

Clinical Usefulness of the Oral Ascorbic Acid Tolerance Test in Scurvy

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THE ascorbic acid content of blood serum (or plasma) reflects within limits the dietary intake of this nutrient. When, however, the concentration approaches zero the simple demonstration of an absence of vitamin C from the serum does not permit one to predict the tissue stores of the vitamin. The concentration of ascorbic acid in the plasma approaches zero some weeks prior to the appearance of clinically detectable lesions of scurvy.¹ The ascorbic acid content of the white cell-platelet layer is a somewhat more sensitive index of tissue stores, but this tedious and difficult determination is not readily adapted to routine use. There is need for a simple, reliable and informative measure of ascorbic acid nutriture whenever the concentration of the vitamin in the serum has dropped to the vanishing point.

Several years ago the reports of Wolfer et al.,² Butler and Cushman³ and Kajdi⁴ attracted the attention of one of us toward the possibility of using a "saturation" or "tolerance" type of test to estimate tissue levels of the vitamin. Usefulness was noted of one such procedure which measures serum ascorbic acid in establishing the diagnosis of scurvy in adults⁵ but the evidence for this usefulness in spontaneously developing scurvy has not previously been published. The purpose of this report is to present

evidence of value of such a procedure, which is suitable for wide clinical application.

A variety of tests has been proposed for the determination of ascorbic acid nutriture. The earlier ones, such as used by Abbasy et al.⁶ and Johnson et al.,⁷ were based upon the premise that persons with low tissue reserves of ascorbic acid excrete less of a test dose in the urine than do subjects with adequate stores. Tests based on urinary excretion of vitamin C do not distinguish between varying degrees of deficiency at the lower levels of nutriture and we agree with Sinclair's⁸ suggestion that their usefulness is limited by several considerations, including lack of conclusive knowledge of metabolism of the vitamin and the mechanism of its renal excretion.

Lund and co-workers⁹ observed that two hours after an oral dose of ascorbic acid normal persons had a much higher serum level than did patients with scurvy. Wolfer et al.² confirmed this finding in a study of induced scurvy, but no application of the test in the diagnosis of scurvy was described. Stotz and associates¹⁰ used an oral dose of 6 mg./kg. body weight and measured serum levels at hourly intervals for the next five hours. Subjects with fasting levels between 0 to 0.2 mg. per cent had four types of response that were classified as (1) undersaturated, (2) low normal, (3) high normal and (4) saturated. No patients with scurvy were studied. Rinehart and Greenberg¹¹ used an oral dose of 15 mg./kg. body weight and measured fasting, three-hour and five-hour serum levels. They similarly classified the resulting curves as (1) flat (peak below 0.5 mg. per cent), (2) medium (peak 0.5 to 0.9 mg. per cent) and (3) high (peak above 0.9

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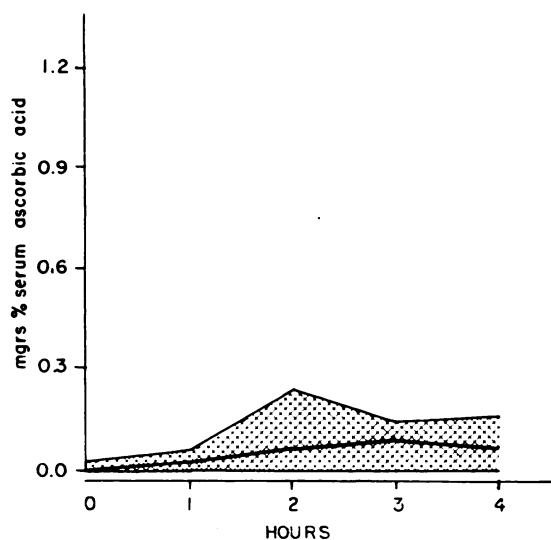


FIG. 1. Mean and range of serum ascorbic acid in nine patients with scurvy after a load test.

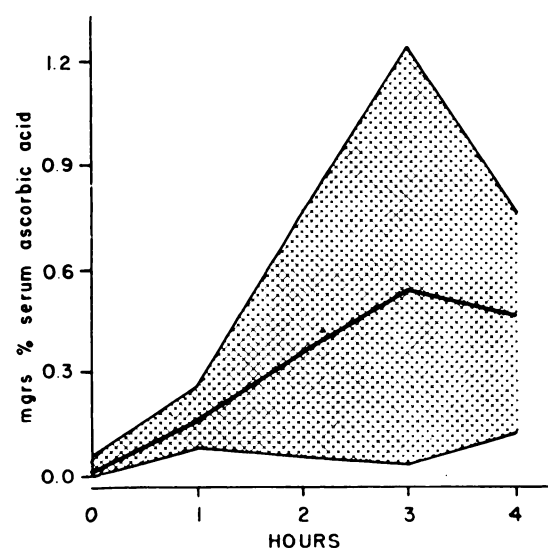


FIG. 2. Mean and range of serum ascorbic acid in eleven patients without scurvy after a load test.

mg. per cent). Again, no patients with clinical scurvy were studied.

Other investigators¹²⁻¹⁴ have used similar tests but with intravenous administration of the vitamin. This route may result in a sudden flooding of the kidney with ascorbic acid and a greater opportunity for enhanced urinary loss.

For rapid assessment of the ascorbic acid stores of an individual the type of test used by Wolfer and associates,² Stotz et al.¹⁰ and Rinehart and Greenberg¹¹ has proved to be of value in this laboratory.

CLINICAL MATERIAL AND RESULTS

We are presenting results obtained in twenty-four adult patients. All had a fasting serum ascorbic level of less than 0.1 mg./100 ml. Of these patients, nine had clinical scurvy, three had a history of inadequate intake of ascorbic acid but they did not have clinical scurvy, one had sprue and the remaining eleven patients were hospitalized for reasons unrelated to nutritional disease. They are included because of low fasting serum ascorbic acid levels.

After a fasting blood sample was obtained, an oral dose of ascorbic acid (15 mg./kg. body weight) was given. Successive determinations of serum ascorbic acid levels were made at one, two, three, four and, occasionally, five hours after ingestion. Serum ascorbic acid was meas-

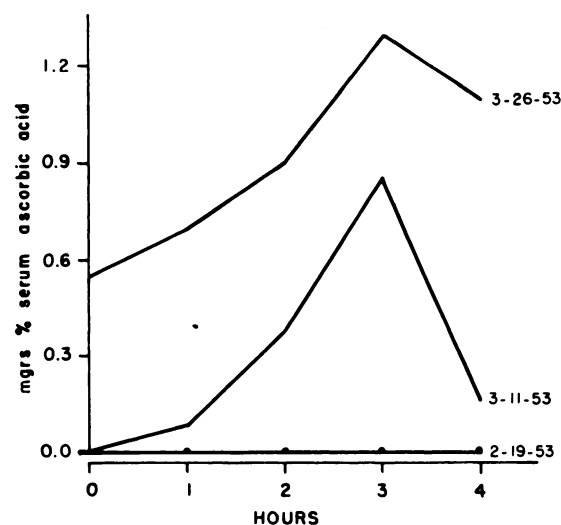


FIG. 3. Successive responses to a load test in a patient with scurvy.

ured using a modification of the 2,6-dichlorophenolindophenol method of Mindlin and Butler.¹⁵ In some of the patients with clinical scurvy, successive load tests were performed after periods of therapy.

The values obtained on the nine adults with clinical scurvy are plotted in Figure 1. Similar data obtained on the eleven patients without scurvy who had low serum ascorbic acid levels are plotted in Figure 2. Finally, the results of three successive load tests on a patient with scurvy are expressed in Figure 3.

COMMENTS

Examination of Figure 1 reveals that the patients with clinical scurvy exhibited a "flat" response to the test dose. In no instance did the maximum rise in ascorbic acid level exceed 0.25 mg./100 ml. It was considerably less in most of the cases and averaged approximately 0.1 mg. The mean maximum obtained at three hours. This response was similar to that found by Lund et al.⁹ who reported that the ascorbic acid levels in four patients with scurvy did not exceed 0.25 mg./100 ml. two hours after an oral test dose of 10 mg./kg. body weight. In children with scurvy Kajdi et al.⁴ demonstrated that the serum level did not exceed 0.2 mg./100 ml. four hours after an intramuscular injection of 200 mg. of ascorbic acid. The three patients with a history of grossly inadequate ascorbic acid intake who did not have clinical scurvy gave the same "flat" response as did those with scurvy. These responses are interpreted as evidence of greatly diminished tissue stores.

Figure 2 depicts the range of results obtained in the group of patients having fasting serum levels of ascorbic acid less than 0.1 mg./100 ml. but whose dietary histories did not appear to be markedly deficient in ascorbic acid. This group exhibited an average rise of 0.5 mg. at three hours with only three failing to have an increase above 0.2 mg. The range of responses within this group suggests varying levels of ascorbic acid nutriture.

The changing response to the load tests (Fig. 3) reflects the increased ascorbic acid stores of a patient with scurvy who was given 300 mg. of ascorbic acid orally daily following the initial load test. After twenty-two days the fasting serum ascorbic acid level was still zero, but the maximum increase in serum level at three hours was 0.8 mg. The patient had received approximately 7 gm. of ascorbic acid during this intervening period. The second load test reflects the relatively good stores which had accumulated in the tissues despite the fasting zero concentration in the serum. The response pattern fifteen days later, and after the fasting serum level had risen, showed a higher maximum. Other patients with scurvy treated with larger amounts of ascorbic acid (600 to 1,000 mg. daily) showed fasting levels

above 0.2 to 0.3 mg./100 ml. and a normal response pattern to the load test within ten days.

A patient with sprue had a fasting serum level of zero. A level of 0.3 mg./100 ml. was attained only nine hours after the load test. This patient's history indicated a poor dietary intake but he did not show clinical signs of scurvy. The absorptive defects in this disease involve both fat-soluble and water-soluble nutrients.¹⁶ The flat tolerance curve of ascorbic acid and the delayed maximum are consistent with the impaired absorption of water-soluble nutrients as well as a degree of "tissue depletion." Other disorders of absorption might give similar misleading results in the clinical application of this test, and, hence, these should be considered in the interpretation of results in order to avoid erroneous conclusions. Whenever defects of intestinal absorption exist, a parenteral load test should be employed.

SUMMARY AND CONCLUSIONS

The tolerance test (in which 15 mg. of vitamin C/kg. of body weight is administered orally and the ascorbic acid concentration in the serum determined three hours later) is useful in assessing vitamin C nutriture. In patients with scurvy the serum concentration will not increase above 0.25 mg./100 ml. and is usually much less. A maximum rise of ascorbic acid concentration in excess of 0.25 mg./100 ml. is not consistent with the diagnosis of scurvy. In states of severe depletion of tissue stores, or in marked degrees of malabsorption, extremely low values may be encountered in the absence of scurvy. Hence, this test may be of conclusive value in excluding scurvy as a diagnosis and of considerable usefulness in sustaining the diagnosis of scurvy. In its simplest form an initial and a three-hour estimate of serum ascorbic acid will suffice. This is more convenient and widely applicable than measurement of white cell ascorbic acid content or other procedures. The normal rise in serum concentration following the oral dose indicates the presence of appreciable tissue stores even though the fasting serum level of vitamin C may be zero. Informative supplementary information might be obtained in nutrition sur-



veys among populations with less than 0.1 mg. of ascorbic acid /100 ml. serum by first dosing with 15 mg. of ascorbic acid per kg. body weight and then taking the blood sample for estimation of the vitamin three hours later.

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