The Genesis of Medical Myths

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A medical myth is an aggressive defensive device used by orthodox medicine to retain the status quo and impede progress in the introduction of new and valuable therapies. It is the same technique and disorganized thinking as that used by the surgeons of a century ago in savagely refusing to wash their hands before performing surgery.

The myth originates in some inadequate sloppy in vitro or animal experimental work from which unwarranted broad conclusions are drawn as to possible effects on man. There is never any hard human evidence involved, just pure speculation. The second step is that the news media pick it up and being more interested in sensationalism than in facts, magnify these speculations and terrify a gullible public. Further repetition of these unwarranted conclusions by the medical press gives them the status of medical dogma to be quoted and requoted.

Megascorbic and megavitamin preventive medicine and therapy has been particularly subjected to this sort of attack in the past. Three more biased reports have recently appeared which will form the basis of future attacks. They suggest that "massive" doses of ascorbic add will cause cancer, will cause gout, and will cause scurvy in infants of mothers consuming these doses. These speculations will surely be accepted, not as ideas, but as facts, and the public will be solemnly warned to avoid these high dangerous doses. This, in spite of 23 years of clinical observations (AH) on several thousand patients consuming "massive" daily doses of ascorbate, which have failed to reveal a single case of scurvy in infants or any serious toxicity because of this ascorbate intake (Hoffer, 1971). For this reason it is essential to examine closely the three reports.

The publication in the April 22, 1976, issue of Nature, by Stich et al. (1976) of the paper, "Mutagenic Action of Ascorbic Acid," has started a new wave of unwarranted criticism and sly innuendo against the use of "mega" doses of ascorbate in humans. Even the title of their paper is biased and misleading, because they promptly show that ascorbic acid is harmless and not mutagenic and only becomes so when it is chemically oxidized or mixed with soluble copper ions, "in vitro." The responsibility for this unconscionable laxity in title must be shared both by the authors and the editors of Nature.

It has been known for many years that the oxidation products of ascorbate are toxic to humans. In fact, the main reason that the several oxidation-reduction

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(O-R) systems were evolved during the early evolution of life on this planet (Stone, 1972) was to maintain the O-R potential of the protoplasm at the optimal low levels and protect it from oxygen toxicity. This protection was so important that many biochemical systems were evolved for this purpose. They include, besides the ascorbate-dehydroascorbate system, back-up systems like the sulfhydryl-disulfide, the cytochromes, the reduced polyphenol-oxidized polyphenols and other sul-fhydryl-containing proteins rich in cysteine. One-and-a-half grams per Kg of dehydroascorbic acid —the oxidized form—will produce-diabetes in rats. This is prevented by the presence of reducing compounds such as the sulfhydryls. Stich et al. found:

(1) Ascorbic acid alone and "not oxidized" did not have any mutagenic effect.

(2) Cultured human fibroblasts treated with oxidized ascorbate or with a mixture of ascorbic acid plus the oxidation catalyst cupric sulfate for two hours increased DNA fragmentation and in-Creased repair synthesis and chromosome aberrations. Cupric sulfate alone had no effect. Flushing nitrogen through the ascorbic acid solution neutralized the effect. The amount of oxidized ascorbic acid required is high compared to the amount of a known mutagen.

These findings prompted these authors to conclude "the potential mutagenic capacity of ascorbic acid products should be taken into consideration when a potential health hazard, due to the addition of relatively large quantities of vitamin C to food products which contain nitrosamine compounds, is evaluated."

But they also caution, "It is difficult to evaluate the degree of genetic hazard posed by vitamin C, its decomposition products and its interaction with metal ions in man."

"A too simple application of these in vitro data to man can lead to erroneous conclusions. Catalases may inhibit ascorbic acid-initiated DNA cleavage within the human body. Metabolic products of ascorbic acid may reach the intranuclear DNA molecules only if present in excessive amounts. The ascorbic acid-metal mixtures may have no effect because of the lack of free cupric or ferric ions within the cells."

As is often the case, a finding made from pure cells in pure culture which indicates a possibility of a deleterious effect is immediately translated by many as an event which will occur with a high degree of probability. This preliminary report which still must be checked by other laboratories will be jumped upon with enthusiasm by those who erroneously believe that doses of ascorbic acid are useless therapeutically, therefore it is fair game to use every possible shred of evidence, no matter how slender, to damn these high doses.

This has already happened, and in a few days we have received worried letters from correspondents, physicians, and patients. For example, it was reported in the **New York Times** that Dr. R. San, not a clinician, suggests that people should avoid massive doses of vitamin C. But he does not define what a massive dose is. Also in the Swedish paper **"Sydsvenska Dagbladet"** for May 21, 1976, the headline is "Too much C-Vitamin can cause cancer." Under the lead it says, "If you eat too much of the C Vitamin you will run a risk for cancer. This is claimed by a team of Canadian researchers." There was a second headline, "Do not prevent colds with C-Vitamin." "It can be dangerous to eat too much of the C-vitamin. It can cause fetal cancer and fetal malformation." The June 17, 1976, **New York Times** carried an article headlined, "Researchers find large doses of Vitamin C may damage gene material." The **N.Y. Times News Service** distributed this article, so it also appeared in many smaller local papers.

These are samples of how a simple finding is finally presented to the public. The newspaper conclusions are, of course, nonsensical.

It is clear that ascorbic acid alone (free of oxygen and free of ionized copper) is nontoxic. It is equally clear that ascorbic acid is readily oxidized by oxygen when

catalyzed by cupric ions. This is why flushing out the solution with nitrogen prevented any effect. We can then conclude that, not ascorbic acid; but some of its oxidation products are weak mutagens.

Because of a 60-million-year-old genetic defect, humans have been deprived of the ability of making their own ascorbate in their livers. The other mammals for the past 165 million years have been making it in large daily multigram levels, in the daily range that Stich et al. and others consider "dangerous." Ever since humans and their hominid ancestors have been on this earth they have suffered constantly and severely from this genetic defect that prevented them from adequately protecting themselves against this oxygen toxicity and other forms of stress. One of the main reasons for supplying these large daily doses of ascorbate to humans is to correct this genetic disability and keep the ratio of oxidized products of ascorbate at a minimum by having an adequate large excess of the reduced form of ascorbate always present. In case anyone has forgotten their elementary facts of physical chemistry, it is the ratio of the components of an O-R system that determines the O-R potential, and healthy human tissues demand a high ratio of reduced ascorbate and a low ratio of the oxidized forms.

Stich et al. in their research protocol flew in the face of these facts and rigged their experimental conditions to make sure the ascorbate was thoroughly oxidized. Their few "in vitro" tests showed that the reduced ascorbate was virtually non-mutagenic, while their oxidized forms showed the effect they were looking for. This is something that the physiology of the mammals has known for the past 165 million years.

The mammals found this out 165 million years ago and have been producing ever since the high levels of ascorbate that the doctors consider "dangerous." When the mammals appeared they had to make more ascorbate to survive. They did this by changing the site of synthesis of ascorbate from the small kidneys to the liver, the largest organ in the body (Stone, 1972), and also developed a new physiological feedback mechanism to produce more ascorbate under stress (Subraman-ian et al., 1973). Any mammal that couldn't do this didn't survive and became extinct. Can anyone argue with the results of this "in vivo" test that has been going on for 165 million years?

While we are on the subject of evolution, humans also evolved another protective mechanism against oxygen toxicity by conserving and reusing the bare subsistence levels of ascorbate that are normally found in their bodies as a result of their genetic defect. A human enzyme utilizing sulfhydryl cofactors is present which converts oxidized ascorbate back into the reduced form as long as sulfhydryl compounds are available. This, of course, was not a part of Stich et al.'s experimental "in vitro" protocol.

The summary of the paper, "Association between drugs administered during pregnancy and congenital abnormalities of the fetus," Mathilda M. Nelson, John O. Forfar (1971) contains the statement, "On the other hand, deficiencies such as those of ascorbic acid and folic acid may have a teratogenic effect." Another "in vivo" bit of evidence in favor of ascorbate.

While Stich et al. suggested caution in applying their "in vitro" test results on tissue cultures and typhoid bacteria to "in vivo" conclusions in humans, such warnings are never heeded by the press. They are more interested in sensationalism at the expense of facts. The damage has already been done in the public mind with the newspaper articles stating that large doses of ascorbate increase the risk of birth defects and cancer, when just the opposite is the truth. The 1971 paper showed that birth defects increase from a deficiency of ascorbate, and recent work on cancer shows that large doses of ascorbate are being used to prevent and treat cancer successfully (see article on cancer by Stone, this issue.)

The choice of test material in Stich et al.'s Table 2 (salmonella typhimurium) was poor because of ascorbate's known

toxicity for typhoid-type bacteria and the many references where ascorbate has been used therapeutically in typhoid fever (Stone, 1972a).

From the in vitro findings, which still must be validated, there is a mega leap to conclude that dosages commonly used will cause cancer in man. There has been no report anywhere in the literature that this has occurred. There is little doubt that if there were even a single case, it would have been reported in the medical literature and widely disseminated in the press. On the contrary there are a number of reports that ascorbic acid has anticarcinogenic properties. Who is one to believe—a tentative suggestion based upon a study of cells "in vitro" which still requires a lot of investigation, or the vast cumulative experience of thousands of physicians on millions of people among whom not a single case of cancer attributable to ascorbic acid has been found? Also clinical evidence is accumulating that large doses of ascorbate can prevent cancer and is used in cancer therapy.

In a second similar type of paper Stein et al. (1976) summarized the results of their research as follows: "Two to six hours after the ingestion of 4.0g of ascorbic acid, the fractional clearance of uric acid increased to 20.2%—21% of the control value." "Ascorbic acid did not diminish protein-bound uric acid. In 3 subjects who ingested 8.0g of ascorbic acid for 3 to 7 days the serum uric acid decreased by 1.2 mg to 3.1 mg/dl as a result of a sustained uricosuria." "Theoretically it could precipitate attacks of gouty arthritis or renal calculi in predisposed persons."

Ascorbic acid is relatively nontoxic. In this way it does not resemble any of the drugs normally not found in the body. In order to establish it as a drug, since physicians are unused to dealing with nontoxic nutrients, elaborate attempts are made to convert theoretical dangers into real ones. In sharp contrast real therapeutic effectiveness is downgraded on theoretical reasons.

The fact that a single dose of 4 g of ascorbic acid increases excretion of uric acid and that 8 g per day does the same over a period of time ought to be a cause for rejoicing since it suggests that a new treatment for gout is possible. The modern treatment for gout calls for a reduction of serum uric acid levels. In fact these authors in a personal communication to AH had thought of this, but concluded that because of the large amount required it would be no cheaper than standard uricosuric drugs. But there is no reference whatever in this paper to the possible benefit and instead we are warned that "diminution in the serum uric acid may precipitate acute gouty arthritis in predisposed individuals."

One of us (AH) has used doses of ascorbic acid from $1^1/_2$ to over 10 g per day on perhaps several thousand patients since 1952. Never has there been a single case of gout precipitated in any individual. Two were patients who now and then suffered gouty attacks before they started on ascorbic acid and after, but at no increase in frequency. We would therefore conclude that the real probability of ascorbic acid inducing gouty attacks must be much less, if it occurs at all, than the natural incidence. When the first case appears where it is shown that the gout has been caused by ascorbic acid, then it will be time to look at it as a potential hazard.

In the biased nomenclature used in their "Discussion" on page 387, the authors speak of "chronic administration of 8 g of ascorbic acid per day." What they consider as "chronic" only happens to be a period of eight days, but even in this short time the serum uric acid levels were reduced about 30 percent from the starting values. What would have happened to the serum uric acid levels if the ascorbate administration was really "chronic" and continued throughout the subject's entire lifetime? Besides eliminating the chronic subclinical scurvy that afflicts all who are not taking many grams of ascorbate daily, its long-term uricosuric effect may have a very salutary action in preventing gout. The end product of purine metabolism in humans, uric acid, is different from most

other mammals because of the genetic lack of the enzyme uricase in Man. This is the enzyme that converts the rather insoluble uric acid into the more soluble allantoin. Research should be started to determine whether the chronic daily use of megadoses of ascorbate can catalyze the non-enzymatic transformation of uric acid to allantoin in Man. If it can, then the uric acid-stone formation problems would be solved.

In another ascorbic acid study, Norkus and Rosso (1975) examined the idea that high intake in pregnant guinea pigs would make the offspring more vulnerable to scurvy when placed upon a scorbutic diet.

Control group animals were given 25 mg of ascorbic acid daily (in human terms 3,500 mg per 70 kg human, assuming the experimental guinea pigs weighed about 500 g). They calculated that 300 mg per kg in the guinea pig is equivalent to 1,500 mg per human because there is a faster turnover in the guinea pig.

The ascorbic acid was added to the feed. They do not say how frequently the animals were fed, but it is logical to assume that they ate ad libitum, i.e., nibbled throughout the day as do rodents when food is freely available to them.

From Day 11 after birth the pups were caged individually and weaned onto the ascorbic acid-free diet. They were weighed and examined every third day for physical signs of scurvy. This was not done double blind. Once signs appeared they were examined every day.

As one would expect, the animals with higher ascorbic acid levels metabolized more as measured by radioactive CO_2 release studies.

There was no difference between the groups in weight gain, but animals from high ascorbic acid mothers developed scurvy about four days earlier—in about 18 days compared to about 22 days for the other pups. The variation was four times as great for the first group, i.e., 0.96 compared to 0.21 S.E. for the control group. Four of the nine high ascorbic acid group developed scurvy in about 22 days.

The high ascorbic acid group died in about 22 days compared to the control group which died in about 31 days.

On the basis of this work Norkus et al. concluded that "although one can not directly extrapolate these results to the human, because of different modes of ascorbic acid catabolism in guinea pig and Man, the results clearly support Cochrane's hypothesis that an ascorbic acid dependency in the young could be induced by exposure to high levels of this vitamin in utero." Then they advise "massive doses of ascorbic acid during pregnancy should be discouraged."

The emphasis in their conclusion is wrong. In our view these experiments with guinea pigs suffer from the following methodological errors: (1) The control group also received massive doses of ascorbic acid. It is amazing that modern diets for guinea pigs include daily doses of ascorbic acid in the range which we have been recommending. The usual megadoses for human adults are from 3 to 20 g per day, and only for severe stresses and deadly diseases such as viremias, cancer, and so on are doses larger than these used. The authors state that 300 mg per kg per guinea pig is equivalent to 1,500 mg per human adult, so why in designing their experimental protocol did they not use the guinea pig equivalent of the human RDA of 45 mg ascorbate per day for their control group, which calculates to 9 mg per kg? The weights of the guinea pigs were not given; if we assume they were closer to 500 g than a kilogram, then each control pig should be receiving 4.5 mg ascorbate per day instead of the 25 mg given. Did they use over 500 percent more than the RDA equivalent because they realized that the guinea pig mothers and pups may not have survived the stresses of pregnancy and birth on the bare subsistence levels recommended for humans?

Norkus et al. completely disregard the clinical work of Klenner (1971) in over 300 cases of human pregnancy and childbirth, in which the mothers were given throughout pregnancy, labor, and postpartum, 4 to 15 g ascorbate daily. Most

also received a booster I.V. shot of 10 g of ascorbate on entering the hospital for labor. This resulted in great clinical benefits in avoiding the usual clinical problems of maternal health and labor and produced exceedingly robust healthy babies.

Any obstetrician following Norkus et al.'s advice contained in the last sentence of their paper, "massive doses of ascorbic acid during pregnancy should be discouraged," based on their highly theoretical, scant guinea pig evidence, and ignoring Klenner's exciting practical clinical data on humans, would seem to be skirting the borderline of malpractice by withholding beneficial information and depriving patients of the great health and life-saving benefits of mega-doses of ascorbate.

In the discussion following the presentation of the Norkus et al. paper at the New York Academy of Sciences conference, Dr. C. W. M. Wilson of Dublin, Ireland, commented in part, "However, to draw such a conclusion for human beings seems completely wrong, because when a mother produces a child she does not deliberately expose him to scurvy by stopping ascorbic acid intake. Therefore, I think your conclusions for the latent human being are completely unjustified."

Dr. Pedro Rosso, the co-author of the guinea pig paper, quibbled in answering Dr. Wilson's comments by stating, "The only conclusion we are drawing is if you feed high intakes of ascorbic acid during the last 30 days of pregnancy in the guinea pigs, the pups develop signs of scurvy earlier when they are put on a deficient diet." If nothing else, Dr. Rosso set quite a speed record in disclaiming responsibility for statements presented only minutes before regarding the in-advisability of pregnant women taking large doses of ascorbate.

The authors of all these three highly critical reports still do not realize that in scurvy we are not dealing with a simple nutritional disturbance, but with a potentially fatal genetic liver-enzyme disease, Hypoascorbemia, whose terminal sequelae are what Medicine now regards as "scurvy." The terminal symptoms can be allayed by the RDA of 45 mg of ascorbate, but this is far too little to fully correct this human genetic defect. This RDA leaves the victim suffering from chronic subclinical scurvy throughout life and is our most widespread disease (Stone, 1972b). To fully correct for this genetic defect requires amounts of ascorbate similar to that normally produced in the livers of other mammals each day. On a 70 kg body weight basis, this is in the range of 10 to 20 g per day (Chatterjee, 1973), so for humans this is not a "high" intake, but is the "normal" intake.

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