CORRESPONDENCE

Letter by Linus Pauling, read carefully

Vitamin C and the common cold

To the Editor:

The review of my book, *Vitamin C and the Common Cold,* which was published in the August 21 issue of the Journal as a "Viewpoint", contains some serious misstatements and misrepresentations which I wish to correct.

The statement is made that the author and his critics seem to agree on one central point—at the moment there is no scientifically valid evidence that "Pauling's proposed prophylaxis" will work.

This statement is wrong. Some of the scientifically valid evidence is discussed in the following paragraphs, essentially as it was in my book. In my book I stated that the well-designed investigations that have been carried out have involved the use of rather small quantities of ascorbic acid (1000 milligrams per day or less), and that no large-scale study had been carried out with ascorbic acid in large amounts. The statement by Beaton and Whalen was probably based on their misunderstanding of this comment by me.

The reviewers also say that the doses that I propose, 1 to 2 g. per day, have never been subjected to controlled clinical trials. This statement is false. The investigation by Dr. G. Ritzel, a physician with the Medical Service of the public schools of the city of Basel, Switzerland, published in 1961, was carried out with 1000 mg. of ascorbic acid per day, and gave results with high statistical significance.

Beaton and Whalen make an astounding misrepresentation of the carefully controlled double-blind study carried out by Drs. Cowan, Diehl, and Baker of the University of Minnesota. These physicians carried out a very good double-blind study with nearly 400 subjects, half of whom received ascorbic acid in average amount 180 mg. per day, and the other half a placebo, over a period of 28 weeks. Careful records were kept of the number of colds and the manifestations of illness. The observations showed a decrease in incidence of the common cold by 14% in the ascorbic-acid subjects, relative to the placebo subjects. Moreover, there was a decrease in integrated morbidity, as measured by the average number of days lost from school because of colds, per subject, by 31% in the ascorbic-acid subjects, as compared with the placebo subjects. Both of these decreases are statistically significant. Cowan, Diehl and Baker state that statistical analysis of the data reveals that a difference as large as this would arise only three or four times in a hundred through chance alone, and that one may consider this as probably a significant difference, and vitamin C supplement to the diet may therefore be judged to give a "slight" advantage in reducing the number of colds experienced, although one might question the practical importance of such a difference. It is my opinion, as stated in my book, that a decrease in incidence by 14% and decrease in integrated morbidity (days of illness) by 31% is more than a "slight" advantage, and that it does indeed have practical importance.

Beaton and Whalen misrepresent this study by introducing a confusing discussion of an insignificant matter. Cowan, Diehl and Baker asked their subjects to make an estimate of the number of colds that they had had during the preceding year, and the averages of these estimates are given in the paper. It is pure nonsense to lay any weight on these values for estimated number of colds during the preceding year, based upon the memory of the subjects. Yet Beaton and Whalen have chosen to introduce in their review a table comparing these unreliable numbers with the observed numbers of colds during the period of the investigation, and have minimized the discussion of the reliable decrease in incidence of colds during the period of the study.

Moreover, Beaton and Whalen mention that the number of complications might be considered a measure of severity and that this was reported in the original paper to be somewhat higher in the experimental group than in the control group. Cowan, Diehl and Baker say "those who took the vitamin C had, if anything, more complications such as bronchitis, otitis, and sinusitis than did those in the control group." The fact is that the number of complications in these groups is so small that the difference does not have statistical significance, and accordingly cannot be used as an argument for impeaching the statistically significant results of the careful study by Cowan, Diehl and Baker.

Before 1961 there might have been some justification for saying that more evidence is needed before the conclusion is accepted that ascorbic acid has greater value than a placebo in providing protection against the common cold for subjects who receive ascorbic acid regularly over a period of time beginning before the colds have been incurred, and who are exposed to cold viruses in the ordinary way, by contact with other people.

In 1961, however, the careful study by Ritzel was published in *Helvetica Medica Acta*. This study involved 279 subjects, of whom 140 received 1000 mg. of ascorbic acid per day and 139 received an identical placebo. The study was a double-blind one, with neither the subjects nor the physicians knowing which subjects received ascorbic acid and which received the placebo. Only after the conclusion of the work were the records turned over to a completely independent team of professionals, who carried out the statistical analysis, and were provided with the identification of the tablets. Each subject was examined every day by physicians, and the number of subjective symptoms of illness reported were noted, and verified to some extent by objective examination (measurement of body temperature, inspection of the respiratory organs, auscultation of the lungs, and so on). Persons who showed cold symptoms on the first day were excluded from the investigation. The results were that the ascorbic-acid subjects had 45% fewer colds than the placebo subjects, and that the average number of days of illness per subject was 61% less for the ascorbic-acid subjects than for the placebo subjects, and the integrated number of symptoms (recorded daily) was 64% less. Accordingly the number of colds was found by Ritzel to be 45% less, and the integrated morbidity (total amount of illness per subject) was found to be 61 to 64% less. Each of these results is statistically significant. The null hypothesis that ascorbic acid has no more value than a placebo is rejected with high statistical significance, at the level P(one-tailed) less than 0.01. This investigation was very well planned and executed. I have not seen any significant criticism of it that would justify rejection of the observations.

My conclusion is that the regular ingestion of about 200 mg. of ascorbic acid per day leads to a decrease in incidence of colds by about 15%, and a regular ingestion of 1000 mg. a day leads to the decreased incidence of colds by about 45%. Moreover, these quantities of ascorbic acid ingested are indicated by the reported results to lead to a decrease in total illness (integrated morbidity) by about 30% and 60%, respectively.

No double-blind investigation that has been published has led to the result that the hypothesis that ascorbic acid has the foregoing amount of protective value, relative to a placebo, is to be rejected with statistical significance.

There is no doubt that vitamin C is far less toxic and has far fewer side effects than aspirin and other commonly used cold medicines. As mentioned above, there is evidence showing with high statistical significance that vitamin C, taken in proper amounts, has the effect of decreasing the incidence and severity of the common cold, whereas the ordinary cold medicines do not have this effect. I find it shocking that physicians and nutritionists should misrepresent the facts and should refuse to recognize the value of this important food, vitamin C, in improving health.

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To the Editor:

In response to Dr. Pauling's letter we would disagree that we have misrepresented either his book or the controversy that has surrounded its publication. In our view we have clearly identified our personal responses to a series of pertinent questions. We would encourage the reader to examine the book and the many reviews that have been published before reaching his own conclusion.

While we have no wish to alter any part of our statement, we would again emphasize our major conclusion. In our opinion, Dr. Pauling's proposal has had insufficient field testing to warrant the widespread implementation he advocates. The solution, as we suggest in our article, is further field testing with full clinical supervision. Until such testing is done, the controversy will continue or the proposal, sound or unsound, will be gradually forgotten. Perhaps a Canadian clinical group would be prepared to undertake a study designed to provide definite answers.

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Levodopa and amyotrophic lateral sclerosis

To the Editor:

In a recent paper[1] we suggested that the use of high doses of levodopa might be useful in the treatment of progressive amyotrophic lateral sclerosis (ALS). This statement was based on biochemical observations in