indicates that at no time is the difference in growth rate of the 2 series sufficiently great to have a real significance.

Conclusion. Allantoin stimulates slightly but not to a significant degree the growth of fibroblasts from cardiac explants in tissue culture.

8903 C

Intramuscular Injection of Ascorbic (Cevitamic) Acid and Excretion in the Sweat.

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The value of the oral and intravenous methods of administration of cevitamic acid has been well established in the treatment of vitamin C undernutrition.[1-9] In order to determine the efficacy of the intramuscular route, a group of patients was given the substance by this method, and the cevitamic acid values of the blood and urine were followed. The patients selected were of varying ages and degrees of vitamin C saturation and were all afebrile. The solution used was made up by mixing one mole of cevitamic acid with one mole of sodium hydroxide and contained 50 mg. of the vitamin per cc. The pH is about 6.3. It has remained stable during the 3 months of the duration of this experiment.* The use of sodium bicarbonate for this purpose, just preceding injection, was suggested by Fisher and Leake.[10]

The cevitamic acid content of the urine of the 2 preceding 24-hour

1 Schultzer, P., *Lancet*, 589, Sept. 9, 1933.

2 Schultzer, P., *Acta Med. Scand.*, 1934, **81**, 111.

3 Schultzer, P., *Acta Med. Scand.*, 1934, **83**, 544.

4 Schultzer, P., *Acta Med. Scand.*, 1934, **83**, 555.

5 Schultzer, P., *Acta Med. Scand.*, 1935, **85**, 563.

6 Wright, I. S., PROC. SOC. EXP. BIOL. AND MED., 1934, **32**, 475.

7 Wright, I. S., and Lilienfeld, A., *Arch. Int. Med.*, 1936, **57**, 241.

8 Dalldorf, G., and Russell, H., *J. A. M. A.*, 1935, **104**, 1701.

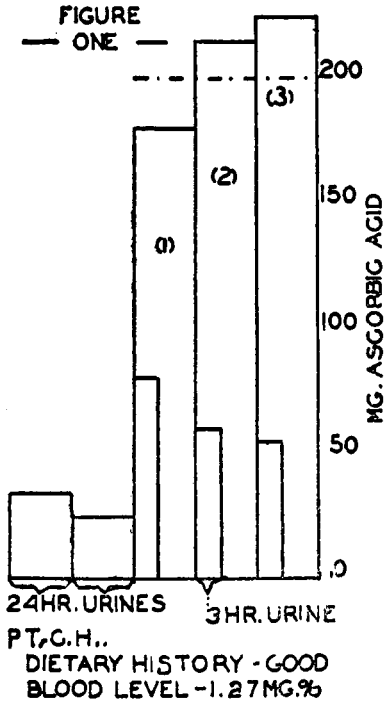
9 Van Eekelen, M., Over opname, Verbruik in Vitscheiding Van Vitamine C Door De Mens, Drukkerj. Fa. Schotanus and Jens, Utrecht, 1936.

*Prepared and supplied through the courtesy of Merck and Co., Inc., Rahway, N. J.

10 Fisher, B. H., and Leake, C. D., *J. A. M. A.*, 1934, **103**, 1556.

periods[11] and the blood level of the vitamin[12, 13] were determined as a control in each instance. Four cc. of the solution (200 mg.) was then injected into the gluteal region daily. Urine specimens were collected every hour for 3 hours and as passed for the remainder of the 24-hour period. This was repeated for 3 days, and, on the third day, 3 hourly blood specimens were taken after the injection, to determine the level of cevitamic acid in the blood plasma. It is important to note that the injection did not produce, on any occasion, evidence of local irritation or inflammation.

Effect on Urinary Excretion. Results. The results may be divided into 3 groups: 1. Cases in which the dietary history with respect to vitamin C was good and in which the initial values for 24-hour urinary excretion and blood level were high. Here, the first injection was followed by an immediate increase of cevitamic acid in the



Urinary excretion during control period (2 days) and following the injection of 200 mg. of ascorbic (cevitamic) acid intramuscularly daily for 3 days. Small columns represent urinary excretion during first 3 hours after injection. Typical curve following previous history of good vitamin C intake.

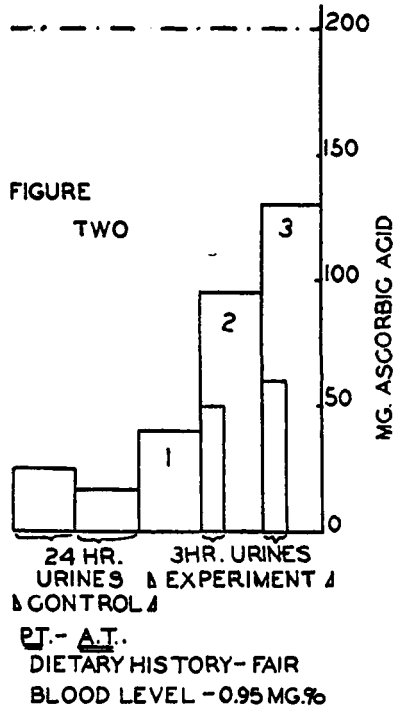
11 Harris, L. J., and Ray, S. N., *Lancet*, 71, Jan. 12, 1935.

12 Abt, A. F., and Epstein, I. M., *J. A. M. A.*, 1935, **104**, 634.

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

urine. This increase was maintained as long as the injections were continued. A typical experiment with a patient (CH) in this group resulted in the following findings: original blood level, 1.27 mg. %; 24-hour urinary output of vitamin C: first control day, 38.6 mg.; second control day, 25.2 mg.; 24-hour urinary output after first dose of 200 mg. of Cevitamic Acid intramuscularly: 179.4 mg. (first 3 hours, 84.8 mg.); after second daily dose, 218.8 mg. (first 3 hours, 63.1 mg.); after third daily dose, 222.6 mg. (first 3 hours, 59.3 mg.).

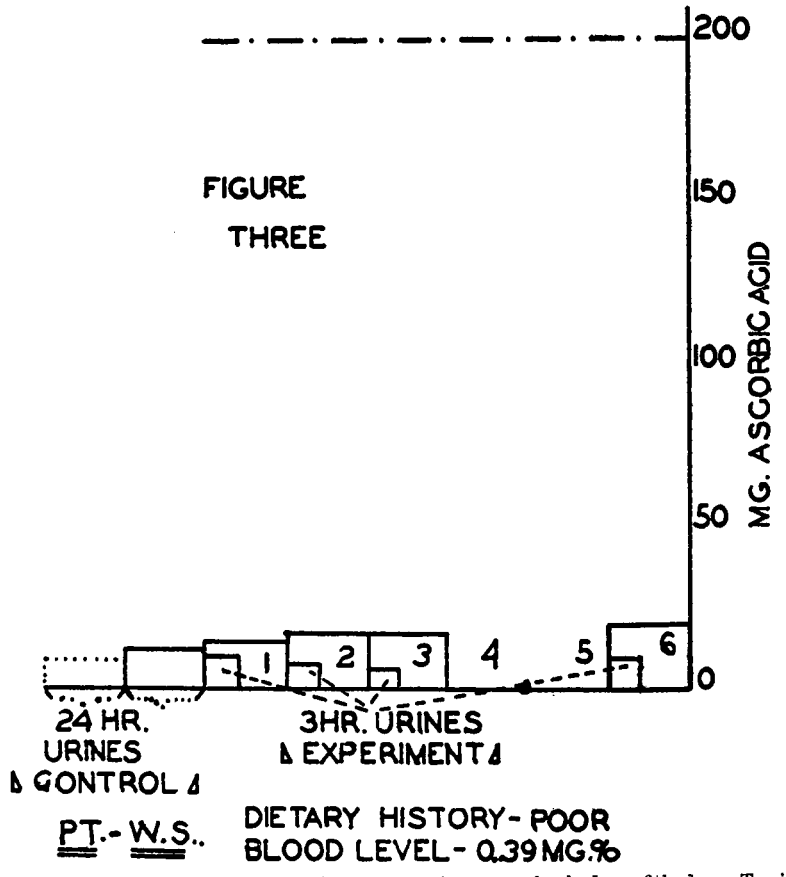
2. Cases in which the dietary intake of vitamin C had been only fair and in which the initial urinary and blood levels of cevitamic acid were correspondingly reduced. Here, an immediate increase in urinary excretion was still apparent, but it was not as sharp as, nor was it to the extent noted in group 1. (Fig. 2.) A typical experiment with a patient (AT) in this group resulted in the following findings: original blood level, .95 mg. %; 24-hour urinary output of vitamin C: first control day, 22.6 mg.; second control day, 16.1 mg.; 24-hour urinary output after first dose of 200 mg. of cevitamic acid intramuscularly, 39.2 mg. (3-hour studies not done); after second daily



Same of Fig. 1. Typical curve following previous history of fair vitamin C intake.

dose, 98.5 (first 3-hours, 42.56 mg.); after third daily dose, 135.2 mg. (first 3 hours, 38.4 mg.).

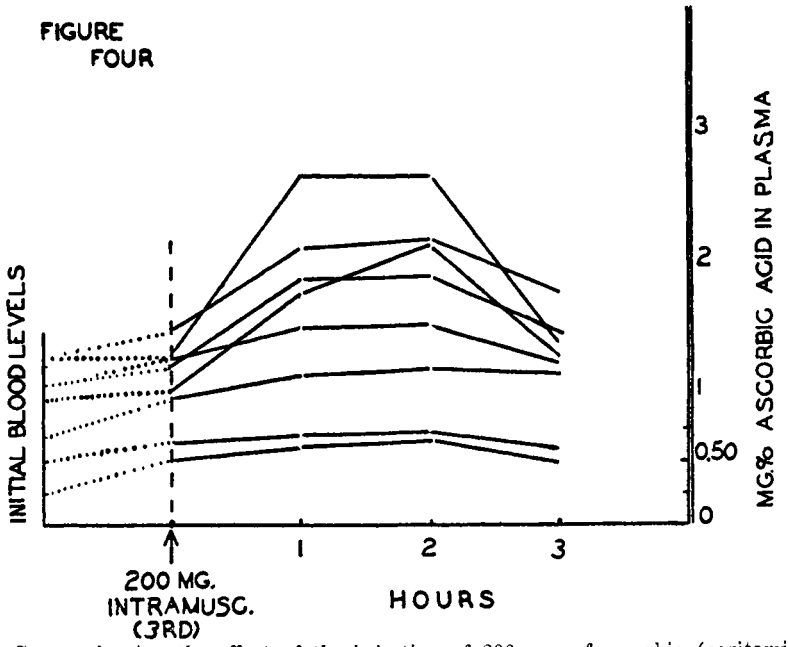
3. Cases in which the dietary history of vitamin C was frankly inadequate. The 24-hour urinary levels and blood plasma content of cevitamic acid were definitely low, and 3 days of the intramuscular injections did not suffice to raise the urinary excretion above the original values. In one patient who was followed for an additional 3 days, a slight increase was noted in the 24-hour urinary excretion of the latter period. A typical experiment with a patient (WS) in this group resulted in the following findings: original blood level, .39 mg. %; 24-hour urinary output of vitamin C: control day, 6.7 mg.; 24-hour urinary output after first dose of 200 mg. of cevitamic acid intramuscularly, 13.39 mg. (first 3 hours, 5.28 mg.); after second daily dose, 13.94 mg. (first 3 hours, 3.45 mg.); after third



Same as Fig. 1 except that urinary excretion was checked on 6th day. Typical curve following previous history of poor vitamin C intake.

daily dose, 14.36 mg. (first 3 hours, 3.11 mg.); after sixth daily dose, 18.18 mg. (first 3 hours, 6.35 mg.).

Effect on Cevitamic Acid Level of Blood Plasma. In all 3 groups of vitamin C saturation, the blood level of cevitamic acid was increased, the height of the concentration being reached and maintained in the first and second hours and dropping rapidly in the third hour towards its original level. In 24 hours, the original level or a slightly higher one was reached. The rise in the first 2 hours was most abrupt in cases where the original nutritional state with regard to vitamin C was good. (Fig. 4.) The blood level was, however, influenced even in those cases of poor dietary history in which the 24-hour urinary excretion was not increased after 3 days of intramuscular injection of cevitamic acid.



Curves showing the effect of the injection of 200 mg. of ascorbic (cevitamic) acid intramuscularly on its level in the blood plasma.

The height of rise of the blood level following the intramuscular injection of cevitamic acid was reached more slowly and was maintained for a longer period of time than after intravenous injection.

In one case, belonging in the group of fair vitamin C nutrition, there was an unexpected decrease in the 24-hour urinary excretion of vitamin C following the second injection (115 mg. after the first, 93 mg. after the second, and 165 mg. after the third). No portion

of the urine had been lost, as far as could be ascertained, and there was no increase in body temperature. During the day, however, the outside temperature had risen to 102°F., and the patient perspired profusely. The possibility was, therefore, suggested that significant amounts of cevitamic acid may have been lost through the skin in the sweat. We have since found that the sweat may contain appreciable amounts of vitamin C. This problem is being investigated at the present and will be reported upon shortly.

Conclusions. 1. Cevitamic acid, properly buffered, may be administered intramuscularly without discomfort or damage to tissue. 2. Studies of the urinary excretion and the blood content of vitamin C following the administration of cevitamic acid intramuscularly demonstrated that it is used by the body when administered by this route. 3. The height of increase in the blood level following the intramuscular injection of cevitamic acid is reached more slowly and is maintained for a longer time than after intravenous injections. 4. In cases of vitamin C deficiency, where cevitamic acid is improperly absorbed through the gastro-intestinal tract, or where the intravenous mode of administration is not feasible, the intramuscular route may be used.

8904 C

Variability of Metabolic Response of Different Children to a Given Intake of Calcium.

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As the metabolic balance studies on the "so-called normal" adults[1, 2] and 22 children[3, 4] as well as the growth observations on 530 infants[5] have progressed in this laboratory over several years

[1] Macy, I. G., Hunscher, H. A., Nims, B., and McCosh, S. S., *J. Biol. Chem.*, 1930, **86**, 17.

[2] Hunscher, H. A., Donelson, E., Erickson, B. N., and Macy, I. G., *J. Nutrition*, 1934, **8**, 341.

[3] Hunscher, H. A., Cope, F., Noll, A., Macy, I. G., Cooley, T. B., Penberthy, G. C., and Armstrong, L., *J. Biol. Chem.*, 1932, **97**, LXIV.

[4] Hunscher, H. A., Cope, F., Noll, A., and Macy, I. G., *J. Biol. Chem.*, 1933, **100**, LV.

[5] Unpublished data from this laboratory.