the vitamin C they need through a balanced diet (my comment, "If you are content to be minimally healthy and close to scurvy, especially under any

unusual stress"). He also said "There is a paucity of evidence that vitamin C supplements are really good for you (my comments - "where has he been living for the past thirty years?") Thus he is quoted as telling the Philadelphia Inquirer Staff Writer, Faye Flam. " There isn't a single study to show that vitamin C does anything to reduce cancer risk." This statement is not true as any cursory examination of the internet will show. The lead author, by sending this mixed message, called a double bind, can never ever be wrong for he presents two contradictory claims (1) That this study is not relevant and (2) It is relevant since he draws conclusions from it that are not warranted.

As I expected, the critics found this study very helpful. For example Dr Arthur Grollman concluded that vitamin C could contribute to DNA damage that could cause cancer. Grollman is an expert in cancer: "It just adds more evidence that there could be a significant risk to ascorbic acid." I enjoy these meaningless statements because exactly the same statement can be made by changing the words "vitamin C" to "water" or "food." It would probably be more accurate if the word were food.

I began to use megadoses of vitamin C in 1952 for treating schizophrenia patients. The first patient was admitted after she became psychotic following a mastectomy. The lesions became ulcerated and she became psychotic. Her psychiatrist booked her for electroconvulsive therapy, the only treatment then used, I persuaded him to postpone it so I could try vitamin C but he only gave me a weekend. I had planned to give her 1 gram three times daily. I therefore ordered she be given one gram every hour, day and night. She was started on Saturday morning and on Monday morning, 48 hours later, she was mentally normal and the ECT was cancelled. Her lesions had started to heal. She was discharged and died six months later but still mentally normal. She was not given follow up vitamin C

because I did not have any idea that it might be helpful. Gradually I used more and more vitamin C and within a few years almost every one of my patients was advised to take 1 to 3 grams of vitamin C daily as part of their treatment protocol. During the past 45 years of practice I must have given vitamin C to over 10,000 patients. Perhaps about 5,000 were schizophrenic. When I became interested in the studies of Cameron and Pauling and used vitamin C in large doses I eventually discovered that very few of my schizophrenia patients, now about 1,200 seen since 1976, developed cancer.

There are a few studies which suggest that cancer is less frequent in schizophrenia patients. I have seen 10 who were schizophrenic and developed cancer. But on treatment they all recovered and are well. I have not seen a single schizophrenic patient die from cancer. The relationship is not as strong with their first order relatives, their families. From 300 families with schizophrenia very few had cancer and many were psychotic. From 300 families with cancer few had schizophrenia and many suffered from cancer. Just published is a report by Lichtermann et al² who found from a very large cohort study of nearly 27,000 schizophrenic patients treated between 1940 and 1969 and their first order relatives that the risk of schizophrenia was increased in their patients treated in hospital which they ascribed to the smoking but the risk was decreased in their relatives compared to the population at large. They concluded, "Although specific lifestyle factors, particularly tobacco smoking and alcohol consumption, probably account for the increased cancer risk in patients with schizophrenia, the decreased risk in relatives would be compatible with a postulated genetic risk factor for schizophrenia offering selective advantage to unaffected relatives." A previous study in a New York Mental hospital showed that schizophrenic patients given vitamin C had a decreased

incidence of lung cancer, even though they were heavy smokers.³ It is possible that this significant difference is due to one or all of the following factors (1) the presence or absence of schizophrenia. Our adrenochrome hypothesis predicted this would happen since adrenochrome is a potent anti-mitotic agent and an hallucinogen. A gene has been recently discovered missing in schizophrenia which helps the body eliminate adrenochrome.(2) The fact that almost all of them were given vitamin C which they took for many months or years. (3) The fact that seeing me gave them hope and by some placebo effect was the positive factor. However I consider the last one the least likely since it has now become clear that the whole concept of the placebo was based upon a faulty biased study in the early fifties.⁴ If vitamin C increased the tendency to become cancerous then one would have to assume that the schizophrenic factor was overwhelmingly powerful. It follows that if you do not want to get cancer, become schizophrenic, and come to me for treatment. Better still would be for you to start taking optimum amounts of vitamin C and then to become schizophrenic. It is clear that I have no sympathy for the nay sayers who continue to hypothesize that vitamin C *may* cause cancer. You will note that they are very careful not to say that it will cause cancer, I challenge them to provide the kind of proof they demand from orthomolecular physicians, that vitamin C has ever caused cancer in even one patient. By now you realize I am biased in favor of the enormous therapeutic value of vitamin C because I have seen what it has done to my patients over the past 45 years. To show that my bias is shared by other scientists, clinicians and observers I asked a few to let me have their views on the current *Science* report for publication in this editorial. They are biased, based upon observations and not trammled by adherence to any creed, guild, drug company, university medical school or school of thought. We all freely

admit our biases. I also challenge the critics of the use of megadoses of vitamin C to provide us with their biases.

Robert Cathcart, MD

Dr. Robert Cathcart has been using megadoses of vitamin C for over 30 years and probably has single handedly placed more patients on vitamin C than any other physician in the world. He first observed that the ability to tolerate large amounts depended upon the need. In other words, the sicker a person is the more vitamin he can take without experiencing bowel intolerance characterized by gas and loose stools.

"In regard to the *Science* report saying that vitamin C might cause cancer, I find this ridiculous. With approximately 25,000 patients I have put on large doses of vitamin C since 1969, you would expect a massive epidemic of cancer. If anything, I think I see less cancer than expected. My greatest interest now is the finding by Hugh Riordan, M.D. that many cancers can be cured by daily intravenous ascorbate in doses from 60 to 120 grams going in at the rate of 1 g per minute. His hypothesis is that these high levels of ascorbate cause the formation of peroxide in all the cells and that since cancer cells do not contain catalase as do normal cells, the peroxide selectively kills the cancer cells. All of these scare stories about vitamin C keep the public from acknowledging the therapeutic effects of massive doses of ascorbate. As Mark Levine points out there is a kidney threshold for oral ascorbate that causes the excretion of almost all of moderate doses of ascorbate, so that blood levels, level out for a time as doses are increased. It is obvious however, that with even higher doses, we can ingest ascorbate faster than the kidneys can excrete it. This will obviously raise the serum levels. These are the levels that those of us who advocate bowel tolerance levels of ascorbic acid and massive intravenous doses of sodium ascorbate achieve. When one takes ascorbic acid in low doses

early in a cold, many mild colds are ameliorated. This is because the free radical cascade is not severe enough with the mild cold to completely eliminate all the vitamin C in the nose and throat, sinuses, eustachian tubes and bronchial tubes so the extra C can prevent the acute induced scurvy in these tissues. However, if there is delay in starting the large doses, or if it is a severe cold, the acute induced scurvy can still be prevented by either bowel tolerance doses of ascorbic acid or intravenous sodium ascorbate. Severe acute infectious diseases will respond similarly. Klenner described how massive doses intravenously will cure polio. Several interest groups, including especially the drug industry, will do anything to prevent this information from becoming well known because the proper use of ascorbate would be a disaster for the drug industry.

L. John Hoffer, MD, Ph.D, Professor Medicine, McGill University, Montreal

John chaired a conference about two years ago to consider alternative therapies, vitamin C. His recent report to *Can Med Assoc J* is influential in arousing interest among cancer therapists.

"The editors of *Science* may be right in flagging this article about test-tube findings for media attention, because it could be important. Let me say first that I don't see anything here that indicates a health risk from the vitamin C supplements so many people take. After all, the diet of the prehistoric hunter gatherer ancestors we evolved from contained around 500 mg of vitamin C each day, maybe twice that. It is interesting that Mark Levine at the NIH has shown that serum vitamin C levels peak around this level of intake, at least in normal people. It is also worth noting that most animals, unlike humans, make vitamin C in their own bodies, and, intriguingly, they dramatically increase this production when exposed to carcinogens. So when considered in a biological context, it hard

to credit the notion that vitamin C is toxic to normal cells except under artificial test tube conditions. What is fascinating and perhaps important about this article, if it means anything, is its support for Ewan Cameron and Linus Pauling's contention that high dose vitamin C, given by intravenous injection, could benefit some cancer patients. Something which really ought to be looked into now is whether the genotoxic effects of high-dose vitamin C could synergize with radiation or cytotoxic chemotherapy. Both of these standard treatments of course kill cancer cells through genotoxicity, and they are useful in this regard precisely because cancers are especially susceptible to genotoxicity."

Stephen Lawson , Formerly CEO, Linus Pauling Institute in California, now Administrative Officer at Oregon State University

Stephen worked closely with Linus Pauling and with the Linus Pauling Institute in Oregon since it was formed. He has had to face both the supporters and the critics of the Institute. I imagine he receives tons of mail whenever a report such as this one in *Science* appears from people expecting reassurance or demanding that the Institute reply to these reports.

"The recent study on vitamin C and oxidative damage from the University of Pennsylvania is the latest of several negative reports about vitamin C discussed in the media in the last few years. The first strike against vitamin C came from the Podmore study published in *Nature* in 1998 purportedly demonstrating that 500 mg supplements of vitamin C caused genetic damage to DNA in human lymphocytes. However, lymphocytes are saturated with vitamin C when the dietary intake is about 100 mg/day, so ingesting more should have no further effect on lymphocyte levels. The investigators reported levels of 8-oxoguanine, a marker of DNA damage, that are much higher than what others have found with experimental protocols that

eliminate *ex vivo* artifacts, leading to speculation that their findings were mainly artifactual.

The next strike against vitamin C came from a meeting of the American Heart Association in San Diego in March 2000. Dr. James Dwyer gave a presentation suggesting that 500 mg supplements of vitamin C taken daily for a year increase carotid artery wall thickness. His study, which has not been published and was based on 573 subjects, conflicts with an earlier study published in *Circulation* with 11,000 subjects in which it was found that those consuming more than 1,000 mg/day of vitamin C had reduced carotid artery wall thickness compared to those consuming only about the RDA. The Dwyer study was followed closely by a presentation by Dr. David Golde at the American Cancer Society meeting, also in March. Golde had previously showed that dehydroascorbic acid enters cancer cells through the glucose transporter and then is converted to ascorbic acid. At the meeting, he speculated that the accumulation of vitamin C in cancer cells might protect them from radiation and chemotherapeutic drugs. The preponderance of clinical evidence, however, does not support this hypothesis. In a lengthy review published in 1999 in the *Journal of the American College of Nutrition*, Dr. Kedar Prasad explains that the accumulation of antioxidant vitamins in cancer cells exerts favorable biochemical effects, including the inhibition of oncogenes and the induction of factors that inhibit cell growth, favor differentiation, or induce apoptosis. The third strike against vitamin C came from the Food and Nutrition Board of the Institute of Medicine in the Spring of 2000. For the first time, a Tolerable Upper Intake Level (UL) was established for vitamin C. The UL of 2 grams/day was based on osmotic diarrhea, the induction of which is quite variable among individuals and transient. It is certainly a very weak factor for the determination of a UL, which many others have

wisely refrained from attempting to set for vitamin C because of its utter lack of toxicity. The good news—the increase in the RDA to 90 mg/day for men and to 75 mg/day for women—was almost completely ignored by the media. The latest strike against vitamin C was published in *Science* in June 2001. Dr. Ian Blair of the University of Pennsylvania found that the incubation of vitamin C with lipid hydroperoxides generated genotoxins. But the study examined only the chemical behavior of vitamin C in the test tube. While the concentration of vitamin C was physiologically relevant (i. e. the range that would be expected from consuming about 200 mg/day), the concentration of lipid hydroperoxides was about 10,000 times the normal physiological concentration. Furthermore, in the body, vitamin C helps prevent lipid hydroperoxides from forming in the first place. Lipid hydroperoxides are enzymatically converted to alcohols in the body in fractions of seconds, but the incubation time in this study was two hours. Has vitamin C struck out? On the contrary, the negative reports have struck out because they contradict the accumulated scientific and clinical evidence. Some suffer from seriously flawed methodology; others have no demonstrated physiological relevance. If vitamin C consumed in the small dietary amounts used in these studies is, indeed, dangerous, an unequivocal risk for supplement users would have been clearly identified by epidemiological studies. Instead, the epidemiological studies continue to validate the protective role for vitamin C against cancer and heart disease. The warnings about vitamin C generated from the recent set of negative studies are unwarranted and may dissuade people from an intake of vitamin C that supports good health and affords prophylaxis against disease. In particular, the media have unnecessarily fanned these flames without exerting proper judgment, thereby endangering public health rather than informing readers with thoughtful, balanced presentations.”

Conclusion

In my opinion authors of this *Science* report were irresponsible because they left a mixed message thus allowing the press to grossly misinterpret the results of this *in vitro* study. The result has been to unnecessarily frighten and confuse people who are not experienced in the nuances of science reporting and the way the press can distort them. As an example, this e-mail just arrived in which the writer wrote "I have had breast cancer and have for the last 4.5 years been taking 16 grams of vitamin C a day. I had researched Linus Pauling's work to arrive at this quantity. I had a very serious diagnosis and have had no recurrence. Recently our local newspaper carried an article about research on vitamin C in which they suggest that megadoses of vitamin C can actually mutate cells and thereby contribute to a pre cancerous situation. I would be very grateful if you could

respond and let me know whether you would advise any caution to the continuation of vitamin C in megadoses"

—Abram Hoffer, M.D., Ph.D.

References

1. Stone I, Hoffer A: The genesis of medical myths. *J Orthomol Psychiat*, 5:163-168, 1976.
2. Lichtermann D, Ekelund J, Pukkala E, Tanskanen A, Lonnqvist J: Incidence of cancer among persons with schizophrenia and their relatives. *Arch Gen Psychiat*, 58: 573-578, 2001.
3. Kanofsky JD, Norkus EP, Geller B, et al: Schizophrenia, lung cancer and vitamin C. Philadelphia PA, *Am Psychiat Assoc*, Poster Session, May 1994.
4. Hhrobjartsson A, Gotzsche PC: Is the placebo powerless? An analysis of clinical trials comparing placebo with no treatment. *New Engl J Med*, 344: 1594-1602, 2001 www.nejm.org.
5. Hoffer LJ: Proof versus plausibility: rules of engagement for the struggle to evaluate alternative cancer therapies *Can Med Assoc J* 164: 351-353, 2001.