Massive Vitamin C as an Adjunct in Methadone Maintenance and Detoxification

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Vitamin C and Physiology

Scurvy, an ancient plague, was mentioned by Hippocrates as the cause of debility, bleeding gums, and hemorrhages. Cities under siege, as well as ships at sea, were often devastated by this progressive and undefinable entity. During the Crusades, St. Louis and all of his knights were said to have been defeated and captured because of scurvy. During the 1497-98 voyage of Vasco de Gama, 100 of his crew of 160 died of scurvy, and in 1577, a Spanish galleon was found adrift with all dead of the disease. A story goes that on one of Columbus' trips, a number of Portuguese sailors were put ashore to die of scurvy. However, on a return trip, these men were found to be alive and healthy since they had out of desperation and hunger eaten the local wild plants and fruits they found on the island which subsequently came to be called Curacao, meaning "cure" in Portuguese.

James Lind, a Scotch physician, published his Treatise on Scurvy in 1753, which demonstrated that the disease could be abated, cured, or prevented through the use of citrus fruits, and 50 years later the British Navy, in 1795, ordered a daily ration of citrus fruits for its seamen, thus eliminating this fearful condition.

Classical scurvy has been described many times. It includes general debility, weakness, restlessness, irritability, pale complexion, sunken eyes, tender bleeding gums, muscular and joint tenderness, and pain. There is often anemia and due to capillary and collagen fragility, a tendency to bruise. There will be eventually bony weakness and loss of teeth. Night blindness and other visual disorders will occur as well as a tendency to easy fractures. Finally, adrenal exhaustion, lung, kidney, and liver damage terminate in death.

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Physiologically, the functions of vitamin C are still very much up in the air. Ascorbic acid and dehydroascorbic acid form a readily reversible oxidation-reduction system. Both the oxidized and reduced form of the vitamin are equally effective antiscorbutically. Vitamin C has been implicated in cellular respiration. It can be oxidized by cytochrome oxidase plus cytochrome C. Dehydroascorbic acid can be reduced by glutathione. Ascorbic acid is important in maintaining SH-activated enzyme systems in their reduced form, and it can act as a hydrogen donor. Vitamin C is important in tyrosine metabolism, since it protects the enzyme, P-hydroxyphenyl-pyruvic acid oxidase, from inhibition by its substrate. Ascorbic acid is also involved in carbohydrate metabolism, since scorbutic animals exhibit hyperglycemia, reduced glucose tolerance, low hepatic glycogen content, and are resistant to insulin. Vitamin C is also important in the conversion of folic acid to folinic acid (Goodman and Gilman, 1970).

Ascorbic acid is highly concentrated in the cortex and medulla of the adrenals. In the latter location it tends to prevent the oxidation of epinephrine. Under the stress of administering ACTH, there is an increased secretion of adrenocorticoster-oids, associated with a rapid decrease in the amount of adrenal ascorbic acid and cholesterol. The mechanism for the relationship between ascorbic acid and intercellular ground substance and collagen is unknown. But a recent theory suggests that there is a direct effect on collagen-synthesis by facilitating the conversion of peptide-bound proline to hydroxyproline (Jeffrey and Martin, 1966).

In other words, at the present time, we are very little further ahead concerning our understanding of the effects of vitamin C upon such conditions as scurvy than were the early sailors who accidentally discovered the empirical relationship between limes and the cure and prevention of the condition. Much of what happens in medicine, as most of us well know, is often a matter of art, accident, lucky guess, intuition, or chance observation. And it may well be that the tale we will tell here falls in one or several of these categories.

In a series of papers, Irwin Stone (1966, 1966a) proposed a concept of "hypoascorbemia" as a kind of human genetic insufficiency. It has, further, been known for some time that man, other primates, and the guinea pig are the only mammals known to be unable to synthesize ascorbic acid. Burns (1954) has suggested that these species lack the hepatic enzyme necessary to carry out the conversion of L-gulonolactone to L-ascorbic acid, because of a gene-controlled enzyme "deficiency." Linus Pauling in his book **Vitamin C and the Common Cold** (1970) picked up the suggestion given by Stone, and following earlier studies of Cowan et al. (1942) suggested that vitamin C was essentially a specific preventative in the development of the common cold. Stone went further, in his book **The Healing Factor: Vitamin C Against Disease** (1972), and indicated that this agent was mandatory in the prevention, mitigation, or cure of a great number of other conditions not readily accessible to more specific treatment.

It has been known for some time that there are individual variations in biochemical needs. In fact, Professor Roger Williams has, a number of years ago, written an important book, **Biochemical Individuality** (1956), stipulating this fact. For example, he stated:

"Some inbred rats on identical diets excreted eleven times as much urinary phosphate as others . . . some voluntarily consumed consistently sixteen times as much sugar as others . . . some appeared to need about forty times as much vitamin A as others . . . some young guinea pigs required for good growth at least twenty times as much vitamin C *as others."*

Rosenberg and Feldzamen **(The Doctor's Book of Vitamin Therapy,** 1974) report that in a group of geriatric patients suggesting mild scurvy, 700 mg of vitamin C daily initiated improvement. However, despite regular checks for

urinary vitamin C, it took three weeks for the ascorbic acid to appear in the urine. This is echoed by a recent report by E. S. Wagner (1973) who found that despite the fact that the usual claim is that excess vitamin C is readily excreted, only about half appears in the urine. There seems, therefore, to be an unknown reservoir for storing the vitamin with which we have not been familiar before.

Food, Drug, and Environmental Allergies

In 1945, Coca published the first of a series of reports by a number of authors discussing what he called **Familial Non-Reaginic Food Allergy** (Coca, 1950). Rinkel et al. (1950) amplified this in their discussion of food allergy. And Randolph broadened the whole concept considerably in his discussion of **Human Ecology and Susceptibility to the Chemical Environment** in 1962 (Randolph, 1962).

Food allergies, ecological mental illness, ecological allergies, etc., are various names for an unusual and rather poorly defined class of conditions which are of untold importance and devastating effect in an advanced society such as ours. All of the contaminants, pollutants, preservatives, drugs, and other agents with which we are continually bombarded have been having a disastrous effect upon man, only barely currently recognized. As noted above, a number of studies and much clinical observation bear out the reality of the food and environmental allergic conditions which relate to none of the ordinary allergic conditions with which we are medically familiar. They do not generally produce hives and rashes, but their effects are very real nonetheless.

These hypersensitivity reactions have a rather characteristic history and effect. Generally speaking, the individual tends to progressively prefer exposure to the implicated agents. For example, he may be a "chocolate addict," or a "potato-chip fiend," or some other chronic persistent user of the very agent that tends to, in the long run, produce the damage. We are all familiar with people who progressively require more and more cigarettes, more and more coffee, etc. Initially, these agents, whatever they may be, will be merely foods, or relatively innocuous substances. However they will progressively take on the quality of becoming demand substances. That is, the individual will feel that he *must* have a smoke, or a cup of coffee, or whatever it may be to "get him started in the morning." This idea that the particular agent is stimulating is an accurate one, at least initially. However, as the hypersensitivity process progresses, a number of rather surprising effects will develop.

The allergic and addicted individual, as well as developing the compulsive need for the offending agent, will begin to suffer a number of withdrawal effects in the absence of the agent. He will feel irritable, tense, perhaps begin to sweat, develop muscular tensions, joint pains, cold hands and feet, as well as tense and restless hands and feet. He will find that most of these symptoms will be alleviated initially by the use of whatever the sensitizing substance may be.

Should he persist in the chronic misuse of the particular agent, or agents, he may discover a number of additional symptoms beginning to develop as well. There will be a tendency toward acute and chronic exhaustion and tiredness despite the use of what had previously been a stimulating and relieving agent. There will be a kind of "brain fag," in which will occur problems of retention of recent events and experiences, as well as difficulty in holding, conceiving, and developing ideas, as well as finding and using the right words. There will generally be a progressively reduced level of effective functioning intellectually. There may also develop a number of physical symptoms, including reduced libido, impotence, constipation, cold clammy skin, inefficiency in finer movements of limbs, a general awkwardness, and any number of frequently called hypochondriacal complaints. For example, there may be headaches resembling, imitating, or conceived as migraine, pains of chest, stomach, back,

and other body parts. These will often call down the unfortunate medical epithet of "crock," and cause such patients to wander peripatetically from doctor to doctor and nostrum to nostrum.

Unfortunately, many of these nostrums will include tranquilizers, amphetamines, barbiturates, sedatives, and even at times narcotics, as well as unnecessary operations for nonexistent conditions. There is a kind of conspiracy which condemns such patients in their desperate and fruitless perambulations from physician to physician and clinic to clinic until they are finally called chronic neurotics or chronic psychotics.

It has been due to the efforts of several heroic and generally insufficiently recognized specialists in this area that at least a number of these patients have been spared the necessity of perpetual and unhappy pursuit of their illness. This is particularly disturbing since such conditions are strikingly easy to diagnose and incredibly easy to treat.

Diagnosis is based largely on history. For example, a patient chronically exposed to a particular agent will usually be able to tell you so. He will say that he is addicted to, or constantly finds himself compelled to use, this or that food, etc. Or in taking a work or environmental history of him, you will find that he is persistently exposed to a petroleum product, a gas, etc.

A recent example of this phenomenon received worldwide attention when Ben Feingold, an allergist at California Kaiser-Permanente Medical Center, reported on 25 hyperkinetic school children. These children who were uncontrolled and uncontrollable at school and at home, he said, could be "turned on and off at will, just by regulating their diet." It was his impression that by restricting the amount of processed food which contained artificial flavors and colors, such as hot dogs, soft drinks, and ice cream, he could completely control the hyperkinetic syndrome (Feingold, 1975).

Randolph and other specialists in this field diagnose such patients by putting them in the hospital on a distilled water diet initially in order to clear out the residues of the offending agents which will take several days. Once this is done, they progressively introduce differing classes and types of foods and agents into the patient's diet so that the offending agent will, when introduced, produce a replication of the symptoms at that time. The treatment is the soul of simplicity itself. Elimination of the disturbing agent will completely resolve the condition and eliminate all of the symptoms.

What is curious about the phenomenon is that, initially, as stated above, the offending agent acts as a stimulant and the hypersensitive individual seems brighter, more physically and emotionally content with himself. Therefore he will be drawn back to the use and misuse of the agent until it begins to have its whole pathological effect. At that time, the initial stimulatory phase passes over so quickly, and the symptomatic and exhaustion phase takes over very fully. All the patient is aware of at that time is the pain, anguish, and disturbance of mind and body that he cannot seem to shake off and that no one can seem to either diagnose or help him with.

Although it is impossible to estimate accurately the number of persons afflicted with this condition, surely it numbers in the many millions. The description we have given above, for example, certainly applies to the alcoholic, who number at least 10 million. It applies to the "foodaholic," whose numbers are vastly greater. It probably applies as well to the narcotic addict, who may number as many as a million. And with the tremendous increase in offending environmental and polluting agents, one must multiply the victims of these conditions many times over.

A Personal Experience

It is not infrequent for many physicians given to sophistication, skepticism, and their predilection for what is called the "scientific methodology," to doubt the

reality of the symptom complex and the clinical phenomenology we have described above. But it is at least the very personal experience of one of us (JS) to know quite intimately the effect of the food-allergic mechanism and its deleterious and devastating personal assault. Having discovered long ago the reality of these symptoms in the course of chronic and progressive excessive use of coffee and tobacco, he knows and can attest at firsthand that these symptoms are all too real.

As a result of these discoveries, and after a number of years of suffering the condition, the individual referred to above, unfortunately unaided by medical assistance, which seemed as puzzled by his condition as was he, spontaneously discovered that the elimination of the offending agent completely cleared up the disturbing conditions. Thus he was enabled to have a period of some four or five years without the burden of these painful symptoms interrupting the course of his life. But as in all food-allergic and food-addicted patients, he was drawn back inevitably to the misuse of the offending agents, since he longed for and knew of the initial and satisfying stimulatory effects of them. Beginning again to enjoy the ecstasies —for the food addicted—of coffee (sic!) he very quickly moved into the phase of exhaustion and symptom production, a totally expected and predictable result.

But as in many scientific discoveries, serendipity and accident were to have a role. A friend, perhaps caught up in the then fashionable and still current vitamin faddery, suggested he try some vitamin C, since it might make him feel better on general principles. To his great amazement, the food-allergic individual mentioned above, after scoffing a handful of vitamin C tablets, very shortly noticed a distinct tendency toward alleviation and relief of the exhaustion, brain fag, and tension phenomena. It became possible to overcome for a considerable period of time most, if not all, of the phenomena associated with his particular food-allergic coffee addiction problem. In fact, he was able to go back to a progressively greater and greater amount of coffee misuse as he had done prior to the realization of the devastating symptomatic effects he had experienced previously. This relief was only made possible through the use of truly massive amounts of chewable vitamin C ingested by the handful almost continuously during the course of every 24-hour period. In fact, 20-50,000 mg per day was not unusual. Unfortunately, ultimately the protective effect of vitamin C seemed to diminish and be overcome by the more prominent and pervasive food-allergic symptoms, so that the individual in question was compelled again to completely abstain from the offending agent perhaps for the final time.

Vitamin C and Methadone

This purely serendipitous effect caused the individual referred to above to experiment with the use of massive vitamin C in other conditions which might be suggestive of food, drug, or environmentally allergic disturbances. For example, he experimented with the use of large doses of vitamin C to resist the effects of alcohol, as well as to reduce the degree of symptomatic tension and disturbance experienced in both the hangover phenomena in patients as well as the recovery stage of acute and chronic alcoholic intoxication and alcoholism. An abstract of some of these findings was reported in an international alcoholism meeting in Liverpool in August, 1973. Since that time Pauling has written *us* confirming these suggestions and reporting on an abstract of E. Cameron and G. M. Baird (Shute, 1956).

In a strictly empirical basis we have observed that patients in a state of narcotic withdrawal often show symptoms of irritability, muscular tensions, a tendency toward exhaustion, and other phenomena suggestive of both the food allergic syndrome as well as the magnesium depletion syndrome. We have also observed clinically, as well, that certain patients on methadone seem to react in a highly stimulated fashion,

with an almost amphetamine effect, while others may tend to be more sedated and suppressed. These are, of course, not the majority of methadone-maintained patients who, if they are not misusing other drugs, will generally be relatively "normalized" through the use of methadone. This also takes into consideration the inevitable slight high produced in the course of total single daily dose administration and slight withdrawal some 18 to 24 hours later.

It is frequently the experience of methadone-maintained patients to discover that they have a tendency toward constipation, reduction of libido, and, in many, a more restless sleep pattern. Based on the analogy of similar symptoms in the food-allergic patient, it was decided to administer megadoses of vitamin C with a suggested average of 5,000 mg per day to all methadone-maintained patients. Over the course of the past three years when this policy has been enforced, it has been found that most patients who complain of these minimal side effects of methadone treatment will be relieved of these and other annoying symptoms. For example, many methadone patients will show low-grade irritability, minor and discomforting emotionality, debility, and mood shifts. After vitamin C, these patients will seem to feel an enhanced sense of comfort and well-being.

These symptoms, though minimal and annoying, are discovered to be more disturbing than the patients had originally realized when they are relieved through the use of large doses of vitamin C. In fact, they frequently comment that they had not expected the vitamin C to do anything at all, but are quite surprised by the fact that they feel considerably better in a general way when they are using it.

Again, based on the analogy of the use of vitamin C on an empirical basis to relieve the acute and chronic symptoms of food allergy otherwise, it was decided that ascorbic acid might well play an alleviating role in the course of detoxification and methadone withdrawal. As is well known, ascorbic acid has a role in oxidative processes, collagen, muscular, vascular, and adrenal metabolism. It was therefore hypothesized that since all of these areas seem to be implicated symptomatically in the process of detoxification, ascorbic acid may very well play a role here, too.

Ascorbic Acid as a Tranquilizer

Consequently, the same regimen is a standard feature of our outpatient and inpatient detoxification process. Furthermore, it would appear that ascorbic acid seems to have a moderating and tranquillizing influence on behavior and emotional states, so that it is of great assistance in the management of patients who are in the process of detoxification. Early on, when we first began the use of ascorbic acid, a double-blind program with the use of placebos in each of these areas was employed, that is, in the withdrawal state, with minor methadone side effects and in detoxification. In each of these instances, on a clinical basis, it was clearly apparent that vitamin C had a marked effect in relieving the fatigue state, the tension state, muscular pains and cramps, vasoconstriction and cold limbs, constipation and impotence. In all of these areas and conditions, there was relief in 60-70 percent of instances, or more. The area where the relief was least successful was in that of reduced libido and impotency, where the relief was in more like 50 percent of the cases. But restless sleep and the other symptoms mentioned above were distinctly alleviated in a considerable proportion of the cases so compared. It was therefore felt that vitamin C represented a clear addition to the armamentarium of narcotic addiction treatment on a clinical and statistical basis, despite the fact that we could not demonstrate biochemically or pharmacologically what the relief was based on.

The tranquillizing effect of vitamin C was again a distinctive plus which had not been anticipated and one to which we feel more attention should be paid. If vitamin C is a mild benign physiological

tranquilizer, it might well stand in the stead of more powerful and possibly more disrupting or problematic pharmacologically tranquillizing agents as a first choice in mild anxiety states.

In fact, it may be that many so-called mild anxiety states, as well as mild depressive states, may represent subacute hypovitaminosis, perhaps more specifically the hypoascorbemia to which Stone refers (1966, 1966a). The other alternative is that many individuals suffering mild symptoms of the kind described above may be really reacting to some kind of environment or food-allergic assault at a relatively low level, and about which they have no real concept. If this is the case, and if ascorbic acid can and may be used in a fashion in which we are describing here, many of these conditions may be somewhat alleviated in their early phases, or controlled for a considerable period of time. Unfortunately, as in the anecdotal incident cited above, it may well be that the ecological hypersensitivity may outrun and overcome the prophylactic effect of the ascorbic acid eventually with the result that the patient may have to omit the use of the offending agent altogether.

Since ecological and environmental and food allergies are at this point so poorly understood, unfortunately many individuals suffering from them will not be so lucky as to be able to identify and eliminate the source of their problem. Only a much broader educational and awareness program will permit this vital necessity to occur in the future.

Vitamin E and Multivitamins

Again on a purely empirical basis, and without the benefit of a double-blind study, alpha-tocopherol, or vitamin E, was added to the ascorbic acid as part of a general program of megavitamin treatment. The scientific rationale for this is no clearer than that for the use of ascorbic acid, except that in the latter case we have clinical and statistical evidence of effectiveness. With the use of vitamin E we only have the analogy that it, too, is an antioxidant, as is ascorbic acid, and therefore we felt it might be additive in the process of alleviating some of the symptoms cited above. The work of the Shutes and others (1956) suggests that vitamin E might also be instrumental in alleviating a number of vague symptoms, many referring to the circulatory system. Clearly we cannot offer a scientific basis for the use of these agents, but we do feel that the use of vitamin E in doses of 250 to 400 international units three to four times a day will have no deleterious effect and may well be helpful in the conditions described above.

It has been our policy also to be sure that patients on methadone, in a withdrawn state and/or in the process of detoxification, also take two to four high-potency multivitamins with minerals a day such as Theragran M. Again we cannot offer any scientific basis for this, but do believe that It follows that most important rule of medicine, "premum non nocere," first do no harm. It also follows that second most important and ancient rule of clinical medicine, perhaps it will do some good. Clinically and in terms of general senses of well-being, the patients have reported subjective benefit. This is particularly conspicuous in the speed of bounceback in the postalcoholic binge or run.

Vitamins and the FDA

There is today considerable discussion about the restriction by the FDA of the general unprescribed use and overuse of poly-and megavitamins. The state of the art, and the state of our knowledge, despite the pretentions of the knowledgeable and the assertions of the faddist and the man on the street, leaves much to be desired. We do not know who is right and who is wrong. We do know that there are very real economic interests involved in the forefront and behind the scene of this presumably scientific discussion. Should vitamins be limited in ready availability and restricted to what many would consider minuscule doses, this would certainly

throw into turmoil many people deeply committed to personal megavitamin programs. Such restrictions, including the limitations of vitamins to a prescription-only basis, would also doubtless please the drug companies for whom it would mean untold millions in financial reward.

It is not our intention to get into this discussion and this argument here, but we do feel that there is a legitimate place and a legitimate use for megavitamin treatment in a rational way on a purely empirical basis. We feel that we have demonstrated the usefulness of this program to ourselves and our patients, even if scientifically much, as elsewhere, remains to be demonstrated. We also feel that our practice of megavitamin therapy may be adopted usefully by those who are involved in methadone maintenance and detoxification programs elsewhere. We have not found any of the side effects others have claimed, such as stone formation, or any involvement at all with oxalic acid in the course of this use of ascorbic acid or the other vitamins cited.

One other clinical suggestion. We feel also that attention should be paid to the use of trace elements, but have not seriously studied the effects or relationship of these to the problems of addiction. We do, however, recommend to our patients the use of kelp tablets, on general principles, since kelp is well known to have a rather adequate supply of all of the known trace elements.

Comment

Finally, we would like to make a plea for an acknowledgement of the serendipitous in medicine and science generally. Had it not been for certain personal experiences cited above, these thoroughly salubrious uses of a common vitamin would not have been developed. And if we were to wait for the methodological absolute confirmation and knowledge of why ascorbic acid operates as it does, we might have to wait a long time indeed. In fact, as is well known, we know very little about how or why aspirin does what it does, or indeed why narcotics such as
morphine or methadone do what they do. So let us hope that in the spirit of enlightened acceptance of what works, the true panchreston of medicine, we are able to accept this very practical and useful remedial measure for what it is worth in the treatment of the addictive process, methadone maintenance, withdrawal, and detoxification.

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