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Effect of Vitamin C Deficiency on Uterine Smooth Muscle in Sensitized and Non-Sensitized Guinea Pigs.

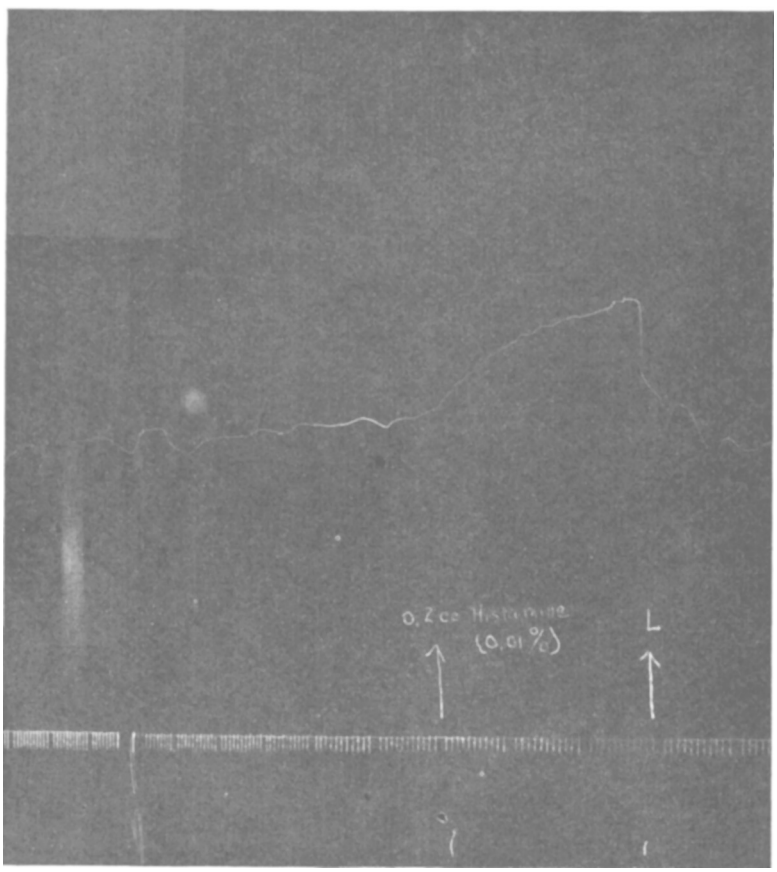
SAMUEL H. HURWITZ AND ELIZABETH G. NICHOLLS.

From the Departments of Medicine and Pharmacology, Stanford University School of Medicine.

During a study of various factors on the mechanism of anaphylaxis in the guinea pig, we observed that excised strips of the sensitized guinea pig uterus suspended in warmed Locke's solution failed to respond upon the addition of antigen. That this loss in tonus is not limited to antigenic substances was shown by the failure of the same uterine segments to respond to pharmacologic agents such as histamine, pituitary extract and barium chloride which are powerful stimulants of normal uterine muscle. The effect of a vitamin C deficient diet on the smooth muscle of the bronchi and its relation to the mechanism of anaphylactic shock will be presented in a later study. This paper records the evidence for the conclusion that the removal of vitamin C from the diet produces a loss of uterine smooth muscle reactivity.

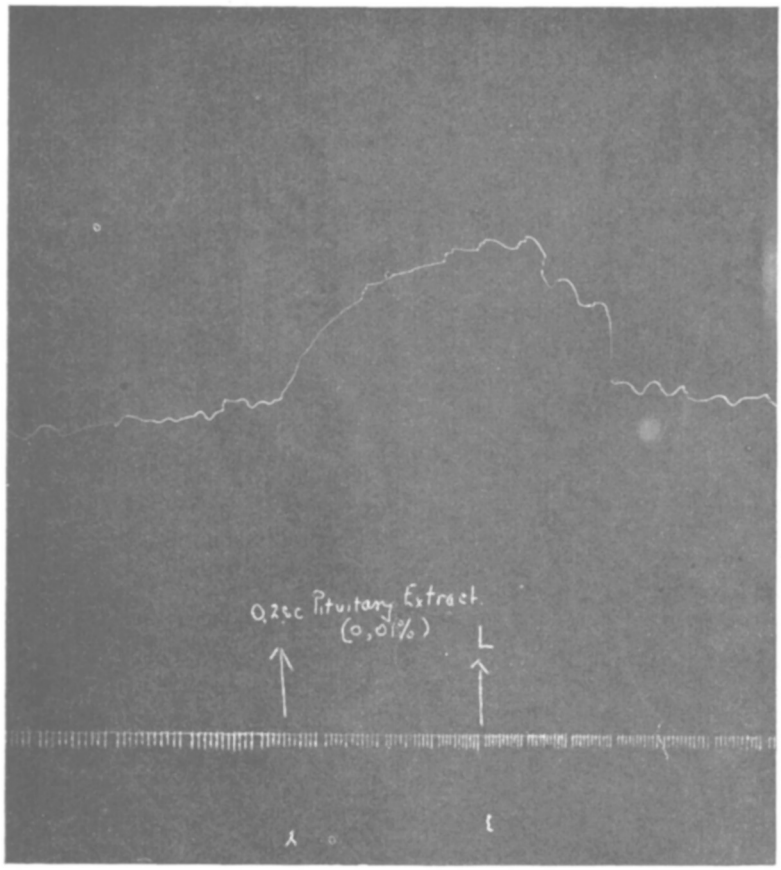
Virgin female guinea pigs weighing 250 to 350 gm. were used. Animals of this weight are particularly suited to these experiments because the responses of the sensitized uterine segments in them are more constant and also because experimental scurvy can be produced in such animals in a shorter period of time. The diet used in our observations was not fundamentally basic, but calculated to be fairly complete from a nutritive standpoint except for vitamin C. It consisted of rolled oats and pasteurized milk, a little bran being added to prevent possible intestinal obstruction from the hard fecal

masses produced by the oats and milk. In some instances evaporated milk was substituted for pasteurized milk with no change in the results. The amount of milk was not limited. The animals did well on this diet until the beginning of the third week when they began to show some loss of appetite and a considerable loss of weight, amounting in some of the experiments to over 50% of the initial body weight. In spite of this inanition the animals continued moderately active, suggesting that little functional change had been produced in the skeletal musculature. The pathological lesions resulting from such a diet were analogous to those described by previous workers, notably Cohen and Mendel,[1] McCollum and



Control observation showing response of uterine muscle of an animal on a normal diet to a 1-2,500,000 dilution of histamine.

[1] Cohen, Barnett, and Mendel, LaFayette B., *J. Biol. Chem.*, 1918, **35**, 425.



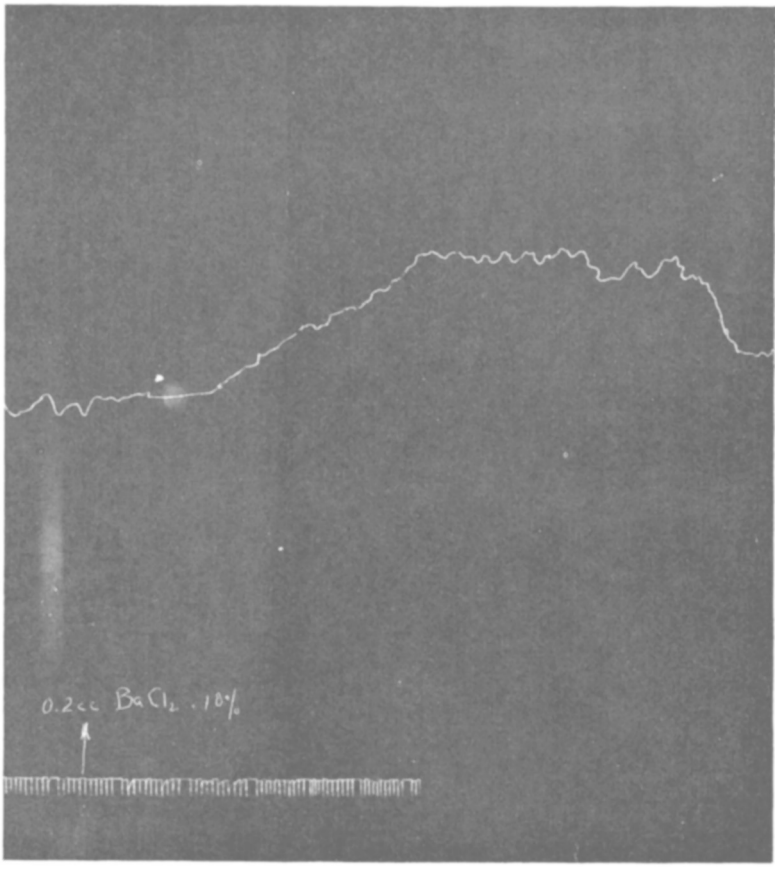
Control observation showing response of uterine muscle of an animal on a normal diet to a 1-2,500,000 dilution of pituitary extract.

co-workers,[2] and Meyer and McCormick.[3] Hemorrhagic effusions were the most characteristic and constant finding. These were found in the skin, the subcutaneous tissues, under the periosteum of the long bones, and in the intestinal tract. Bleeding from the gums was only rarely observed. The most constant lesions were subcutaneous and muscular hemorrhages about the joints of the hind legs and a tendency to epiphyseal separation of the bones, usually present even though the animals showed no subcutaneous hemorrhages.

The uterine horns of these animals were strikingly pale and flabby

[2]McCollum, E. V., and Simmonds, Nina, "The Newer Knowledge of Nutrition," Macmillan Company, 1929.

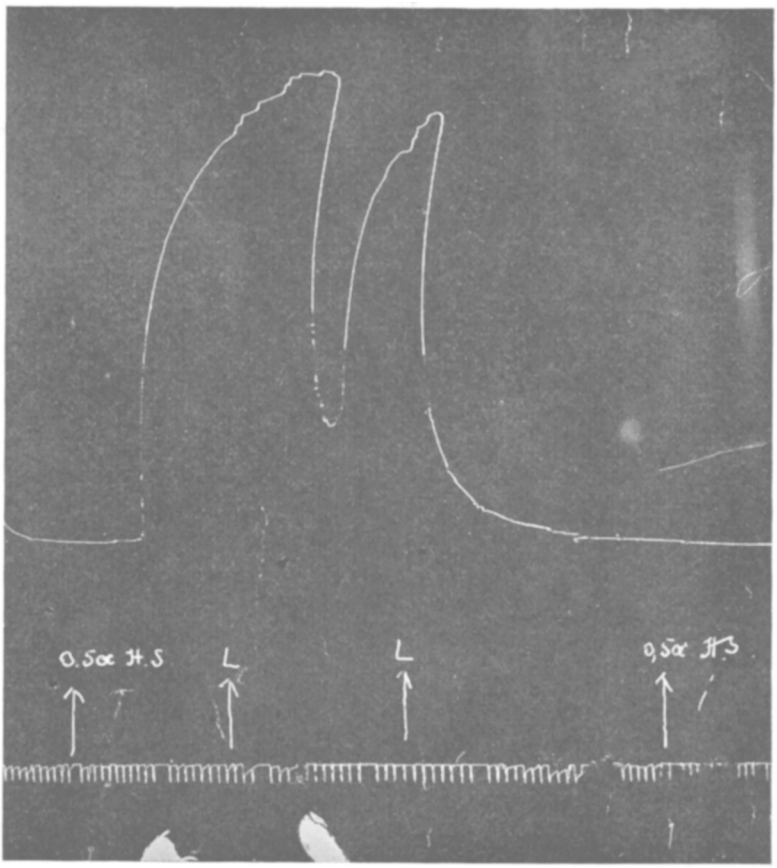
[3] Meyer, A. W., and McCormick, Lewis M., "Studies in Scurvy," Stanford University Press, Medical Sciences, 1928.



Control observation showing response of uterine muscle of an animal on a normal diet to a 1-3,000 dilution of barium chloride.

and stringy. Sections of several such horns showed an uneven staining and an indistinct appearance of the muscle. Many small degenerative areas were noticed. In some sections the nuclei were particularly affected in this degenerative process and in others the muscle fibers. There was considerable vacuolization due probably to fatty degeneration.

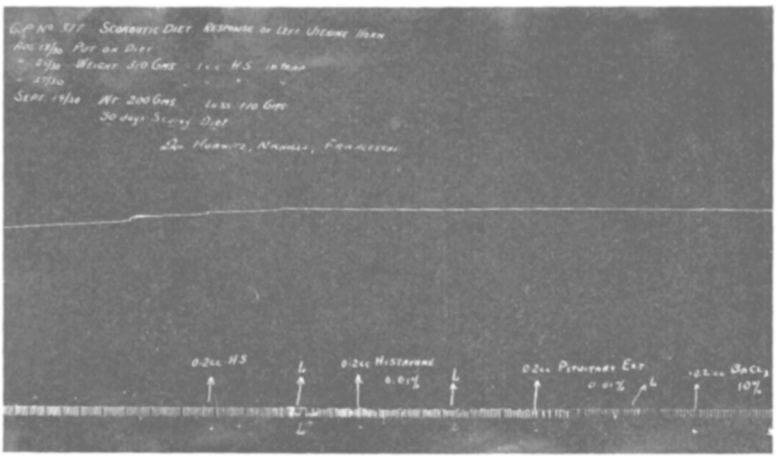
Observations were made on the responses of the uterine segments of 7 sensitized and 9 non-sensitized animals. Only 2 of the sensitized uterine segments gave slight responses on the addition of horse serum. In these instances the vitamin C deficient dietary had produced only a very slight loss of weight. These animals were of a group weighing between 300 and 400 gm. Where heavier guinea pigs are used the scorbutic lesions are produced more slowly and



Guinea Pig 376. Response of left uterine horn of a control animal on a normal diet to horse serum 33 days after sensitization with 1 cc. of horse serum intraperitoneally. The graph shows the desensitization of the muscle following a second injection of serum. The letter L represents the point at which the muscle was washed in Locke's solution.

this may account for the slight responses obtained in them. In the non-sensitized group graphic records were made of the uterine responses of 13 segments to high dilutions of histamine, pituitary extract and barium chloride. Whereas control observations showed typical and very marked responses to 1-2,500,000 and lower dilutions of histamine and pituitary extract and to 1-3,000 and lower dilutions of barium chloride, the uterine smooth muscle of pigs on a diet deficient in vitamin C failed to show any response to dilutions as low as 1-50,000 of histamine and pituitary extract and 1-1,000 of barium chloride.

The significance of these observations in their relation to anaphylactic shock will be recorded in a subsequent study. Inasmuch as the



Guinea Pig 377. Response of left uterine horn to horse serum, histamine, pituitary extract and barium chloride after 30 days on a scorbutic diet, and 25 days after sensitization. Histamine and pituitary extract were used in dilution of 1-2,500,000 and barium chloride in dilution of 1-3,000.

functional pathology of body tissues removed from animals on a diet deficient in vitamins has been little if at all studied, we felt that the recorded observations on the loss of smooth muscle reactivity in such animals are of interest. We have, as yet, no proof that other vitamin deficiencies may not produce similar results. Experimental work is in progress to determine what effect chronic anaemia and inanition in themselves might have on smooth muscle responses to antigens and to pharmacological agents such as those used in this study. Such observations are important because these two conditions are striking clinical accompaniments of vitamin C deficiency.

This loss of smooth muscle reactivity in animals on a diet deficient in vitamin C may result from degenerative changes in the muscle cell or from a loss of intercellular cementing substance[4] or from both lesions.

[4] Aschoff, L., and Koch, W., *Scorbut—Eine Pathologish—Anatomische Studie*, Gustav Fischer, Jena, 1919.