Eight Decades of Scurvy. The Case History of a Misleading Dietary Hypothesis.

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This paper will discuss the history of scurvy in this country over the past eight decades and try to explain how a potentially-fatal and insidious genetic disease of such wide incidence in our population could become an unrecognized, phantom disease, to which most present day doctors pay little or no attention and are unconcerned. It will also discuss the widely accepted dietary theory which has been applied by nutritionists attempting to solve this problem in medical genetics. The author believes that the wide acceptance of this misleading dietary hypothesis is the source of the medical complacency and apathy and the dangerous continuing high incidence of Chronic Subclinical Scurvy.

Scurvy is a disease which during the course of human prehistory and recorded history has killed more victims, caused more disease and suffering and has shortened the human life span more than any other single factor. (Stone, 1972). This disease has been epidemic among humans ever since they appeared on this earth. If it weren't for the high mortality of scurvy and its efficient control of population growth, our problems of over-population would have overwhelmed us centuries ago.

Many people believe that scurvy is not a modern disease because they think the problem was solved in the 18th Century when Dr. James Lind of Britain's Royal Navy (Lind, 1753) found that one ounce of fresh lemon juice would prevent the appearance of the terminal symptoms of this dread disease in his scorbutic sailors.

Others, including nutritionists, home economists and a large proportion of the medical profession believe that the minute daily doses of "Vitamin C" proposed in 1912 in the "Vitamin C-Dietary Deficiency Disease Hypothesis" (Funk, 1912) has completely solved the problem of scurvy and there is nothing further to worry about. Nothing could be further from the truth.

Let us take a look at the sequence of historical events in scurvy of the past 80 years and try to see what went wrong and what finally went right:

The first notable date in this century is 1907 which records the first important scientific advance in our knowledge of scurvy beyond what was known to Dr. Lind in 1753. Hoist and Frohlich (1907) stumbled accidentally upon this important evidence while they were investigating ship beriberi which was causing problems in the

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This paper was originally prepared for presentation at the Conference On Controversies In Human And Clinical Nutrition, Boston University School of Medicine, Hyannis, Massachusetts, July 16, 1978 and also presented at the Annual Meeting of the Orthomolecular Medical Society, September 17,1978, San Diego, California.

Norwegian Fishing Fleet.

Up until 1907, scurvy was considered to be solely a human disease because none of the animals used in medical experimentation up to that time, appeared susceptible to this disease. No matter how deficient a scorbutic diet was fed laboratory rats or mice, none ever died of scurvy. In ship beriberi the standard test animal in 1907 was the pigeon. Hoist and Frohlich wanted to use a small mammal instead of a bird so they tested guinea pigs by feeding them a diet that caused beriberi in pigeons. To their amazement they found that the guinea pigs developed scurvy instead. We now know why this is so, but in 1907 it was a complete mystery. Guinea pigs suffer from the same genetic defect as humans. The result of Hoist and Frohlich's work was to provide a small test animal that could be used in laboratory experiments on scurvy. Later, monkeys were also found to be susceptible to scurvy. Guinea pigs or monkeys are the only test animals that should be used in any medical experiments where results are to be extrapolated to humans. Rats, mice, rabbits, dogs and all other animals capable of synthesizing ascorbate endpgenously are unsuitable as test animals in this medical experimentation.

The second date is 1908. This is a date that is not usually connected with the history of scurvy, but 57 years later in 1965, the work reported in 1908 supplied the clue which placed scurvy into its rightful place as an inherited illness, a potentially-fatal genetic liver-enzyme disease. It was in 1908 that Sir Archibald Garrod, a noted English physician, who was at least 50 years ahead of his time, published his series of Croonian lectures describing a new type of disease, an "inborn error of metabolism" which is caused by a missing or a defective, inactive enzyme. As is usual with great medical discoveries, Sir Archibald's exciting concept and clinical results were ignored for forty years before being "rediscovered" in the 1950's. Now there are thousands of "missing enzyme" diseases, including "Hypoascorbemia", the actual cause of scurvy.

Four years later in 1912, nutritionists led by the Polish biochemist, Casimir Funk summarized the nutritional knowledge of the 19th Century and early 20th Century and came up with the revolutionary idea that ^ouie diseases could be caused by the lack of some trace substance in the diet. They cited three diseases as typical of these deficiency diseases: xerophthalmia, an eye disease, beriberi, a deadly neurological disease of the Far East, and the third one -scurvy. The unknown, hypothetical missing substances in the diet causing these diseases were named "vitamines" A, B and C respectively for each of these diseases. This "vitamin" hypothesis appeared to be a perfectly logical explanation of the state of the nutritional knowledge available in 1912. Later research on these diseases has shown that the results on the diseases caused by the lack of vitamin A and the B vitamins have stood the test of time better than scurvy and vitamin C.

Any hypothesis is only as good as the con-firming later research and a theory has to be revised periodically in the light of this continuing research. The research of the past 15 years has exposed serious flaws jn. the. vitamin C-Dietary Deficiency Disease

Hypothesis for the etiology of scurvy and broad revisions are required in this hypothesis to bring it in line with the current facts.

In 1912, the antiscorbutic factor was arbitrarily named vitamin C and its existence was neither proven or even known to exist at the time. There were many other theories prevalent at this time, such as that scurvy was caused by tainted meat or by constipation, so in 1912 this was a very tenuous hypothesis. It took twenty years and much intensive chemical and biological research before it was proven in 1932 that the hypothetical antiscorbutic substance, "Vitamin C" was actually ascorbic acid.

At that time the chemical structure of ascorbic acid was worked out and its synthesis was devised and for the first time in the history of mankind, ascorbate, the specific antidote for scurvy was available in unlimited quantities as the pure unadulterated crystalline product.

Before this, large quantities of fresh foods had to be used to provide precious little of this wonder substance. The potato, for

instance, which was the main antiscorbutic foodstuff of the entire population of countries like Ireland in the 19th Century, requires the ingestion of at least 44 pounds of boiled potatoes to obtain a level teaspoonful of ascorbic acid (3 grams). So you see that in the early days before the synthesis of ascorbate everyone was thinking in terms of minute food related dosages. This is why the early workers became misorient-ed in the direction of minute inadequate daily intakes of vitamin C. They could not use more because they were always limited to foodstuffs containing only minute quantities of vitamin C. Then when pure ascorbic acid suddenly became available, they could not change this enforced pattern of thinking and continued to look into smaller and smaller daily doses.

As a consequence, the nutritionists and home economists who dominated the research effort at that time, conducted test after test to find the smallest amount of vitamin C which would prevent the appearance of the Classical Terminal Signs of Frank Clinical Scurvy and still avoid death, the so-called "Minimal Daily Requirements". However, in their entire research effort since 1912 they have never conducted a single, long-term test to determine the optimal level of the daily intake of vitamin C, the amounts of daily ascorbate intake that are needed for full health and to maintain this health and freedom from disease throughout a person's lifetime. This record of research short-sightedness by the nutritionists over the past 66 years is only paralleled by the lack of hard data for setting the current Recommended Dietary Allowances (RDA) Tor ascorbate to maintain the full health and freedom from disease of the American people. The present adult RDA for ascorbate is not based on any tests or clinical data but is just a collection of guesses and assumptions. The Food and Nutrition Board that sets the official RDA's has been steadily reducing the RDA for ascorbate with each new edition of its book in face of the mounting evidence that more and more ascorbate is needed to combat the present increasing stresses of living. The present RDA's for ascorbate is at least 300 times less per unit body weight than the amount of ascorbate produced en-dogenously each day by other mammals to maintain their own bodies in a good healthy condition and fight off their stresses. This is a discrepancy that I've never seen adequately explained by the current low-ascorbate-dosage enthusiasts.

Several other grave errors have been made with this hypothesis from the early days. The classical signs of scurvy are used as a means of diagnosing "scurvy". These classical symptoms are really the terminal sequelae of Frank Clinical Scurvy and this theory ignores and bypasses the relatively asymptomatic, insidjous Chronic Subclinical Scurvy which is epidemic in our population. Another early grave error was equating good health with the mere lack of these terminal symptoms. The present RDA of 45 mg will prevent the appearance of these terminal symptoms but it won't do much for correcting the Chronic Subclinical Scurvy. This is like saying cancer victims are in good health as long as the terminal signs of the disease are not evident.

Biochemical research in the *195Cfs* showed that the lesion in scurvy is the absence of the enzyme, L-Gulonolactone oxidase (GLO) in the human liver (Burns, 1959). This enzyme is the last enzyme in a series of four which converts blood sugar, glucose, into ascorbate in the mammalian liver. This liver metabolite, ascorbate, is produced in an unstressed goat for instance, at the rate of about 13,000 mg per day per 150 pounds body weight (Chatterjee, 1973). A mammalian feedback mechanism increases this daily ascorbate production many fold under stress (Subramanian et al., 1973).

The lack of the enzyme GLOHrthe human liver completely blocks the endogenous biochemical synthesis of ascorbate and has destroyed the ability of humans to produce their own ascorbate. There are a few other mammals afflicted with this same genetic defect as humans, such as, guinea pigs and other members of the Primate Sub Or-der,Anthropoidea. Complete deprivation of ascorbate is rapidly fatal. It takes several months for humans to die from scurvy

depending upon the incident stresses, but a guinea pig succumbs in two weeks. Scurvy, therefore, meets all the criteria of the genetic diseases, the "inborn errors of metabolism" the "missing enzyme" diseases described by Sir Archibald Garrod in 1908.

In 1956-67, in a series of four papers (Stone, 1965) it was shown that scurvy was not a separate dietary disease entity but merely the premortal sequelae of a genetic liver-enzyme disease, Hypoascorbemia. Thus instead of being a simple dietary disturbance due to the lack of vitamin C in foods, the basic cause of our susceptibility to scurvy is the much more serious potentially-fatal inherited presence of a defective gene for GLO in the human gene pool. This defective gene appears to have originated by a mutation in a primitive primate ancestor of Man, some 60 million years ago (Stone, 1972) and its incidence is in 100 per cent of the human population.

We now have the paradoxical situation of a basically inaccurate hypothesis dominating the thoughts and research for over 60 years in a field where no attempts have been made during this time to bring this theory into line with established facts. It has been a record of a serious potentially-fatal genetic liver-enzyme disease, an "inborn error of carbohydrate metabolism" being investigated by nutritionists and home economists, under the mistaken impression that it is a simple dietary disorder. Such little progress in improving human health in the past 80 years of clinical research can be attributed to the narrow outlook and low dosage orientation of the investigators due to the fact that they were neither qualified by training or competent by experience to be investigating a complicated problem in medical genetics. The most serious result of-this long exposure to misleading nutritional propaganda is that this hypothesis has become current medical dogma and has prevented the easy and simple elimination of Chronic Subclinical Scurvy (the CSS Syndrome) in our population and has permitted this disease to reach epidemic proportions (Stone, 1977).

Because of this misleading hypothesis, the current impression in the minds of a large segment of physicians is that 1. scurvy is a rare disease in this country; 2. that if you take 45 mg of ascorbate a day scurvy is "cured" and there is nothing further to worry about; 3. the only disease that ascorbate (or "vitamin C") can treat is scurvy; 4. doses of 150 mg of ascorbate a day for a human adult are not only unnecessarily high, but may be toxic and are "wasteful".

The clinical research of the past decade has shown these impressions to be sheer nonsense. 1. Chronic Subclinical Scurvy (the CSS Syndrome) is our most widespread disease (Stone, 1972). 2. 45 mg of ascorbate will prevent the appearance of the terminal symptoms of the disease but will not do much else. To correct Chronic Subclinical Scurvy requires at least 10 grams of ascorbate a day depending upon the incident stresses (Stone, 1977). Under heavy stresses the daily ascorbate requirement may be 200 grams or 300 grams to keep ahead of the CSS Syndrome. .3. The long term biochemical results of Chronic Subclinical Scurvy set the stage for the development of the serious medical problems of later life; the heart attacks, the cancer, the collagen diseases and many more. Preliminary clinical tests indicate that mega levels of ascorbate are useful in the prevention and treatment of cancer (Stone, 1974,1976), heart disease, and many others (Stone, 1972). In the case of viral diseases (Pauling, 1978, Stone, 1972), research of the past 30 years indicates that no one should succumb to a viral infection any more. Ascorbate is a non-specific, nontoxic virucide and when used at the proper daily dosage (up to 300 grams intravenously and/or orally) any viral infection can be relieved within 96 hours (Klenner, 1974, Cathcart, 1978, Pauling, 1976). The Sudden Infant Death Syndrome (SIDS) or Crib Death, has been shown by the Australian workers, A. Kalokerinos and G. Dettman, to be a manifestation of infantile scurvy, due to the fact that all infants, born of mothers who depended solely on their diet as their only source of ascorbate, are born with the CSS Syndrome after nine months of intrauterine scurvy (Stone, 1978). SIDS can be prevented by increasing the infant's intake of ascorbate (Cook, 1978). This has been known and

published since 1974 (Kalokerinos, 1974). Yet 8000 to 10,000 babies die of SIDS a year because the doctors and others involved with the management of these babies permit this annual slaughter to take place because they have become so complacent with scurvy that they refuse to even try this harmless treatment. 4. Ascorbate is one of the least toxic substances known. Therapeutic doses up to 300 grams can be administered without unfavorable side reactions. The daily doses that we recommend for humans are based on amounts normally synthesized by the mammals and should not be regarded as "high" or "abnormal" a-mounts. We are using the "normal" mammalian levels. It is the "micro" daily amounts recommended under the "Vitamin C-Dietary Deficiency Disease" theory that are the inadequate abnormally low levels.

Over the past 8 decades the use of these "micro" daily levels of ascorbate intake, much below the levels needed to overcome our current daily stresses of living, has served to wipe out acute Frank Clinical Scurvy as a common disease but has preserved the epidemic incidence of the CSS Syndrome, the more insidious and more dangerous, relatively asymptomatic form of scurvy. The full correction of the CSS Syndrome is the first step in any Preventative Medicine procedure.

As soon as the term "Vitamin C" is discarded in favor of "Ascorbate" when speaking of this missing Human Liver Metabolite, we shall know that some progress has been made in understanding this killer disease.

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