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Vitamin C and Cancer - Storm of Controversy

by Nicholas Calvino DC and Stephen Levine (more info) listed in cancer, originally published in issue 71 - December 2001

Overview of the Cancer Problem and the Vitamin C Controversy

The World Health Organization has estimated there will be more than ten million documented new cases of cancer next year. Since 1971, according to official figures, over $1 trillion has been spent on conventional cancer research and treatment in the US. The current cost is at least $110 billion a year – over 10% of all US medical expenditures – and 2% of the entire gross national product (GNP). Despite, or perhaps because of, these unprecedented costs, the cancer establishment remains largely closed to most truly independent, innovative treatments. More people make a living from conventional cancer research and treatment than die from the disease on an annual basis. Also, the average cancer patient spends in excess of $100,000 treating the disease via the conventional medical protocol.[1] Thus, there is a tremendous vested interest in the status quo of current cancer therapy. A 1986 report in the New England Journal of Medicine assessed progress against cancer in the US during the years 1950 to 1982. Despite progress against some rare forms of cancer, which account for 1-2% of total deaths caused by the disease, the report found that the overall death rate had increased substantially since 1950. "The main conclusion we draw is that some 35 years of intense effort focused largely on improving treatment must be judged a qualified failure." The report further concluded, "we are losing the war against cancer."

Clearly, there are appropriate conventional treatments that seem able to remove the immediate threat to life. Surgery, chemotherapy and radiation can be used with some degree of success in killing cancerous tissue. However, that degree of success must be viewed in the context of and weighed against the possible side effects and after effects that are to be expected. The ideal agent to treat cancer would be cytotoxic to tumour cells, but non-toxic to normal cells. Vitamin C has long been known to fulfil these requirements but is obscured, ridiculed and criticized by conventional medicine in favour of more powerful and toxic chemotherapeutic agents.[2]

Since it was made popular by Dr Linus Pauling, vitamin C therapy has remained one of the most controversial axioms of alternative healthcare to this day. Two main controversies surround vitamin C. The first claims that vitamin C can actually cause DNA damage, and theoretically cancer, in high doses. The second is the use of vitamin C therapy in cancer, especially when used concurrently with chemotherapy. We will provide evidence that high doses of vitamin C are not only safe, but also therapeutic – whether used concurrently with chemotherapy/radiation or on its own. Because it has a wide therapeutic dosage range and an even wider safety margin, it can be supplemented even up to 100-200 grams daily safely, while it takes only a few milligrams to prevent scurvy.

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Stephen Levine PhD received training in biochemistry and genetics at the University of California at Berkeley and has published a well-known textbook on free radical biochemistry in health and disease, as well as numerous technical and lay articles in diverse areas, with an emphasis on antioxidant and free radical chemistry in areas of cancer and chemical hypersensitivity. He presently publishes regular newsletters for Allergy Research Group, a company that he started in l979 and for which he functions as President and Chief Executive Officer. He can be contacted via salevine@ix.netcom.com

Misconceptions about Orthomolecular Doses of Vitamin C

In the 1998 Journal Nature, researchers reported that vitamin C may act as an oxidant.[3] These concerns led to later studies like the one in the 15 June 2001 issue of Science, in which researchers at the University of Pennsylvania Center for Cancer Pharmacology reported that the daily equivalent of 200mg vitamin C could potentially cause cancer. This was quickly picked up by the news media and reported globally, causing a storm of controversy. Unexplainably, the researchers and press overlooked many items of contradictory evidence. Common sense and evolutionary evidence clearly contradict findings that 200mg of vitamin C cause DNA damage and cancer. The concentration of vitamin C in animals – most animals make their own vitamin C endogenously (only guinea pigs, fruit-eating bats, the red-vented bulbul bird and primates/humans cannot make their own vitamin C) – is equal to or greater than what the researchers at the University of Pennsylvania allege would cause DNA breaks and

promote cancer (see Table 1). There have been over 90 studies to show that vitamin C intake is inversely related to cancer, with protective effects shown for cancers of the pancreas, oral cavity, stomach, cervix, rectum, breast and lung.[4] The authors found that the oxidation of guanine (a purine) in DNA was significantly reduced after vitamin C supplementation, but the oxidation of adenine (also a purine) was significantly elevated. The oxidation of nucleic acids is indicative of oxidative stress being placed on DNA with the concomitant exposure to reactive oxygen species, such as hydroxyl radical. The reduced level in the oxidation of guanine suggests that vitamin C acts as an antioxidant. Failure to report this finding is a significant oversight.[5] Furthermore, these studies were only done in vitro, with no in-vivo evidence. Finally, and most importantly, six concurrent studies disproved the notion that high-dose vitamin C causes DNA damage.[6-11] In light of the weight of evidence against the media hype and research biases against vitamin C, it seems irresponsible to present and report such one-sided and biased findings.

Table 1.

Vitamin C produced per day by different animal species

(equivalent for 70kg man)

Animal	Mg
Goat	2,000-13,000
Rat	2,500-14,000
Rabbit	1,500-15,000
Mouse	2,000-19,000
Cat	350-2,500

Concern about Concurrent Use of Vitamin C and Chemotherapy

The Mayo studies of Creagan and Moertel, which rebutted Pauling's and Cameron's notorious findings, have closed the issue on vitamin C and cancer in the minds of many oncologists and allopathic physicians.[12],[13] However, Pauling pointed out serious design and interpretive flaws of these studies in a rebuttal paper which he was unable to get published. Clearly, the case is not closed. Clinical data demonstrate that ascorbic acid potentiates chemotherapy effects.[14-17] However, there are still theoretical concerns from conventional oncology questioning the use of antioxidants, such as vitamin C, concurrently with chemotherapy. The majority of clinical evidence indicates the usefulness of antioxidants, like vitamin C, concurrently with most types of chemotherapy.[18],[19] In a recent review paper in The Journal of American Nutraceutical Association, Block and Evans reviewed all English articles listed in Index Medicus between the years 1990-2000 related to antioxidant and interactions with anticancer drugs or radiation and concluded that "there is a rational basis for the continued use of antioxidant agents as a therapeutic adjunct in cancer therapy".[20]

The theoretical concern of antioxidant use concurrently during chemotherapy lies in the knowledge that many current clinical oncology drugs induce cellular toxicity and death through mechanisms of intracellular free radical generation, and it is thought that antioxidants may block this action. In the September 1999 issue of The Journal of Oncology an article appeared in which the authors discuss possible theoretical negative interactions of cancer chemotherapy drugs and concurrent use of antioxidants.[21] The experimental evidence for such a hypothesis is lacking and actually, in the majority of cases, shows the opposite.[22] There are only three presently known examples in which any agent classifiable as an antioxidant has been shown to decrease the effectiveness of radiation or chemotherapy in vivo, none of which applies to vitamin C.[23] Vitamin C has been shown in both animal and human studies either to increase the efficacy and/or decrease the toxicity of the following chemotherapeutic agents: alkylating agents (cyclophosphamide, ifosfamide, busulphan, melphan), antibiotic type agents (doxorubicin [adriamycin], bleomycin, epirubicin, daunorubicin), anti-metabolites (5-Fluorouracil, methotrexate), platinum compounds (cisplatin), radiotherapy, hormone therapies (tamoxefin) and plant alkaloids (etoposide, vincristine, paclitaxel).[24] For further review, the reader is referred to the study by Lamson and Brignall, Alternative Medicine Review, April 2000.[23]

Vitamin C has been extensively tested in vitro and in vivo for its ability to prevent the adverse effects of, decrease resistance to, and increase the effects of chemotherapeutic agents.[25] Combined administration of vitamin C (1g/kg) and vitamin K given prior

to chemotherapy increased survival and the effect of several chemotherapeutic agents in a murine ascitic liver tumour model.[26] The vitamin combination did not increase the toxicity of these agents to healthy tissue. Splenic and thymic weights of the vitamin-treated animals were higher than those receiving cytotoxic treatment alone, suggesting an immune-stimulating action of the vitamins. As well as being safe to use concurrently with chemotherapeutic agents, vitamin C has also been shown safe to be used concurrently with radiation.[27] Vitamin C has been shown to have a radioprotective effect on normal cells while concurrently having a radiosensitizing effect on malignant ones.[28],[29]

Abraham Hoffer, who has seen over 970 patients suffering from cancer in the last 20 years, has concluded that "the optimum treatment for cancer today is a combination of xenobiotic and orthomolecular therapy and that the treatment must be started as soon as possible." Hoffer's view is that orthomolecular treatment improves the quality of life, decreases side effects and is palatable. Furthermore, he states, "There can be no logical reason today why most of the research funds should go only toward the examination of more chemotherapy and more ways of giving radiation. There must be a major expansion into the use of orthomolecular therapy to sort out the variables and to determine how to improve the therapeutic outcome of treatment."

Theoretical and Experimental Applications of Vitamin C in Cancer

Proposed mechanisms of vitamin C activity in the prevention and treatment of cancer include:

* enhancement of the immune system by increased lymphocyte production;

* stimulation of collagen formation, necessary for 'walling off' tumours;

* inhibition of hyaluronidase, keeping the ground substance around the tumour intact and preventing metastasis;[30]

* inhibition of oncogenic viruses;

* correction of an ascorbate deficiency, often seen in cancer patients;

* expedition of wound healing after cancer surgery;[31]

* enhancement of the effect of certain chemotherapy drugs, such as tamoxifen, cisplatin, DTIC and others;[32]

* reduction of the toxicity of other chemotherapeutic agents;

* prevention of cellular free radical damage; and

* neutralization of carcinogenic substances.[33]

Vitamin C is so important because it is considered the main redox stabilizer, stabilizing oxidation reactions in the body. The redox potential of an element is an expression of potential energy and potential ability to do work (the energy potential of a molecule is related to the minus number of electrons). The redox potential is directly linked to the effectiveness of the immune system and inflammatory resolution. Therefore, effective cancer modulation can be thought of as a product of the redox potential, or, in other terms, antioxidant capacity. The role of antioxidants as cancer modulative, palliative and a treatment agent is a topic of hot emotional and scientific controversy. What is not commonly appreciated is that tumours exhibit sensitivity to free radical damage and to high concentrations of antioxidants. From research on investigating the antioxidant status of tumour cells and their ability to utilize antioxidants, what is apparent is that tumour cells lack 'antioxidant adaptation' and 'antioxidant homeostatic' mechanisms. Numerous studies have shown that tumour cells are lacking in catalase, glutathione peroxidase, manganese SOD (superoxide dismutase) and copper-zinc SOD. This indicates that tumour cells lack free radical protective mechanisms. Further evidence for this lies in the fact that many of the chemotherapeutic agents utilized today act via the generation of highly reactive free radicals, which cause damage to malignant cells (and normal cells too, unfortunately).

The million-dollar question is: If malignant cells lack antioxidant protection mechanisms, how then can antioxidants be employed against tumour cells? The answer, again, seems to lie in the fact that tumour cells lack antioxidant homeostatic mechanisms and can neither protect themselves from the damages of free radicals nor adapt to high doses of antioxidants and incorporate them into their defence mechanisms. Therefore, high-dose antioxidant therapy has two beneficial modes of action. One is through direct tumourcidal effects and one is by protecting normal cells from the damage of the immune system generating free radicals. Ascorbic acid and ascorbic acid salts are preferentially toxic to tumour cells, which is thought to be related to intracellular generation of hydrogen peroxide.[34],[35] In vitro, ascorbic acid has been shown to induce cellular DNA strand breaks in human mammary carcinoma cells and has been shown to slow tumour growth in mice.[36],[37] Simultaneously, cancer cells are sensitive to high doses of antioxidants, which has a direct tumourcidal effect, again, because they lack the ability to regulate antioxidant status in the cell (too little or too much). This paradox is explained by the lack of antioxidative homeostatic mechanisms of malignant cells versus normal cells. The main mechanism thought to be responsible for this is the lack or relative deficiency of

catalase in tumour cells.[38] There is a reported 10- to 100-fold greater content of catalase in normal cells than in tumour cells.[39]

The redox potential of the body is like a cellular battery where oxygen is the positive terminal. Antioxidants act as electron carriers, coenzymes act as electrical circuits, and fats and antioxidants are the insulation. Some theories of cancer are that the 'cellular battery' has become drained and, due to reduced levels of electrons, the energy in the system is reduced and the ability to do work (on a micro-cellular level) is compromised. Irwin Stone demonstrated this brilliantly with his work in showing that the ratio of reduced to oxidized ascorbate was highly correlated to morbidity, convalescence and mortality. He found that when the ratio was equal to one, the patient would die. In other words, when the electric potential was zero, life ceased. The electrical systems for generating energy, blocking extra free radical production, creating immunity and protecting against cancer are the same electrical system. That electrical system is redox. Why then is ascorbic acid so important? Because it is considered the main redox stabilizer, stabilizing oxidation-reduction reactions in the body. In support of this theory is evidence showing thatcancer patients suffer from a decreased level of ascorbic acid, and other antioxidants, relative to non-cancer patients and the use of orthomolecular doses of vitamin C may act to 'recharge the cellular battery' in such cases.[40-44]

Clinical Data on the Usefulness of Vitamin C in Cancer

Dr Linus Pauling in 1968 in his famous paper in Science formulated the term 'orthomolecular' and provided a rational basis for the use of optimum, even if large, doses of nutrients. His theory explained how evolution was shaped by the loss of the chemical machinery required to make essential nutrients. His first paper appeared in 1970, his last one in 1992. He contributed nine reports. Dr Abraham Hoffer was coauthor with him for the two vitamin C cancer reports. The claim that vitamin C is useful in the treatment of cancer is largely attributable to Linus Pauling, PhD. In 1976 and 1978, he and a Scottish surgeon, Ewan Cameron, MB, ChB, reported that patients treated with high doses of vitamin C had survived three to four times longer than similar patients who did not receive vitamin C supplements. The study was conducted during the early 1970s at the Vale of Leven Hospital in Loch Lomonside, Scotland. Dr Cameron treated 100 advanced cancer patients with 10,000 milligrams of vitamin C per day. The clinical course of these patients was then compared with that of 1,000 patients of other doctors whose records were obtained from the same hospital, but who had received no vitamin C. The findings were published in 1976, with Pauling as co-author, in the Proceedings of the National Academy of Sciences. The 1976 report emphasized that 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 patients were reported to have a mean survival time of 300 days longer than that of the controls. Moreover, the vitamin C patients were said to have shown an improvement in their quality of life. In response to doubts about the validity, reliability and quality of the control population, Cameron and Pauling replaced some of the patients and controls and published another analysis in September 1978 in the same journal.[45] In 1979, two Japanese researchers affiliated with the Linus Pauling Institute claimed similar results in two studies totalling 130 cancer patients treated during the 1970s.[46] Pauling later contributed further evidence of vitamin C's efficacy in mammary tumours in mice.[47] Furthermore, Riordan, from the Bio-Communications Research Institute, and Jackson have reported on cases of cancer successfully treated with intravenous vitamin C therapy.[48-51] And, The Journal of Oncology reported two cases of complete cancer regression in response to high-dose ascorbic acid therapy.[52]

Treatment Protocols

Although very safe and non-toxic, there are a few contraindications or cautions when using orthomolecular doses of vitamin C therapy in cancer. One established contraindication is a glucose-6-phosphate dehydrogenase (G6PD) deficiency. Under oxidative stress, G6PD deficiency can give rise to haemolysis of red blood cells.[53] Pauling and Riordan have also noted that it may be necessary concurrently to detoxify patients who are undergoing IV vitamin C due to the large amounts of tumour cell death by-products, which can cause massive necrosis in rare instances. For this reason, initially, IV vitamin C should be started at a low dose to ensure that haemolysis or tumour haemorrhage does not occur.

Riordan has done work showing that vitamin C is toxic to several cancer lines at doses that are non-toxic to normal cells. He found that at a dose of 7.04mg/dl, vitamin C is completely toxic to cancer cells while being completely non-toxic to normal cells. Only at eight times the dose needed to kill cancer cells does vitamin C become toxic to normal cells. Thus vitamin C has a very wide therapeutic window.[54]

In some cases, high dosage of IV vitamin C can cause symptoms of ascorbate deficiency. This so called 'rebound effect' can be avoided by concurrently supplementing with oral doses of vitamin C (and possibly bioflavonoids and other antioxidants).[55]

Summary

The employment of high-dose vitamin C in the treatment of canceris wrought in a long history of controversy. Since the initial suggestion that vitamin C, in high doses, was useful in treating cancer was first proposed, it has been opposed and debated with heated emotion. The political agendas intertwined in this debate are some of the most deeply rooted and heavily defended.

Despite voluminous observational, epidemiological, laboratory, clinical and research data supporting a positive role of vitamin C in conjunction with, or without, chemotherapy and/or radiation in the treatment of cancer, the medical establishment remains largely close-minded to the available evidence. Although more research needs to be done, this paper undoubtedly demonstrates the safety and plausible efficacy of employing high-dose vitamin C therapy, with few exceptions. Vitamin C appears to fulfil the role of an ideal chemotherapeutic agent, in that it is selectively toxic to cancer cells, protective of normal cells and has a wide therapeutic safety margin. Vitamin C is also an icon for the vitamin and natural therapies movement and demonstrates the slowness of the conventional medical establishment to accept the power of simple, natural remedies. This should serve as a lesson, and as consolation to those practitioners who employ sound, rational integrative medicine but have been alienated or ridiculed by their colleagues as being 'fringe' or 'unscientific'. Sadly, if we wait until the 'establishment' acknowledges what is outside of their paradigm, we may have to wait a very long time. Our patients cannot wait for the blessings of the medical priests. Let us not forget that it has taken decades for medicine to act on the research linking folate and neurotube defects, homocysteine and cardiovascular disease, vitamin E and stroke, and H. pylori and ulcer. In fact, not only have these ideas been slowly adopted, but they were met with fierce ridicule and opposition – not unlike vitamin C and cancer. Thankfully, Pauling, Cameron, Hoffer, Riordan and others did not wait for 'approval' of their findings, but forged out ahead of us, only in search of 'what works' for the betterment of humankind. To them, we are truly grateful and indebted.

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