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Vitamin C and the Adrenal Gland in the Dog.*

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Harris and collaborators[1, 2] have shown that dogs do not require vitamin C in their diets for adequate nutrition. Others have kept dogs upon synthetic rations, presumably devoid of this vitamin, for periods of 1-4 years without symptoms of scurvy. Tissues from such animals, notably the adrenals and liver, show by chemical and biological tests the presence of large amounts of ascorbic acid. Similar tissues from guinea pigs kept upon scorbutic diets reveal a marked diminution in the content of ascorbic acid as scurvy develops.

The early observation[3] that the cortex of the adrenal gland contained large amounts of "hexuronic acid", later shown to be vitamin C[4, 5, 6] has led to speculation upon the relationship of this vitamin to the functions of the adrenal cortex. The belief that the medulla[7] did not contain "hexuronic acid" supported the idea of a functional significance for this uneven distribution. It has since been demonstrated that other animal tissues contain appreciable amounts of ascorbic acid, *e. g.,* liver,[8] corpora lutea,[9, 10] pituitary[11] thymus.[12] Huszák[13] has shown that the adrenal medulla contains as much vitamin C as does the cortex. Such a wide distribution is hardly indicative of a specific relationship between vitamin C and the functions of the adrenal cortex. In those species that do not develop scurvy one may reasonably consider any tissue containing much vitamin C as having a possible rôle in protecting the animal from this nutritional disorder.

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1 Harris, L. J., quoted by Innes, *Ann. Rep. Dir. Inst. Path.*, Cambridge, 1931, pp. 143-50.

2 Harris, L. J., and Ray, S. N., *Biochem. J.*, 1933, **27**, 580.

3 Szent-Györgi, A., *Biochem. J.*, 1928, **22**, 1387.

4 King, C. G., and Waugh, W. A., *Science*, 1932, **75**, 357.

5 Svirbely, J. L., and Szent-Györgyi, A., *Nature*, 1932, **129**, 576.

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7 Szent-Györgyi, A., *Science*, 1930, **72**, 125.

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10 Bessey, O. A., and King, C. G., *J. Biol. Chem.*, 1933, **103**, 687.

11 Gough, J., and Zilva, S. S., *Biochem. J.*, 1933, **27**, 1277.

12 Euler, H., and Klussman, E., *Z. Physiol. Chem.*, 1933, **219**, 215.

13 Huszák, St., *Z. Physiol. Chem.*, 1933, **222**, 229.

The question arises, is the adrenal gland in the dog concerned specifically with the synthesis and metabolic functioning of vitamin C and the consequent protection of the animal from scurvy?

Six adult male dogs have been adrenalectomized and kept alive with cortical hormone for periods of 15-33 months without any of the commonly recognized symptoms of scurvy (these animals are being used for assay of hormone preparations). During this time their diets have been almost exclusively proprietary dog foods. Only 2 animals have been varied from these diets at any time; one received a lean-meat liver diet for one month 28 months ago, while the other received beef heart for a similar period 17 months ago.

The foods have been tested for vitamin C. Bal-Ra† (Diet I) and Ken-L-Ration‡ (Diet II) were supplemented with yeast,§ salt mixture[14] and cod liver oil to make the rations similar to those fed the dogs. The assays upon guinea pigs indicate clearly that the foods are devoid of this dietary adjuvant.

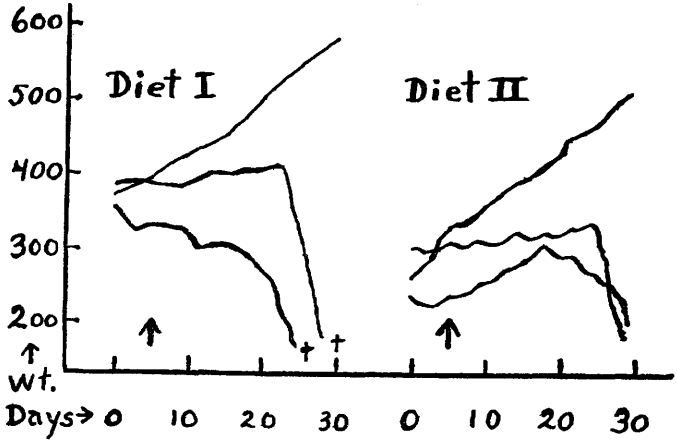

CHART 1.
Typical weight curves of guinea pigs on scorbutic diets of Bal-Ra (Diet 1) and Ken-L-Ration (Diet II).
At ↑ cabbage withdrawn from diets of experimental pigs, control I continuing on 10 gm. cabbage daily, control II transferred to 2 cc. orange juice daily.

Chart 1 gives the details of typical weight curves (selected from data on 18 animals). The 2 experimental animals on diet I died in 23 and 27 days respectively, exhibiting all of the classical symptoms of scurvy. Those on diet II showed the same early symptoms, and

† Valentine Meat Juice Co., Richmond.
‡ Chappel Brothers, Rockford.
§ Northwestern Yeast Co., Chicago.
[14] Cowgill, G. R., *J. Biol. Chem.*, 1923, **56**, 735.

when death was imminent (28th day) both were killed and autopsied. The controls were autopsied at the same time. No evidences of scorbutic lesions were observed in the controls while the experimental animals showed the usual severe abnormalities. Determination of the vitamin C content of the adrenal glands, by the technique of Birch, Harris and Ray[15] gave for the controls 0.38, and the experimentals 0.09 mg. per gm. tissue. These figures compare favorably with data reported by others. The growth curves of the control pigs indicate that the failure of the experimental animals was not due to toxic effects of the diet, *e. g.*, animal protein content.

The method of preparation of the adrenal cortical hormone precludes the presence of more than insignificant traces of ascorbic acid. Three guinea pigs, after the tenth day on a scorbutic diet, received 30 dog units of cortical hormone daily. They were killed on the 15th day of injection. No differences were observed in the weight curves or in the ascorbic acid content of the adrenals and livers of experimental and control animals. All showed marked scorbutic lesions. In this instance the injection of cortical hormone did not retard the development of scurvy. Hartman[16] considers that the cortical hormone delays the onset of scurvy.

The feeding of large amounts of vitamin C to the adrenalectomized dog does not cause any change in the hormone requirement. An assay was repeated on 2 dogs using the same extract. In the latter assay they received daily 5 mg. ascorbic acid per kilo (decitrated concentrated lemon juice) during the whole course of the experiment, *i. e.*, 30 days. The failing dose was the same in both cases. No change was noted in any of the symptoms accompanying insufficiency that would indicate a beneficial effect of the vitamin administered.

Conclusion. No evidence has been obtained that the adrenal gland, as an organ in the dog, is concerned with either the synthesis or the metabolism of vitamin C. If the adrenals do play any rôle in the metabolism of this compound the action is conferred by the adrenal cortical hormone.

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[15] Birch, T. W., Harris, L. J., and Ray, S. N., *Biochem. J.*, 1933, **27**, 590.

[16] Lockwood, J. E., and Hartman, F. A., *Endocrinology*, 1933, **17**, 501.