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High Doses of Vitamin C Are Not Effective as a Cancer Treatment

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The claim that vitamin C is useful in the treatment of cancer is largely attributable to Linus Pauling, Ph.D. In 1976 and 1978, he and a Scottish surgeon, Ewan Cameron, M.B., Ch.B., 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 grams 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 Proceeding of the National Academy of Sciences [1].

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 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 [2]. In 1979, two Japanese researchers affiliated with the Linus Pauling Institute claimed similar results in two studies totaling 130 cancer patients treated during the 1970s [3].

Faulty Design

The Pauling/Cameron study was not a clinical trial in which patients were compared to carefully matched patients chosen at random and followed using a standardized protocol. Instead, Pauling and Cameron attempted to reconstruct what happened to the control group by examining their medical records. Most cancer specialists and journal editors are extremely reluctant to accept this type of study for evaluating the validity of contemporary cancer therapy, primarily because bias may occur in selecting controls.

In 1982, William D. DeWys, M.D., chief of the clinical investigations branch of the National Cancer Institute's cancer therapy program, pointed out that the vitamin C and control groups had not been properly matched

[4]. First he observed that no data had been published to demonstrate that the patients had been matched by stage of their disease, functional ability, weight loss, and sites of metastasis, all of which are important judging the stage of the disease. Then he pointed out that Cameron's patients began getting vitamin C when Cameron judged them "untreatable" and their subsequent survival was compared to that of the control patients from the time they had been labeled "untreatable."

DeWys reasoned that if the two groups were comparable, the average time from the initial diagnosis to "untreatable" status should be similar for both groups. But they were not. He concluded that many of Cameron's patients had been labeled untreatable earlier in the course of their disease and would therefore be expected to live longer. DeWys also noted that more than 20% of the patients in the control group had died within a few days of being labeled untreatable, whereas none of Cameron's patients had died. This, too, suggested that Cameron's patients had had less advanced disease when they were labeled untreatable.

In the Japanese study, the treatment and control groups were treated with various doses and at different times, which made the conclusions even more questionable [5].

Mayo Study #1

In 1978, the Mayo Clinic embarked on a prospective, controlled, double-blind study designed to test Pauling and Cameron's claims. Each patient in this study had biopsy-proven cancer that was considered incurable and unsuitable for further chemotherapy, surgery, or radiation. The patients were randomized to receive 10 grams of vitamin C per day or a comparably flavored lactose placebo. All patients took a glycerin-coated capsule four times a day.

The patients were carefully selected so that those vitamin C placebo groups were equally matched. There were 60 patients in the vitamin C group and 63 in the placebo group. The age distributions were similar. There was a slight predominance of males, but the ratio of males to females was virtually identical. Performance status was measured using the Eastern Cooperative Oncology Group Scale, a clinical scale well recognized by cancer researchers. Most study patients had some disability from their disease, but only a small proportion were bedridden. Most patients had advanced gastrointestinal or lung cancer. Almost all had received chemotherapy, and a smaller proportion had undergone radiation therapy.

The results were noteworthy. About 25% of patients in both groups showed some improvement in appetite. Forty-two percent of the patients on placebo alone experienced enhancement of their level of activity. About 40% of the patients experienced mild nausea and vomiting, but the two

groups had no statistically significant differences in the number of episodes. There were no survival differences between patients receiving vitamin C and those receiving the placebo. The median survival time was approximately seven weeks from the onset of therapy. The longest surviving patient in this trial had received the placebo. Overall, the study showed no benefit from vitamin C [6].

After the study was published, Pauling complained in a letter to the editor that most patients had had extensive prior chemotherapy and were therefore immunologically compromised -- so no benefit from vitamin C in the patient population should be expected [7]. In response, the Mayo researchers pointed out that Pauling's own reports had said that all of his patients had undergone "perfectly conventional" therapy [8]. But Pauling maintained that only 4 of Cameron's 100 patients had received prior chemotherapy [7]. Curiously, at a meeting in February 1985 at the University of Arizona, Pauling stated that vitamin C therapy could be used along with all conventional forms of treatment [9].

A 1975 study at the Mayo Clinic had demonstrated that patients with advanced cancer can mount an immunological response. The study involved forty patients who had undergone chemotherapy for a gastrointestinal malignancy. Many of these patients had immune responses to BCG vaccine, indicating that people with advanced cancer are not uniformly or inevitably immunologically compromised [10]. Nevertheless, the Mayo researcher decided to retest vitamin C.

Mayo Study #2

Patients in the second Mayo study of vitamin C and cancer had tissue-proven colorectal adenocarcinoma that was considered incurable. They were ambulatory and had not had chemotherapy. Most had no symptoms. The patients were carefully classified according to the interval between the diagnosis of inoperable disease and entry into the study, the sites of metastasis, and whether there was a measurable area of tumor. A total of 51 patients were randomly allocated to vitamin C, and 49 patients were assigned to receive a milk-sugar placebo.

There were no objective regressions from either placebo or vitamin C for the 19 patients in each group who had measurable tumors. Among the patients who had symptoms when the study began, 7 (64%) of the 11 vitamin C patients and 11 (65%) of the 17 placebo patients claimed some degree of symptomatic relief. To be sure that patients were following the experimental protocol, urine specimens from five patients selected randomly from the treatment group and six patients from the control group were analyzed for vitamin C. The vitamin C patients had significant levels, while the five of the six placebo patients had negligible levels of urinary vitamin C. (The other patient was taking medications that made it impossible to interpret the test.)

The median survival for all patients was approximately 10-11 months, while that from entry into the study until "progression" was declared was about four months. (Progression was declared if a tumor increased significantly in size, new metastases occurred, symptoms or performance worsened substantially, or weight decreased 10% or more.) No meaningful differences were found between patients on vitamin C and those on placebo. Thus, there was no apparent benefit from treatment with high-dose vitamin C [11]

Mayo Study #3

Following publication of these results, some commentators suggested that the study patients might not have been representative of cancer patients as a whole -- that perhaps there was a subtle selection or referral bias that may have skewed the results. So a third prospective, randomized, stratified study was conducted under the auspices of the North Central Cancer Treatment Group, an international, multi-institutional, collaborative oncology group. Based primarily at the Division of Oncology at the Mayo Clinic, the group also had input from community-based cancer specialists in the Upper Midwest, Louisiana, Montana, Pennsylvania, and Saskatchewan, Canada.

This study included 71 patients on vitamin C and 73 patients on placebo. The patients were carefully matched by age and gender. Performance scores indicated that most of them had some disability from their advanced cancer. The sites of the primary cancers were virtually identical to those of the original study -- primarily lung and colorectal cancer -- and the distribution between treatment groups showed no meaningful differences by diagnosis or site. All had advanced cancer that had progressed after standard treatment.

Most patients had had prior chemotherapy, and a smaller proportion had undergone radiation therapy. The study found that the vitamin C group survived no longer than the placebo group. The median survival time was approximately one month, which is fundamentally the same as in the initial vitamin C study. The data did show something that was somewhat intriguing. At two weeks after the onset of therapy, some patients receiving vitamin C experienced substantial improvement in appetite, strength, and pain relief. However, these advantages quickly dissipated so that by 4-6 weeks, no meaningful advantage from vitamin C remained. The researchers concluded that vitamin C had provided transient symptomatic improvement in appetite and strength for a small pro-portion of treated patients. However, survival was not enhanced by vitamin C [12].

Thus, three prospectively randomized, placebo-controlled studies involving 367 patients documented no consistent benefit from vitamin C among

cancer patients with advanced disease. Moreover, high doses of vitamin C can have significant adverse effects. High oral doses can cause diarrhea. High intravenous dosage has been reported to cause kidney failure due to clogging of the kidney tubules by oxalate crystals [13,14].

Despite these hard facts, many individuals still claim that high doses of vitamin C are useful as a cancer treatment. It is important for responsible health professionals to clarify this issue so that patients neither forfeit scientific care nor put themselves at risk by using a product that has no merit.

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