

New Horizons for Vitamin C

Plain talk review of the day to day uses of vitamin C in colds, cancer, and other conditions seen in daily practice, by one of the leaders in vitamin C research. This is the first of a two-part series,

An editorial relating to Dr. Anderson's article appears on page 14

by Terence W. Anderson, M.D., Ph.D.

The polarization of views on vitamin C that has occurred in the last few years is well illustrated by the following sequence of events: 1970, Linus Pauling's book, "Vitamin C and the Common Cold" was published and became a bestseller,

1972, Irwin Stone published "The Healing Factor: Vitamin C Against Disease" claiming a wide variety of health benefits from large doses of Vitamin C.

1974, the U. S. Recommended Dietary Allowance for Vitamin C was reduced from 60 to 45 mgm per day.

THINKING SCURVY

The books were written by sincere, highly intelligent scientists who feel that the previous 60 mgm recommendation was grossly inadequate. The reduction in the RDA to an even lower level was based on the considered judgment of another group of sincere, highly intelligent scientists who believe that the 60 mgm figure was unnecessarily high.

How can such divergent views develop, since presumably they are both based on the same body of knowledge and by men and women of equal sincerity?

The easy answer is that the men who wrote the books were the wrong sort of scientists—chemists, rather than nutritionists or physicians—and were, therefore, unable to properly evaluate the available evidence. There may be some truth in this answer. But an equally important reason for the divergence may be that the thinking of most nutritionists and physicians is still dominated by the nature of the relation of vitamin C to scurvy.

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Even the chemical name of "a-scorbic" (scorbutus = scurvy: for the skin to be covered with scurf or scale) acid helps to perpetuate this idea. And no wonder, for a cause and effect relationship in human disease could hardly be more obvious and unequivocal. Consider, for example, what a bare trace of vitamin C, contained in a dilute extract of pine needles and bark was able to do for a small group of men as they endured a harsh winter on the site of what is now Quebec City (see cover). According to Jacques Cartier's journal for 1536, they were quickly "healed of all the disorders afflicting them." And what unpleasant disorders they had been:-

"Legs became swollen and puffed up while the sinews contracted and turned coal-black and, in some cases, all blotched with drops of purplish blood. Gums were so decayed that the flesh peeled off down to the roots of the teeth while the latter almost all fell out... by February out of our group of 110 there were not ten left in good health . . . already eight were dead, and over fifty more were given up for lost"

Our modern understanding that this gruesome and deadly disease was due to the lack of a pin-point quantity of a simple chemical compound in the daily diet must surely be one of the most impressive achievements of nutritional science. Yet it may be that the dramatic nature of severe vitamin C deficiency is indirectly responsible for much of the present controversy—the symptoms and signs of scurvy are so drastic, so clearcut that there is no need for large numbers of subjects, enduring double-blind studies with the results measured

**And now given a boost with a new book by Linus Pauling, "Vitamin C and the Common Cold and the Flu." It is reviewed on page 26 Ed.*

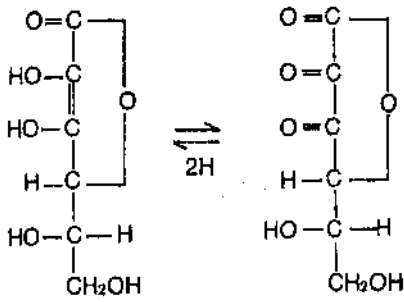
for statistical significance in order to establish the presence of this disease. Scurvy is dramatic and self-asserting, doesn't leave one in doubt. This is the reason why suspicions of more subtle effects from an "adequate" but possibly less than optimal intake of vitamin C have seemed weak and unimpressive in comparison.

The other aspect of scurvy-oriented thinking that has influenced vitamin C research is that the effect of increased intake (above a 5 to 10 mgm a day minimum) has been measured almost exclusively in terms of scorbutic symptoms—gum health, wound healing, capillary haemorrhage, and the like—an increasing the daily intake above 1 mgm has clearly been shown *not* to confer any added benefit in most of these. Only gum health seems to require more than 10 mgm a day. Everywhere, the optimal effects appear to be reached at about 30 mgm a day. The new U. S. RDA of 45 mgm would, therefore seem to provide a generous margin of safety. For years the Canadian figure has been only 30 mgm a day, without any obvious deleterious effect emerging

THINKING BIG

The opposing view that optimal health requires the daily intake of hundreds or even thousands of milligrams of vitamin C has leaned heavily on theoretical arguments and has been weak in substantiation with practically well-controlled scientific studies in humans. This is a serious weakness. It has caused many orthodox nutritionists and physicians to dismiss the ideas of Pauling and Stone as unfounded speculation. However, one must recognize that there is a dilemma here—if all the persons with the necessary expertise and facilities to conduct human studies are on the "inside," how do "outsiders" get about having their unorthodox ideas tested? Perhaps one way is to write

The "Redox" Pair



L ascorbic acid

L dehydroascorbic acid

popular book on a popular subject—in this case the common cold—and thus provoke some of the insiders to try and disprove your extravagant claims! At least, this was the reason why a group of us at the University of Toronto found ourselves involved in conducting a large-scale trial of vitamin C in high doses during the winter of 1972-73.

Professor George Beaton and Sandra Whalen, a graduate student, both of our University, had written a critical but not entirely unsympathetic commentary on Linus Pauling's book for the Canadian Medical Association Journal. In it they pointed out that, although traditionally the burden of proof rests with the proposer of a new idea rather than with his critics, when the proposer is as brilliant a theoretical scientist as Linus Pauling, the health community might be wise to accept the challenge and conduct an appropriate clinical trial. (See also the four critiques, "That Man Pauling" *Nutr. Today*, Vol. 6 (J/F) p. 8-9, 1971.) In a subsequent letter to the editor, Professor Pauling claimed that the Beaton, Whalen review had been unjustifiably negative, and reiterated his conviction that the regular intake of 1000 mgm of vitamin C a day would lead to 45% fewer colds and 60% fewer days of sickness. We, therefore, set about organizing a clinical trial that would test this claim by giving half the subjects a regular daily intake of 1000 mgm of vitamin C and the other half an inert placebo.

Since we anticipated a negative result, we needed a large number of subjects to avoid getting an indecisive answer, so we recruited 1000 volunteers, of whom 818 eventually completed the trial. We also added a therapeutic feature—an increase in the daily dose to 4 grams during the first three days of any illness—to give the regime every possible chance

of success. Subjects were randomly assigned to vitamin or placebo tablets and the experiment was strictly double-blind, i.e., neither the subjects nor the investigators knew which group an individual belonged to until all the sickness records had been coded and the information transferred to punchcards. Special care was taken to ensure that the vitamin and placebo tablets were truly indistinguishable in appearance and taste, since we were relying on individually-kept records of sickness, and it is well-known that psychological factors can greatly influence an individual's perception of illness.

DOUBLE BLIND TRIALS

The trial ran for 14 weeks. When the results were analyzed we found that, although the total number of episodes of illness was 7% lower in the vitamin group, this difference was not statistically significant. Similarly, although there was a 12% difference in the total days of recorded symptoms in the two groups, that difference was also statistically "not significant"—in spite of its being based on more than 2,000 days of symptoms in each group. (This illustrates one of the difficulties of "proving" effects of this nature, namely the great variability of spontaneous human illness patterns and the need for very large numbers if a difference is to be "significant"). However, there was a highly significant difference in the amount of *disability* experienced by the two groups. The vitamin group had recorded 531 days "confined to the house," some 30% fewer than the 769 days recorded by the placebo group. The probability of this being due to chance was less than 1 in 1000 ($P < .001$).

A careful examination of the data failed to reveal any imbalance between the two groups that could account for a difference of this magnitude. So, we were forced to conclude that the extra vitamin C had, in some way, reduced the severity of the symptoms experienced.

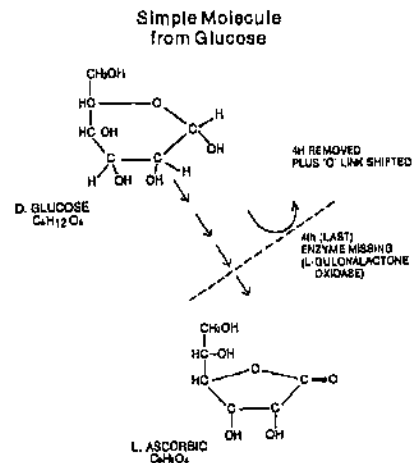
Then we organized a second trial during the following winter. In this, we would try to separate the effect of the regular daily intake from the extra "therapeutic" doses at the time of illness. We also wished to determine whether these effects were dose-related, i.e., could the same result be achieved with lower doses/ and/or would larger doses produce even more effect?

Thanks to the widespread public interest in the vitamin C controversy we were able to recruit more than 3,500 volunteers for this second study. They were allocated to eight different treatment schedules. Unfortunately, the sheer size and complexity of this experiment led to a number of problems, both in its conduct and interpretation, so that some of the results were not as clearcut as we would have desired. However, it was reasonably clear that the regular "prophylactic" dose *alone* had little effect on sickness rate, days of symptoms, or disability. Furthermore, there was no evidence of a dose-related effect across the prophylactic range of 250, 1000, or 2000 mgm a day. There were two placebo groups in this study, and in the accompanying diagram the uncertainty over which to use as the placebo base-line has been resolved by using a weighted average of the experience of both.

SATURATING TISSUES

At first, these results were difficult to understand/ since Coulehan and his colleagues in Arizona had found a substantial reduction in days of symptoms in children given only a regular supplement of 1000 or 2000 mgm daily without any extra therapeutic dosage at the time of sickness. Unfortunately, no information on disability was available in this study.

A subsequent study by the Arizona group has failed to confirm these early findings, but our initial attempts to reconcile the Toronto and Arizona findings drew our attention to an aspect of these large-scale studies that is frequently overlooked, namely, the initial nutritional status of the experimental subjects. Thus, it seemed possible that



the differences between the first Toronto and Arizona studies might be due to the fact that one group consisted of urban, well-nourished adults, while the other consisted of young, possibly less well-nourished, school children on an Indian reservation.

It has been known for years that the level of vitamin C in the blood can only be increased up to a certain point by increasing the daily intake of the vitamin and that this maximum concentration is reached at intakes of between 60 and 120 mgm a day. When one takes larger amounts they are less completely absorbed, greater amounts are excreted, so that although there will continue to be a brief rise in the quantity of vitamin C circulating in the blood, an increase that lasts one or two hours, the background (fasting) blood levels of vitamin C tend, after a few days, to adjust back to their previous level. There is some evidence that tissue levels also reach a plateau. This state of affairs is often referred to by the convenient, although possibly imprecise, term of "saturation." In this state the average adult body store of vitamin C has been estimated to be at about 4000 mgm.

Recently, similar figures have been obtained by E. M. Baker and R. E. Hodges at Davis, California, in a series of studies involving radioactive ascor-

bic acid. They found that, under a wide variety of conditions, the total body store declined at a remarkably constant rate of about 3% a day, so that the U. S. recommended intake of 45 mgm a day was enough to maintain a body pool of 1500 mgm—well above the 300 mgm level at which the symptoms of scurvy begin to appear.

If the maximum body pool is 4000 mgm, the daily intake necessary to maintain this pool would presumably need to be about 120 mgm, assuming the same 3% daily rate of decline.

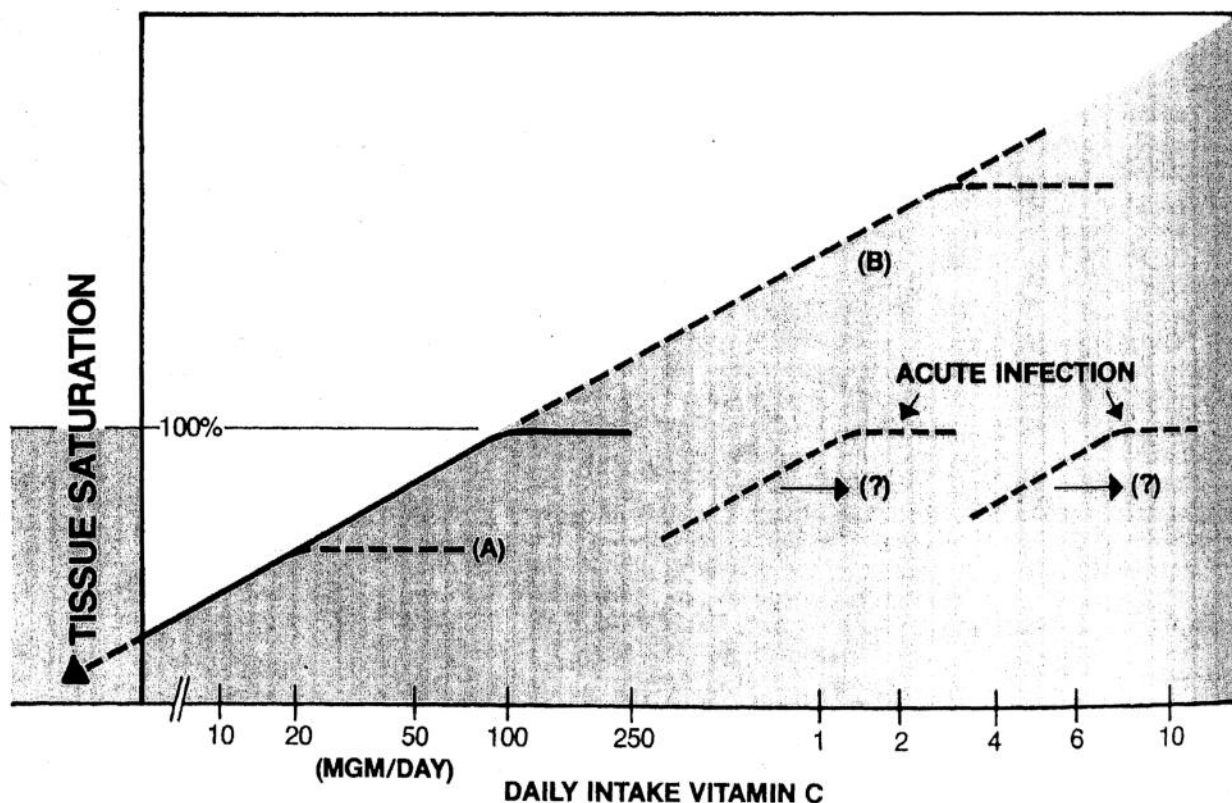
Animals that are able to synthesize their own vitamin C are said to maintain their tissues in a state of full saturation. This is the reason why some nutritionists have long argued that this should also be the aim in human nutrition. It was this point of view that led to the relatively high figure of 75 mgm a day that was used for some years as the U. S. recommended dietary intake. But this point of view has fallen into disfavor in recent years because of the lack of concrete evidence that there is any real advantage to be gained from the higher intake. However, as mentioned earlier, almost all of the human experimental studies on optimum dose-levels have involved measuring the effect on typical scurvy lesions — capillary hemorrhage, wound strength, gum

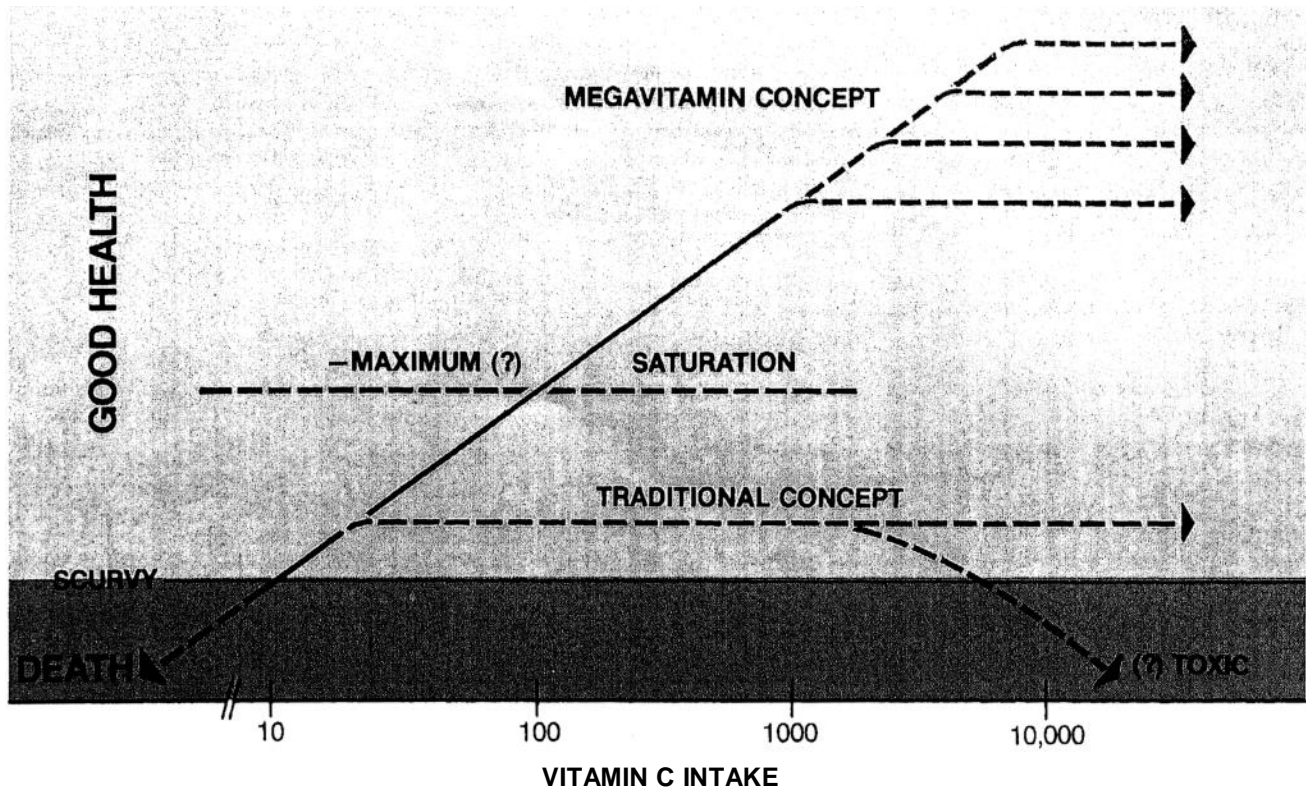
health—whereas perhaps the benefit of saturation is in something less specific and less easily measured, such as resistance to "stress/'

THE STRESS FACTOR

If a saturation/stress relationship exists, it might well help to explain the difference between our results and those of other investigators. Our subjects were a self-selected sample made up approximately ten percent of the population invited to volunteer. Many of them were highly motivated, nutrition-conscious individuals, whose vitamin C intake was well above average (over two thirds reported drinking at least four ounces of juice daily) and most were probably close to saturation. Therefore, it is likely that the group as a whole had little room for improvement in terms of saturation. This may have been the reason that the prophylactic-only dosage schedules showed little effect. In other, less saturated, populations there could conceivably be a measurable effect on disability but there is not, as yet, any experimental evidence to support this hypothesis.

The saturation/stress concept might also explain why we found the prophylactic-therapeutic combination more effective than the prophylactic alone. There is evidence from both animal and





human experiments that many different types of stress can accelerate the utilization of vitamin C. If this is so, then an increased intake would be necessary to maintain saturation in time of stress. Just how big an increase would be needed is uncertain, but both Wilson and Loh in Dublin, and Hume and Weyers in Glasgow have produced evidence for believing that the daily increase required under such circumstances might need to be measured in thousands rather than hundreds of milligrams.

In any case, as far as a regular daily "prophylactic" dose is concerned, if saturation is indeed the limiting factor there would seem to be little point in the average healthy person taking in more than about 120 mgm each day.

To test this idea we have now conducted a third study, in which our subjects took 500 mgm of vitamin C once a week probably equivalent to 50 mgm or less each day, but hopefully enough to ensure full saturation in view of the fact that in most cases it was in addition to a good dietary intake. At the first sign of infection they took an extra 500 mgm dose, repeated this twice at four-hourly intervals, then at 12-hourly intervals for up to four more days, i.e., 1,500 mgm on the first day, then 1000 mgm daily on days two through five.

Half of the vitamin subjects received

a sustained-release form of the vitamin that should be more efficiently retained (and therefore possibly equivalent to higher dose) than an ordinary tablet, since it avoids the rapid absorption and excretion seen with the conventional tablet form of dose. However, there was no striking difference in the results observed with the two types of vitamin dosage, so the results have been combined in the accompanying diagram.

As can be seen, the results of this third study were not greatly different from those obtained in the other two combination prophylactic/therapeutic studies, i.e., little effect on the total number of episodes, little effect on the total days of local (nasal) symptoms, but a 20 to 30% reduction in disability as measured by days spent indoors. This pattern suggests that the extra vitamin C is not protecting against viruses directly, or just helping to dry up nasal secretions, but rather is helping the victim to overcome the general feeling of "malaise" that often accompanies an acute infection, and is probably part of a non-specific reaction to stress.

It must be emphasized that these conclusions are only tentative. Further research is badly needed. The range of experimental variation in this type of study is so great that the impression of uniformity in the three studies may be misleading. Large-scale trials need to

be carried out-preferably with the same dosage schedules but in other populations, with different lifestyles, and at different levels of initial saturation.

TWO THINGS CLEAR

In spite of the uncertainty that remains, two things now seem clear. The first is that Pauling and Stone were over-optimistic in contending that large doses of vitamin C would cure the common cold. Nevertheless, despite this major reservation, one has to acknowledge that the provocative writings of these two men have stimulated interest in an area that very few of us had previously thought worthy of any serious investigation but which might turn out to be quite important. Thus, although the 20 to 30% reduction in disability that we have observed may be dismissed as a relatively trivial benefit, the fact that there is *any* effect arouses enough scientific curiosity that it will inevitably lead to further investigations. The curiosity of the public and, hence ones students, friends, and patients has also been aroused. Now they, too, are asking questions that await satisfactory answers.

To the above conclusions it must be added that, if this applies to one area, the common cold, what of the claims that have been made by Pauling, Stone/

for the common-cold in 1970. Of these, heart disease and cancer are the ones that most urgently need further exploration, since these diseases are responsible for more deaths than all other causes combined, and our present methods of prevention and treatment leave much to be desired. Unfortunately/ however, as in so many other areas of the Vitamin C controversy, although there are some intriguing and tantalizing scraps of evidence, there are many frustrating gaps in our knowledge, and—particularly in terms of human evidence—a sometimes bewildering mixture of conflicting reports.

For example, serum lipid levels, a well-recognized risk-factor for both ischemic heart disease and stroke, have been clearly shown by some investigators to be raised, by others to be lowered, and by others to be unaffected by giving supplementary Vitamin C! Part of this confusion is almost certainly due to the fact that, as with "colds," the response to supplementary vitamin C is likely to vary according to the initial vitamin C status of the subjects, with those already on a high intake having little or no room for improvement. It also seems probable that the duration of the experiment and the presence or absence of other diseases or metabolic abnormalities will affect the results obtained.

One of the confusing factors is that at a very low vitamin C intake, the serum

cholesterol level is depressed, and supplementary vitamin C therefore leads to a rise in **serum-cholesterol**. This is probably related to changes in lipid absorption from the gut, since Bronte-Stewart and his colleagues in South Africa found in treating patients with scurvy that the serum cholesterol rose more promptly if vitamin C was given by mouth than by injection.

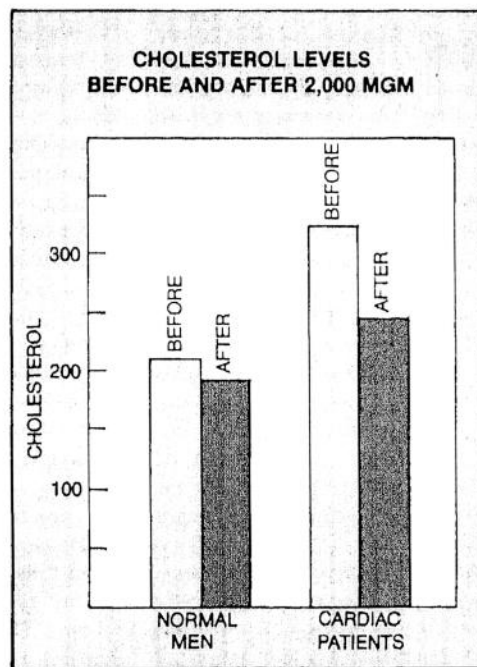
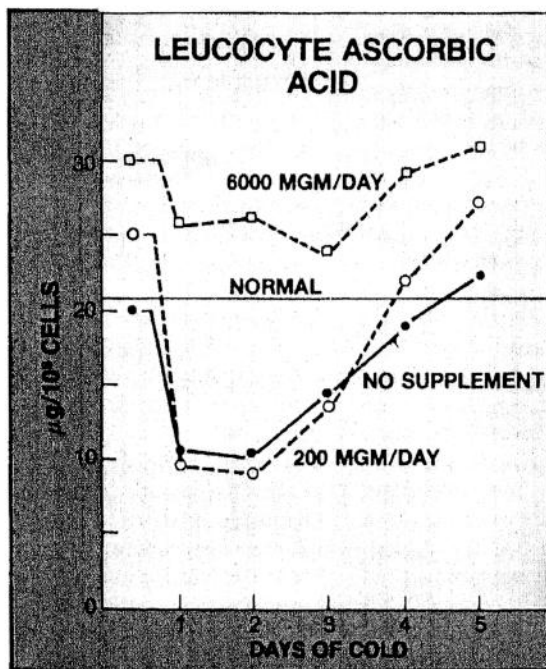
At the other extreme, Boris Sokoloff in Florida and some other investigators elsewhere have found that, with a very large daily dose of 1 or 2 grams of vitamin C, **abnormally** high serum cholesterol levels can be reduced, **particularly** in patients with evidence of ischemic heart disease. Unfortunately, other investigators have either found no change (or even an increase) in cholesterol levels, or that some patients respond while others do not.

Our own limited experience in this area has been disappointing. We were unable to confirm the claim made by Constance Spittle of Wakefield, England, that cholesterol levels could be lowered in healthy young adults. After 1 gram daily for 14 weeks our subjects showed no change in serum cholesterol. However, once again, differences in the initial levels of saturation and in the duration of treatment may account for the different results of the two situations. The encouraging results of Sokoloff and his colleagues indicate that this area should be investigated further.

Some animal studies on blood vessels are also encouraging. Under certain circumstances, atherosclerotic lesions or the arteries can be either prevented or reduced by vitamin C supplementation. The underlying mechanisms that may be involved have recently been well-reviewed by Krundieck and Burterworth (Am. J. Clin. Nut., Aug., 1974). Unfortunately, it does not necessarily follow that we can expect to see the same effect in humans, since in addition to species⁷ variation; animal experiments are usually conducted with diets and time-scales that are quite different from those encountered in the **human** situation.

There is some circumstantial evidence in humans also that a generous supply of vitamin C may help to keep blood vessels healthy. The similarity between the early lesions of atherosclerosis and scurvy led two Canadians, G. C. Willis and VV. J. McCormick, to suggest that these lesions might be a form of "localized scurvy" affecting the connective tissue in the wall of the artery. Willis went on to show that the arterial walls of men dying of heart attacks did indeed show abnormally low levels of ascorbic acid.

The smooth inner surface of veins may also be protected by high tissue levels of vitamin C. Dr. Spittle has reported a small controlled trial in which there were fewer cases of post-operative venous thrombosis in hospital patients



SOME HIGH VITAMIN C FOODS IN AMERICA



ORANGE
1 cup juice/122 mg.



PEPPERS
1 cup (diced)/192 mg.



LEMON
1 cup juice/122 mg.



PARSLEY
1 cup/103 mg.



STRAWBERRY
1 cup/88 mg.



CAULIFLOWER
1 head/671 mg.

given high doses of vitamin C,

Another possible site of action of Vitamin C in heart disease is inside the heart-muscle itself, where the vitamins may affect the ability of the cells to survive a poor blood supply. In recent years it has become recognized that "coronary thrombosis" is often the *result* of a heart attack rather than its cause and that the precipitating event, particularly in the case of sudden death, may be metabolic rather than vascular. In 1757, Lind reported that sudden-death was a common occurrence in men with scurvy. Nearly two hundred years later, two of the subjects in a British scurvy experiment in 1945 had to be withdrawn from the trial because of acute cardiac symptoms. It therefore seems theoretically possible that heart-muscle cells which are fully saturated with Vitamin C may be less vulnerable to a poor blood supply than heart cells with a low or borderline vitamin C content. It must be re-emphasized that these intriguing theoretical speculations and isolated favourable reports should not be accepted, uncritically, to justify indiscriminate Vitamin C therapy in heart disease, but should rather be used as the starting point for precise and well-designed studies.

IN CANCER

Although cancer is responsible for fewer deaths than diseases of the heart and blood vessels, it generates considerably more fear and anxiety. This, combined with the often slow progression of the disease, has led to cancer being a prime target for "quack" cures. The suggestion that vitamin C may help to prevent or cure some cancers, therefore, tends to arouse even more cynical amusement than do some of the other claims for this extraordinary chemical. Yet, once again, such a reaction is unjustified, since there are at least three ways in which an extra intake of Vitamin C *may* help to reduce the impact of this dread disease.

First, the initial step in the development of some cancers could theoretically be blocked by an adequate concentration of Vitamin C. The formation of

carcinogenic substances in the body sometimes involves the oxidation of harmless precursors. Thus, it is not altogether unreasonable to postulate that a reducing agent such as ascorbic acid might prevent this oxidation transformation from taking place. The best known example of this potential use of vitamin C is in the prevention of nitrosamine formation from the nitrates used in curing bacon. As an anti-oxidant, vitamin C should also help to neutralize free radicals, those highly reactive molecular fragments that may be the link between ionising radiation and cancer (see Tappel, *op. cit.*).

Second, an increased intake of vitamin C may be needed to maintain saturation in the face of the stress of illness. This could be particularly important in the case of cancer wherein the stress of treatments such as surgery, chemotherapy, and radiotherapy is significant. Whether the maintenance of saturation will result in a measurable improvement in the quality or (quantity of life for the cancer patient is not yet known, but it should be relatively easy to carry out some appropriate trials.

The third way in which Vitamin C may *possibly* be useful is as an anti-cancer drug when used in huge doses of 10, 20 or 30 thousand mg per day. Most of the recent studies in this area have been stimulated by the ingenious theorizing of Ewan Cameron, a Scottish surgeon. Some years ago he developed a hypothesis about the nature of cancer that focused on the ground substance surrounding the cell, rather than the cell itself. He argued that any cell will multiply rapidly if it is in isolation, and that in normal tissues the ground substance acts as an inhibitor of this uncontrolled (i.e. "cancerous") growth. Hence, for a cell to reproduce, it has to make room for itself by dissolving away some of the ground substance, and it does this by secreting the enzyme, hyaluronidase. This process is normally controlled by a substance circulating in the blood, called "physiological hyaluronidase inhibitor" (PHI).

Later, Douglas Rotman pointed out that the dissolving of the ground sub-

stance was essentially the same process that occurs in scurvy. Furthermore, he added, that part of the PHI molecule was remarkably similar to ascorbic acid. Cameron and Rotman reasoned that large quantities of ascorbic acid might help to inhibit the erosion of the ground substance around cancer cells, and thereby slow down their rate of multiplication.

This attractive theory has yet to be tested by rigorous, unambiguous, clinical trials, but some encouraging preliminary results have been reported. In these a number of terminal cancer patients have experienced relief from pain, and others have apparently survived for a significantly longer period than might otherwise have been expected.

It must again be stressed that an attractive theory and encouraging early results are never enough to justify uncritical, widespread adoption of a new treatment. The history of medicine is replete with treatments that failed to live up to their early promise. However, the risk/benefit ratio relative to the severity of the disease as well as to other available treatments in cancer is so heavily weighted in favour of Vitamin C in this situation that validation or refutation by other groups will presumably occur quite quickly.

"OPTIMUM DAILY REQUIREMENT"

In the opening paragraph of this article, the claims of Pauling and Stone were contrasted with the recent reduction in the Recommended Dietary Allowance from 60 to 45 mgm of vitamin C by the United States Food and Nutrition Board. The contrast is, however, not quite as extreme as it may appear at first sight, since the RDA is, by definition, only intended to meet the *known* needs of *most* people. In this sense, an RDA of 45 (or even 30) mgm of vitamin C is, perhaps, overly generous, in that 10 mgm is enough for most people to completely prevent scurvy—the only disorder that is definitely *known* to be due to inadequate vitamin C intake.

In the present state of uncertainty the possibility that a higher intake of vitamin C *might* be beneficial could perhaps

best be handled by publishing a separate figure for an 'optimum' or 'prudent' intake. This would need to represent a reasonable compromise between possible benefits and possible hazards. In the present state of knowledge it should probably be limited to the amount necessary to maintain saturation. This, as mentioned previously, is unlikely to be much higher than 120 mgm (and the average may well be closer to 100 mgm) for a person in normal health. Since there needs to be some allowance for individual variation, a figure of 150 mgm a day, for an adult might be appropriate. One advantage of having saturation as the goal is that it draws attention to the desirability of an increased intake of vitamin C at the time of illness or other stress. The potential hazard of this level of intake is likely to be close to zero.

Higher intakes than those necessary to produce saturation may eventually prove to be desirable in certain situations, but until we have a clearer idea of the benefit/risk ratios involved, such "mega-vitamin" dosages should only be used on a short-term or experimental basis, or where the potential risk is far outweighed by the nature of the disease being treated. Here, cancer is a good example.

ABNORMAL NORMALS

The need to allow for individual differences in absorption, metabolism, and excretion is at the heart of some of the current vitamin C controversy.

Roger J. Williams, of the University of Texas, has argued, forcefully and with some justice, that we tend to think too often in terms of averages, that we often ignore the great deal of "biochemical individuality" that may affect individual nutrient requirements (see "We Abnormal Normals" R. J. Williams, *Nutr. Today* 2:4, p. 19, 1967). However, most biological characteristics seem to vary within reasonably narrow limits and the coefficient of variation (standard deviation as a proportion of the mean) of physiological variables usually lies between 10 and 15%. The range of values that will include 95% of a population is therefore usually from 70-80% up to 120-130% of the mean (i.e. plus and minus two standard deviations). This is less than a 2-fold variation. A 3-fold variation would cover more than 99% of the population. In light of this, the suggestion made by Williams, and endorsed by Pauling and Stone, that the

human requirement of vitamin C probably extends over a forty-fold range seems rather unrealistic. This is especially true since in human experiments with deliberately induced scurvy, the critical intake appears to have been over quite a narrow range, namely, from around 3 to 6 mgm a day.

At the same time it must be admitted that a forty-fold difference in requirement is theoretically possible in rare individuals who have some genetic abnormality. After all, even the 99% range excludes, by definition, 1% of the population.

It is equally likely that there are also rare individuals with an unusual sensitivity to high doses of vitamin C, so that widespread consumption of very large doses would probably not be an unmixed blessing. In support of this is a report from Australia that, although most people studied were able to consume large quantities of vitamin C without much change in their urinary output of oxalic acid (a breakdown product of ascorbic acid), one individual showed a very large increase. Such an individual must have had some unusual metabolic pathways for ascorbic acid, and could conceivably have developed various metabolic problems as well as having an increased risk of forming oxalic acid kidney stones, if he had continued to take large quantities of vitamin C.

Among other factors that could affect the optimum intake of vitamin C is, as mentioned earlier, 'stress'. This may include emotional as well as physical stress, and could occur in chronic as well as acute stressful situations. Persons with chronic diseases, therefore, probably need higher intakes than healthy individuals. And if this is so, then hospital patients with acute or chronic illnesses should receive an extra allowance. (A recent study in England suggests that even bed-sores, that bane of chronic-care hospitals, may heal more rapidly when bed-ridden patients receive extra vitamin C). It must also be borne in mind that if an individual has developed very low body stores they may require a high dose to reach saturation quickly. Thus, to move from a body pool of 1000 to 4000 mgm would require 30 days at an extra 100 mgm per day, even assuming complete absorption and retention.

On the other hand, after doses of 1000 mgm or more each day have been taken

for more than 1 or 2 weeks there should be a gradual "weaning" off the dose over a 1 or 2 week period in order to avoid the withdrawal depression of blood-ascorbate levels seen in persons who have become accustomed to a very high intake.

One may sum up what has been said in this effort to sort out the various popular ideas about vitamin C that the vitamin is almost certainly more than just an "a-ascorbic" substance. In order to properly define its benefits and limitations there will need to be much more research in human subjects. This research may need to involve large numbers of people enduring prolonged periods of observation because some of the effects of the substance may be subtle or hard to measure. Some of the claims may well prove to be unfounded. Nonetheless the effort should be made, particularly in those diseases where currently available treatments are unsatisfactory. In these, even a partial success may be valuable in both economic and humanitarian terms.

Meanwhile, what, if anything, should the concerned individual do about the current vitamin C controversy?

First, he or she should avoid becoming an extremist. It is very easy to accept all claims uncritically, or to reject all claims out of hand because this only helps to perpetuate and fossilize the controversy. We should aim to be open-minded but not naive; skeptical, but not cynical.

Second, as far as personal intake is concerned, the safest thing is to follow current nutritional guidelines and include plenty of fresh fruit and vegetables in the diet. This should give one an intake that is well in excess of the RDA, and should keep them at or close to saturation if they are in normal good health. At times of illness, it is best to increase intake of vitamin C to, say, 500 mg a day. This is only a "guesstimate": more research is needed. If a person chooses to experiment with higher doses, say in the thousands of mg per day, they should bear in mind the facts that the potential for undesirable side-effects increases with dose and duration; if a person has been on high doses for more than 1 or 2 weeks, the body will have become used to the high dose and will need to be 'weaned' off slowly to avoid a rebound fall in blood level.

This is the current status of Vitamin C in the eyes of one observer. ©