cord into the same intracerebral site and 3.1 cc. of the virus suspension was inoculated intraperitoneally. Both these animals have remained unaffected up to the present time, a period of 19 days.

Summary and Conclusions. Five common Marmoset monkeys were inoculated intracerebrally, intraperitoneally, and intranasally with 10 and 20% suspensions of active poliomyelitic cord. The monkeys remained unaffected by such inoculations. The common Marmoset does not therefore appear to be susceptible to infection with the virus of poliomyelitis.

8970 P

Reduced Ascorbic Acid Content of Blood Plasma in Rheumatoid Arthritis.*

J. F. RINEHART, L. D. GREENBERG, AND F. BAKER.

From the Departments of Pathology and the Arthritis Clinic, University of California Medical School.

Experimental, clinical and other considerations led to the concept that vitamin C deficiency may operate as a contributory factor in the etiology of some cases of rheumatoid arthritis.[1]

The present study, based upon the determination of reduced ascorbic acid in the blood plasma, represents an effort to evaluate objectively the validity of this thesis. The report of Abt, Farmer and Epstein[2] and our own,[3] indicate that the method proposed by Farmer and Abt[4] is accurate and a reliable index of the intake of vitamin C in health and in any case of the immediate nutritive status with respect to the vitamin.

On the basis of excretion tests and a comparative study of diet habit and reduced ascorbic acid determinations in a group of "normal" adults,[3] we feel that fasting plasma levels below 0.7 mg. per 100 cc. are probably sub-optimal. Levels ranging between 0.7 and 0.9 mg. per 100 cc. would seem adequate. Optimal levels probably lie

* This work was aided by a donation from the California Fruit Growers Exchange and by the Christine Breon Fund for Medical Research. We are indebted to Hoffmann-La Roche, Inc., for supplies of ascorbic acid.

1 Rinehart, J. F., *Ann. Int. Med.*, 1935, **9**, 671.

2 Abt, A. F., Farmer, C. J., and Epstein, I. M., *J. Pediat.*, 1936, **8** 1.

3 Greenberg, L. D., Rinehart, J. F., and Phatak, N. M., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 135.

4 Farmer, C. J., and Abt, A. F., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1625.

above this range. Reduced ascorbic acid levels below 0.5 mg. per 100 cc. must be considered low. These ranges are somewhat less than those recorded by Abt, Farmer and Epstein.[2] It is pertinent to recall that the estimation of the plasma ascorbic acid is only a measure of the immediate nutritive level, and is dependent upon recent dietary habit to a great degree. Although it is an index of vitamin C nutrition at the time of the test, in a single case a low level does not imply tissue injury or sub-clinical scurvy. This latter results from the operation of sub-optimal or low metabolic levels over some period of time. Conversely, a good or high level would not indicate that deficiency had not operated to produce tissue injury in the past.

The material of this study comprises 36 cases of rheumatoid arthritis. Twelve of these cases serve as a control group in that they had all been maintained for a period of months on a high vitamin C intake. The plasma ascorbic acid levels in this group ranged from 0.90 to 1.39 mg. per 100 cc. with an average of 1.10 mg. This, no doubt, approaches an optimal range.

A second group of 21 cases all showed clinical or laboratory evidence of activity of the rheumatic process. The fasting plasma ascorbic acid levels in this group ranged from 0.14 to 0.66 mg. per 100 cc. They are shown graphically in Fig. 1.† In 5 of the cases a high vitamin C intake had been recommended at some time in the past but for one reason or another the patients had not cooperated to the extent advised (cases stippled in graph). Three other cases

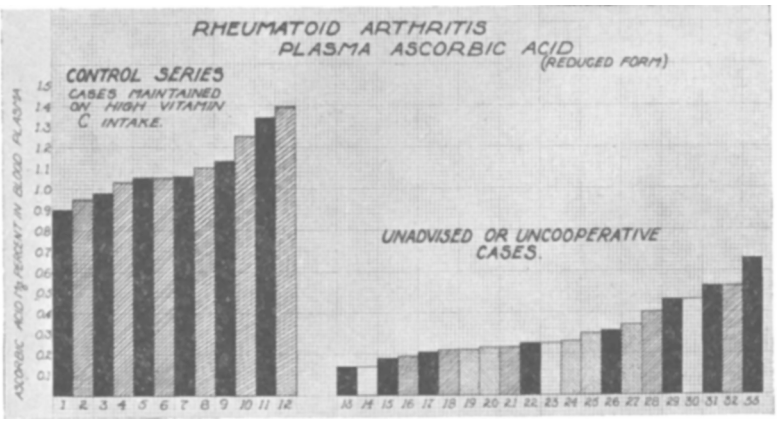

FIG. 1.

† The single value above 0.53 mg. did not represent the habitual nutritive level of the patient because she had been on a raw fruit and vegetable diet for 3 weeks prior to the determination.

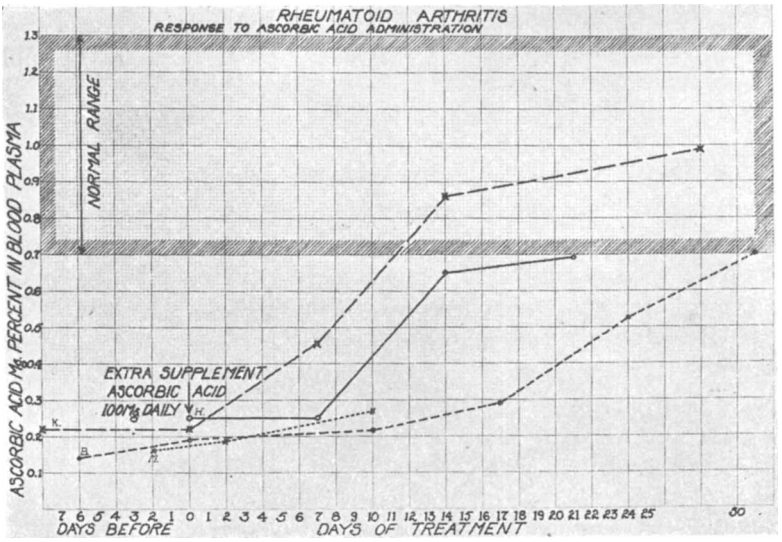

FIG. 2.

are of particular interest in that they had taken a good though not high vitamin C diet supplement for months prior to the examination (cases unshaded in graph). In spite of this the ascorbic acid plasma levels were sharply lowered. Such cases strongly suggest that a fault in absorption or utilization may be the basis for vitamin C under-nutrition in some individuals. In the majority of the cases, definite vitamin C supplements were prescribed following initial observations. In all of the cases which we were able to follow, the reduced ascorbic acid plasma levels rose in response to this regime. The initial levels and responses to therapy in 4 cases are shown in Fig. 2. This graph shows not only the depressed initial levels in rheumatoid arthritis, but the response of the plasma ascorbic acid concentration to an increased vitamin C intake. The refractory responses are to be noted in curves "M" and "B." Curve "H" is of one who had been on a relatively good vitamin C intake for several months (average supplement of 6 oz. of orange or tomato juice daily).

Three cases of old inactive rheumatoid arthritis gave reduced ascorbic acid plasma levels of 0.59 and 0.79 and 1.56 mg. per 100 cc.

The 6 cases of hypertrophic arthritis, in which plasma ascorbic acid was determined, showed high levels ranging from 0.90 to 1.34 mg. per 100 cc.

Lowered plasma ascorbic acid levels are obviously not peculiar to rheumatoid arthritis and, as has been noted, in individual cases, do

not establish the existence of scurvy. The practically uniform finding of sharply lowered levels in initial determinations in a series of 21 cases is, however, considered significant. With the exception of the 5 cases noted these individuals were on their usual dietary regime.

Summary. The blood plasma ascorbic acid (reduced form) in active cases of rheumatoid arthritis is regularly low if the individuals have not been maintained on a *high* vitamin C supplement. Unadvised cases were found to show uniformly lowered levels. The reduction is striking. Such levels rise in response to extra supplements of vitamin C. In many this rise is refractory. Our studies indicate that in some cases the intake required to maintain adequate vitamin C levels in the plasma are much above the average requirement for normal individuals. The mechanism involved is unexplained.

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Reduced Ascorbic Acid Content of Blood Plasma in Rheumatic Fever.*

J. F. RINEHART, L. D. GREENBERG, AND A. U. CHRISTIE.

From the Departments of Pathology and Pediatrics, University of California Medical School.

The thesis was advanced that vitamin C deficiency may be an important factor in the etiology of rheumatic fever.[1] This concept was based upon the experimental production of a disease state with manifold similarities to rheumatic fever, by subjecting guinea pigs to the combined influence of vitamin C deficiency and infection. Epidemiologic and clinical considerations were noted which afforded confirmatory evidence for the validity of the concept. In studies reported by Schultz, Sendroy and Swift,[2] and Perry[3], the clinical significance of this concept was questioned or denied.

* Aided by a donation from the California Fruit Growers Exchange and by the Christine Breon Fund for Medical Research. We are also indebted to Hoffmann-LaRoche, Inc., for supplies of ascorbic acid.

1 Rinehart, J. F., and Mettier, S. R., *Am. J. Path.*, 1934, **10**, 61; Rinehart, J. F., Connor, C. L., and Mettier, S. R., *J. Exp. Med.*, 1934, **59**, 97; Rinehart, J. F., *Ann. Int. Med.*, 1935, **9**, 586; Rinehart, J. F., *J. Lab. and Clin. Med.*, 1936, **21**, 597.

2 Schultz, M. P., Sendroy, J., and Swift, H. F., *J. Clin. Invest.*, 1935, **14**, 698.

3 Perry, C. B., *The Lancet*, 1935, **229**, 426.