

VITAMIN C AND THE COMMON COLD

FOR MANY YEARS the topic of vitamin C in the prophylaxis and treatment of the common cold has provoked considerable interest and controversy both within the medical profession and among the general public. The interest, and certainly the controversy, have been re-kindled in the last 12 months by the appearance of a book (reviewed in last week's Journal, page 1344) with the title "Vitamin C and the Common Cold" by the outstanding scientist, Linus Pauling. Awarded the 1954 Nobel Prize for Chemistry and the 1962 Nobel Prize for Peace, Linus Pauling is the author of over four hundred scientific papers testifying to his status in his own field of chemistry. It comes as a surprise then to find that a man of Pauling's eminence and achievements should have written and published what many people will not hesitate to class as a piece of propaganda, for that is how many will appraise "Vitamin C and the Common Cold".

"Propaganda" is rather a strong word, of course, and its use would certainly require justification. It has been defined¹ as "the calculated dissemination of partisan ideas with the intent of influencing group attitudes and opinions". It will be a matter for the individual reader

to decide whether it is fair to apply this definition to Pauling's book, the main theme of which is the assertion by the author that large doses of vitamin C have a prophylactic and therapeutic effect on the common cold.

This notion has been strongly challenged by a number of reviewers of the book, and in his replies Pauling claims that he has been misquoted. Here are Pauling's own words: "There is evidence that some people remain in very good health, including freedom from the common cold, year after year through the ingestion of only 250 mg of ascorbic acid per day. The requirements of a few people for ascorbic acid may be expected to be even smaller. For some people optimum health may require amounts up to 5 g per day or more" (page 84). In another place, in respect of treatment the author states: "It is wise to carry some 500-mg tablets of ascorbic acid with you at all times. At the first sign that a cold is developing, the first feeling of scratchiness of the throat or presence of mucus in the nose, or muscle pain, or general malaise, begin the treatment by swallowing one or two 500-mg tablets. Continue the treatment for several hours by taking an additional tablet or two tablets every hour. If the symptoms disappear quickly after the first or second dose of ascorbic acid, you may feel safe on returning to your usual regimen [presumably 1 to 4 gm per day]. If, however, the symptoms are present on the second day, the regimen should be continued, with the ingestion of 4 g to 10 g of ascorbic acid per day."

What is the evidence of these statements? Pauling does not offer any scientific data of his own except the experience of himself and his wife and an unspecified number of friends, who have apparently benefited from the regular intake of large doses of ascorbic acid.

For support of his contentions Pauling depends heavily on the experience of Dr Irving Stone, an American biochemist, who introduced the idea of the possible effects of large doses of vitamin C to Linus Pauling in 1866 and who has himself taken large doses of ascorbic acid for many years. So far as we could ascertain, Irving Stone has not published a critical appraisal of the effects of vitamin C on the common cold. The other source of support is Dr E. Regnier, who claims to have treated with success patients with the common cold with up to 4 gm of ascorbic acid per day.²

In addition to quoting these sources, Dr Pauling has reassessed the results of most scientific attempts to test the notion that large doses of vitamin C prevent an attack of the common cold. Since 1942 somewhere about a dozen clinical trials have been made. The numbers of subjects in the experimental groups have ranged from as few as 20 to 1,000. The dose of ascorbic acid administered ranged from 70 mg to 1,000 mg daily, and the experiments lasted from a few days to half a year. The criteria used to test the effectiveness included the incidence of a frank fully developed cold to "scratchiness" of the throat or pharyngitis. Pauling correctly dismisses some studies because of poor planning, too few subjects and the small dose of ascorbic acid used.

D. W. Cowan, H. S. Diehl and A. B. Baker³ found a 15% reduction in incidence of common colds in people who had taken 200 mg of ascorbic acid daily during the

¹ "Sociology", by L. Broom and P. Selznick, published jointly by Harper and Row, New York, Evanston, and London, and John Weatherhill Inc., Tokyo, 3rd Edition, 1965: 282.

² *Rev. Allergy*, 1968, 22: 835, 948 (September).

³ *J. Amer. med. Ass.*, 1942, 120: 1267 (December 19).

winter. Although this could have occurred three or four times in every 100 by chance, Pauling comments: "I think; such a difference does have practical importance." The original investigators made no claim for their findings.

Other studies in which the ascorbic acid was found either to reduce the incidence of common colds or ameliorate the symptoms showed such small benefit for those treated over the controls that the authors made no (positive) claims. Pauling, however, points out that more striking results might have been obtained with larger doses or larger trial periods.

The real problem in this kind of investigation is establishing the criteria for the diagnosis of a common cold or of the prodromal stages. Except for the fully established febrile state, many of the minor symptoms are highly subjective. H. S. Diehl and his co-workers,⁴ who made some of the earlier studies, have pointed out that "untreated subjects may experience symptoms such as sneezing or a mild sore throat, which then disappear without going on to a full cold, and patients' assessments of their colds are much influenced by any treatment owing to the (placebo effect)". It is noteworthy that in one study, that by Cowan, Diehl and Baker in 1942,³ the incidence in the experimental group dropped from a mean annual rate in the previous year of 5.5 to 1.9 during medication, but the control group taking a placebo also showed a fall from 5.9 to 2.2. It is debatable as to how much these reductions were due to the placebo effect. In his comments on this study Pauling restricts his discussion to the difference of one-third of a cold per year per subject (2.2-1.9) between the experimental and control groups and ignores the spectacular fall in both groups. To admit the (possible effect of a placebo may not be in the best interest of his cause.

The most significant experiment to test the effects of vitamin C was made at the Common Cold Research Unit, Salisbury, England, by G. H. Walker and her co-workers.⁵ They "attempted to show by *in vitro* experiments that exposure of cells to ascorbic acid increased their resistance to infection with viruses" (using 11 different types or strains). Though there was no activity *in vitro*, they also attempted to demonstrate a protective effect in animals or man since it was thought that host resistance might be enhanced directly. The human volunteers were given 1 gm of ascorbic acid three times a day, a dose in the range advocated by Pauling. These investigators, who have had considerable experience in this field, "concluded that there is no evidence, that the administration of ascorbic acid has any value in the prevention or treatment of colds produced by five known viruses".

Commenting upon this study Dr Pauling has this to say: "The incidence of colds observed in the subjects receiving ascorbic acid (18/47) was 6% less than that in the control group (18/44). This difference is not statistically significant, and the observation does not rule out the possibility of a considerably larger protective effect."

The subjects in this study lived in at the Research Unit and so were under the constant surveillance of the highly trained staff. It is of interest that for those

volunteers who were told whether or not they had been given ascorbic acid tablets before their colds had finished, "the colds in the treated group were appreciably shorter than in the controls". In other trials the subjects were not told which they had received, and "the duration of colds was similar in both groups". Did suggestion play a part in the more rapid disappearance of the colds in the treated group?

We are justified in asking how much suggestion and subjective evaluation of symptoms has played a part in the assessment of prophylactic effects of ascorbic acid with Dr Pauling, his wife and the few friends who have followed his regimen.

Turning now to the nutritional function of ascorbic acid, we know it has been demonstrated that 10 mg per day will protect the great mass of adults from scurvy and that 30 mg are fully protective. About 60 mg per day are required to produce and maintain tissue saturation. Above this dose ascorbic acid apparently acts no longer as a nutrient but as a foreign chemical substance or a drug which must be handled by the body in the manner consistent with its chemical and physical properties. Because of its high solubility, practically all ingested ascorbic acid enters the blood from the intestinal lumen, and so there must be a rise in plasma ascorbic acid levels with each dose. How long this rise is sustained will depend on the frequency of the doses.

Because of its acidity a certain amount of buffering must take place in the blood, and then the excess in the plasma above about 1.0 mg/100 ml is excreted via the kidneys. In this connection, Dr Grace Goldsmith, Professor of Medicine at Tulane University School of Medicine and one of the world's leading authorities on ascorbic acid metabolism, has commented:⁶ "Although ascorbic acid is water soluble and excessive amounts are excreted in the urine, large doses can have adverse effects. Amounts of 1 gm daily may cause diarrhoea. [This is admitted by Pauling.] Amounts of 4 to 12 gm daily, given for the acidification of urine in the management of certain chronic urinary tract infections, can lead to the formation of urate and cystine stones through precipitation."

The definition of propaganda quoted at the beginning of this comment implies that the propagandist has "the intent of influencing group attitudes and opinions". Dr Pauling is certainly intent on influencing individuals, but he is also trying to influence those in authority in the U.S.A., for he hopes that "the U.S. National Institutes of Health and other agencies will carry out thorough and reliable studies" (page 103). If the experience of the British Common Cold Research Unit is any guide, one wonders how the subjective effects of receiving a drug can be overcome. Dr Pauling's scientific status and reputation lend credibility to his claims, which at the best are "not proven". There are some indications that a substance which is normally consumed as a nutrient and which becomes a drug when taken in massive doses may, in these doses, be harmful to some (people).

We cannot help asking whether Dr Pauling has not done science a disservice by his support for a cause which has not been scientifically proven and which, in fact, has been disproven by the most scientific and elegant investigations made to date.

⁴ *J. Amer. med. Ass.*, 1938, 111: 1168 (September 24).

⁵ *Brit. med. J.*, 1967, 1: 603 (March 11).

⁶ *J. Amer. med. Ass.*, 1971, 216: 337 (April 12).