

been found that the large percentage of subjects will receive convulsions with currents of from 400 to 450 ma, applied for 0.2 or 0.3 seconds.

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Influence of Hyperpyrexia on Ascorbic Acid Concentration in the Blood.

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It has been established^{1, 2, 3} that the plasma ascorbic acid concentration during the course of an infectious fever is lowered, as a consequence, the therapeutic procedure of supplementing the diet of such patients with ascorbic acid is receiving increased attention.

This investigation was undertaken to ascertain whether an artificial fever produced by physical means also produced a lowering of the plasma ascorbic acid. When this work was initiated no such study had been reported; but in the meantime two somewhat similar investigations have been reported.^{4, 5} In addition, Rhinehart's^{6, 7} association of low plasma ascorbic acid levels with the etiology of rheumatic disease further augmented our interest, inasmuch as our patients had been afflicted with this disease.

Method. Seventeen patients suffering from chronic arthritis were subjected to hyperpyrexia. The body temperature was elevated and maintained at 104° to 104.6° F (rectal) for a period of 4 hours, following which it was permitted to return to normal. A combination of fever cabinet and inductotherm was used to elevate the patient's temperature. Treatments were given once weekly.

¹ Farmer, C. J., *Quart. Bull. Northwestern Univ. Med. Sch.*, 1940, **14**, 220.

² Wolfer, J. A., *Surg. Clin. N. A.*, Chicago Number, Feb., 1940.

³ Wolfer, J. A., *Surg. Gynec. Obst.*, 1939, **69**, 745.

⁴ Daum, K., Boyd, K., and Paul, W. D., *Proc. Soc. Exp. Biol. and Med.*, 1939, **40**, 129.

⁵ Zoak, J., and Sharpless, G. R., *Proc. Soc. Exp. Biol. and Med.*, 1938, **39**, 233.

⁶ Rhinehart, J. F., *Ann. Int. Med.*, 1935, **9**, 586.

⁷ Rhinehart, J. F., *Ann. Int. Med.*, 1935, **9**, 671.

The blood plasma ascorbic acid concentration was determined by the micro method of Farmer and Abt.⁸ In 2 of the patients with widely divergent initial plasma levels (0.36 and 0.60 mg % respectively) a supplement of 450 mg ascorbic acid (Cebione Merck*) was given daily for the purpose of observing differences in plasma level behavior under treatment with a more than adequate ingestion of vitamin C.

Seventy-seven observations were made on the 17 patients. The analytical determinations were made on each patient (a) just prior to treatment, (b) when the rectal temperature reached 104° F, (c) after a temperature of 104° F had been maintained for 4 hours, and (d) after the patient's temperature had returned to normal.

Results. Table I gives a summary of the average values and the result of the statistical analysis. Obviously, there are no significant changes in the blood plasma ascorbic acid concentration during or following the course of the artificial fever.

TABLE I.
Summary of Blood Ascorbic Acid Determinations.

	Elapsed time, hrs	Avg of 77 determinations on 17 chronic arthritis patients	$\sigma \pm$	$2 \gamma \text{ diff. } \pm$	Change $\pm$
Control	0	.62	.03		
Temp. reached 104° F.	2	.68	.04	.104	.06
Temp. at 104° F 4 hours	6	.66	.03	.106	.04
Temp. returned to normal	8	.64	.03	.088	.02

Discussion. Investigators vary markedly in their reports as to what constitutes a normal blood plasma ascorbic acid level, either in health or disease. Abt and Farmer,⁹ in their studies on children and young adults, report normal values for patients with adequate intake to range from 0.7 to 1.5 mg per hundred cubic centimeters. Blood plasma values below 0.7 mg they consider to be suboptimal. Furthermore, according to these investigators, active scurvy may occur in children with values up to 0.4 mg %. Abt and Farmer believe that while these values are critical during the period of growth, they may not hold the same significance in the adult. Wolff, Banning, and van Eekelen¹⁰ state a blood level of 0.4 to 1.2 mg % to be adequate but not the optimum. Daum, Boyd and Paul⁴ state that the normal ascor-

⁸ Farmer, C. J., and Abt, A. F., *Proc. Soc. Exp. Biol. and Med.*, 1936, **34**, 146.

* We are indebted to Merck and Company, Rahway, N.J., for the ascorbic acid (Cebione, Merck) used in this investigation.

⁹ Abt, A. F., and Farmer, C. J., *The Vitamins*, Chapter 22, Am. Med. Assn. Press, Chicago, 1939.

bic acid content of the blood ranges between 0.7 to 2.0 mg %. Ralli and Sherry¹¹ in their recent review agree that plasma levels above 0.7 mg % can be considered normal with a white cell platelet content of 25 to 38 mg %.

While the average blood plasma ascorbic acid concentration for our group was 0.62 mg % before treatment, the range varied from a low of 0.28 to 0.72 mg %. Many of the values found in these patients are considered to be subnormal. Thirty-three of the 77 determinations before treatment showed a level below 0.5 mg %. This is of interest in the light of the work of Rinehart,^{6, 7} who as the result of his study expressed the following opinion: "On the basis of experimental data previously reported, the concept was presented that rheumatic fever may be the result of the combined influence of vitamin C deficiency and infection. With respect to the rôle of infection, it may briefly be said that in the presence of adequate vitamin C nutrition, rheumatic type lesions have not been observed."

The claim has been made that fever increases the vitamin C requirement. The most worthy evidence in support of this claim has apparently been submitted by Zoak and Sharpless.⁵ They subjected guinea pigs to a scorbutogenic diet and to artificial hyperpyrexia for from 2 to 6 hours daily. Early in the course of the experiment they found the vitamin C content of the tissues reduced by hyperpyrexia, but as the scorbutic state was approached, little difference was found. This was particularly true of the adrenals. The evidence obtained from human subjects is divergent. The conclusion of Zoak and Sharpless⁵ that no significant change in the blood level of vitamin C occurs, was confirmed by our results. They believed the failure to observe a decrease was due to hemoconcentration; however, our studies¹² failed to show a hemoconcentration during hyperpyrexia when produced by the methods and management employed. On the contrary, Daum, Boyd and Paul⁴ observed a decrease in the blood plasma level. Falke,¹³ Daum, Boyd and Paul⁴ and Zoak and Sharpless⁵ studied the urinary excretion of vitamin C as well as the blood level. These authors with the exception of Zoak and Sharpless interpreted their data as showing that fever increases the need or utilization of vitamin C in man. According to Falke,¹³ who induced a fever with "pyrifer", the need is increased by 100 mg per day. Zoak and

¹⁰ Wolff, L. K., Banning, C., and van Eekelen, M., *Quart. Bull. Health Organ. League of Nations*, 1936, **5**, 566.

¹¹ Ralli, E. P., and Sherry, S., *Med.*, 1941, **20**, 251.

¹² Osborne, S. L., *Arch. Physical Therapy*, 1941, **22**, 407.

¹³ Falke von, *Klin. Wchnschr.*, 1939, **18**, 818.

Sharpless expressed the view that by following the blood level and urine excretion one cannot accurately determine if fever increases the utilization of vitamin C; tissue analysis as performed in the guinea pig studies would seem to yield more direct evidence. The reliability of data on the urinary excretion in regard to the utilization or need for vitamin C is questioned by Abt and Farmer⁹ and Wolff, Banning and van Eekelen.¹⁰ The blood plasma level would appear to be more reliable, since the level at which vitamin C appears in the urine is subject to considerable individual variation. Further, Hawley, Frazer, Button and Stephens¹¹ present evidence indicating that the reaction of the urine is concerned in determining the excretion of vitamin C. Finally, in man, considerable vitamin C is lost through the sweat according to the observations of Cornbleet, Klein and Pace.¹⁵ This, however, is denied by Wright and MacLenathan.¹⁶ Since we could not find a satisfactory method applicable to our patients for the determination of the loss in the sweat, we relied on the assumption that the blood plasma level is the best indicator for the body level of vitamin C. According to this view, a body temperature of from 104° to 104.6° F for 4 hours did not significantly or detectibly increase the rate of utilization of vitamin C.

Conclusions. A study of 77 observations made on 17 patients showed no significant changes in the ascorbic acid concentration as the result of elevating the body temperature to 104°F and maintaining it for 4 hours, using a combination of air conditioned cabinet and inductotherm.

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Destruction of Phenylalanine by Ultraviolet Radiant Energy.

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The following changes have been observed to occur when *dl*-phenylalanine is exposed to ultraviolet radiant energy:

1. Spiegel-Adolf¹ reported that solutions of phenylalanine ex-

¹⁴ Hawley, E. E., Frazer, J. P., Button, L. L., and Stephens, D. J., *J. Nut.*, 1936, **12**, 215.

¹⁵ Cornbleet, T., Klein, R. J., and Pace, E. R., *Arch. Derm. Syph.*, 1936, **34**, 253.

¹⁶ Wright, I. S., and MacLenathan, E., *J. Lab. and Clin. Med.*, 1939, **24**, 806.

¹ Spiegel-Adolf, M., *Biochem. J.*, 1937, **81**, 1303.