



## What's new about scurvy?

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This question was asked, in all sincerity, by one of my colleagues who wondered why another study of scurvy in man was worthwhile. Why indeed? Many physicians have observed and described scurvy over a span of several thousand years and the British Medical Research Council induced scurvy in volunteers during World War II, thereby establishing a minimal daily requirement for ascorbic acid of about 10 mg/day or somewhat less.

The reasons for restudying scurvy are twofold; first, the mechanism of action of ascorbic acid remains obscure, albeit related as a cofactor to certain enzyme systems; and second, there has been a group of determined scientists who have insistently claimed that very large doses of ascorbic acid have health-giving virtues over and above those of preventing scurvy.

Recent reports of experimental scurvy represent the fruits of two cooperative ventures between members of the Metabolic Ward at the University of Iowa and members of the U.S. Army Medical Research and Nutrition Laboratory at Fitzsimons General Hospital in Denver, Colorado. The first study has been published recently in this Journal (1, 2).

Induction of scurvy by dietary means was not new, but the sophisticated radiometric techniques used to measure the metabolism of ascorbic acid in man were. These procedures, performed largely at Denver, permitted accurate measurement of the body pool(s) of ascorbic acid, daily measurement of catabolism of this substance, and correlations between pool size, blood levels, rates of utilization of ascorbic acid, and symptoms and signs of deficiency. As a result, we now

know that body stores of ascorbic acid in healthy, well-fed men approximate 1,500 mg and that they are utilized at an average rate of 3% of the existing pool per day. Thus, after a period of about 3 months of deprivation, the stores become largely depleted and the amount of ascorbic acid available for daily catabolism is less than the amount needed to prevent scurvy (3, 4). Actually the earliest signs of deficiency may begin during the first month of deprivation but, by the time the pool size has decreased to less than 300 mg and the daily rate of catabolism to less than 9 mg, signs and symptoms of frank scurvy become obvious.

A distressing feature is the lack of precision of serum ascorbic acid levels. According to most authorities, deficiency appears after the serum level has fallen below 0.2 mg/100 ml, yet several men in these studies had obvious scurvy at a time when their serum levels were above this value.

Another departure from common knowledge is the observation that bleeding gums are not truly the most characteristic feature of scurvy, although they do occur as late manifestations. Instead, the hyperkeratotic follicle with a surrounding pink halo, the "perifollicular hemorrhage," is almost pathognomonic.

But signs and symptoms observed in these studies were not limited to those usually described in scurvy. In addition to these latter ones, another group of syndromes became clearly identifiable as a result of ascorbic acid deprivation. They included: 1) ocular hemorrhages, especially in the bulbar conjunctivas (5); 2) Sjögren's syndrome, that is, loss of secretion of salivary and lacrimal glands, swelling of parotid and submaxillary

glands, loss of dental fillings, loss of hair, and dryness and itching of skin (6); 3) femoral neuropathy, resulting from hemorrhage into the femoral sheaths (7); 4) oliguria with edema, especially of the lower extremities; 5) psychological disturbances, such as the neurotic triad consisting of hypochondriasis, hysteria, and depression followed by decrements in psychomotor performance (8); 6) impaired vascular reactivity, i.e., poor responses to stimuli that normally activate vasomotor adaptive mechanisms (9); and 7) scorbutic arthritis, which is clinically similar to rheumatoid arthritis with pain, swelling, joint effusions, and limitation of motion.

All of the above syndromes responded completely to therapy with ascorbic acid. Thus, with multiple systems obviously involved and with so few biochemical mechanisms adequately explained, there should be no question about the value of further studies of the metabolism of ascorbic acid, especially in the areas of stress.

Repletion studies demonstrated that remarkable improvement can result from daily doses of only 6.5 mg ascorbic acid. Larger doses resulted in more rapid improvement and in substantial rates of storage in the body pool(s). Once these storage depots had been replenished to approximately 1,500 mg, the rate of urinary excretion of free, reduced ascorbic acid increased. Very large daily doses of nonradioactive ascorbic acid (350 to 600 mg) resulted in an increased urinary excretion of nonradioactive, free, reduced ascorbic acid, indicating that the additional amount had not mixed thoroughly with the radioactively labeled body pool(s).

The recent release of a book entitled *Vitamin C and the Common Cold* (10) emphasizes the need for a careful reappraisal of the evidence pro and con regarding the

potential benefits of "megavitamin" therapy with doses as high as 1,000 times the minimal daily requirement. Although the author quotes a number of references that support this type of therapy, the sum total of the scientific evidence is inadequate to support a valid conclusion. The Iowa City-Denver studies that are published in this issue neither support nor negate the claims made in Pauling's book. Until carefully controlled studies have been performed, further argument must be considered conjectural. ❧

### References

1. HODGES, R. E., E. M. BAKER, J. HOOD, H. E. SAUBERLICH AND S. C. MARCH. Experimental scurvy in man. *Am. J. Clin. Nutr.* 22: 535, 1969.
2. BAKER, E. M., R. E. HODGES, J. HOOD, H. E. SAUBERLICH AND S. C. MARCH. Metabolism of ascorbic-1-<sup>14</sup>C acid in experimental human scurvy. *Am. J. Clin. Nutr.* 22: 549, 1969.
3. HODGES, R. E., J. HOOD, J. E. CANHAM, H. E. SAUBERLICH AND E. M. BAKER. Clinical manifestations of ascorbic acid deficiency in man. *Am. J. Clin. Nutr.* 24: 432, 1971.
4. BAKER, E. M., R. E. HODGES, J. HOOD, H. E. SAUBERLICH, S. C. MARCH AND J. E. CANHAM. Metabolism of <sup>14</sup>C- and <sup>3</sup>H-labeled L-ascorbic acid in human scurvy. *Am. J. Clin. Nutr.* 24: 444, 1971.
5. HOOD, J., AND R. E. HODGES. Ocular lesions in scurvy. *Am. J. Clin. Nutr.* 22: 559, 1969.
6. HOOD, J., C. A. BURNS AND R. E. HODGES. Sjögren's syndrome in scurvy. *New Engl. J. Med.* 282: 1120, 1970.
7. HOOD, J. Femoral neuropathy in scurvy. *New Engl. J. Med.* 281: 1292, 1969.
8. KINSMAN, R. A., AND J. HOOD. Some behavioral effects of ascorbic acid deficiency. *Am. J. Clin. Nutr.* 24: 455, 1971.
9. ABBOUD, F. M., J. HOOD, R. E. HODGES AND H. E. MEYER. Autonomic reflexes and vascular reactivity in experimental scurvy in man. *J. Clin. Invest.* 49: 298, 1970.
10. PAULING, L. *Vitamin C and the Common Cold*. San Francisco: Freeman, 1970.