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Relation of Adrenal Cortex to Development of Scurvy.*

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It is well known that in scurvy (guinea pigs), marked changes develop in the adrenal. The cortex of this gland is rich in hexuronic[1] acid which has been shown by King to be vitamin C.[2] This vitamin, at least in the guinea pig, is not synthesized to any extent in the body and, therefore, its concentration in the adrenal cortex may be indicative of participation of the latter as an intermediary step in its utilization. If this is true, cortin may play some rôle in the process.

To test this hypothesis 3 series of guinea pigs with different amounts of cortin were used. The animals in each group (9 or 10 animals to a group) were balanced for sex and weight and placed on a pre-experimental diet of vitamin C-free ration and lettuce *ad libitum,* for one week previous to the experiment. At the beginning of the experimental period, the lettuce was discontinued. All animals not injected with extract were injected with one cc. of isotonic NaCl solution twice daily so that they would be subjected to the same manipulation.

Series I—Normal amount of cortin (intact adrenals). Group I—Basal diet. Group 2—Basal diet and 0.7 cc. of orange juice daily (one-half protective dose).

Series II—Added cortin (by injection). Group 3—Basal diet and 1 cc. of cortin twice daily (40 gm. whole gland per cc.).

Series III—One adrenal removed. Group 4—Basal diet. Group 5—Basal diet and 0.7 cc. orange juice.

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[1] Szent-Gyorgyi, A., *Biochem. J.*, 1928, **22**, 1387.

[2] King, C. G., and Waugh, W. A., *Science*, 1932, **75**, 357.

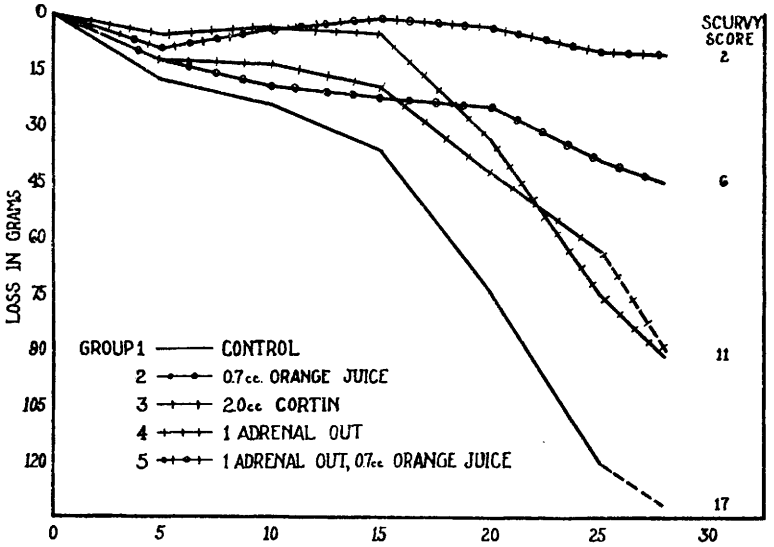

CHART 1.

The results are shown in the accompanying chart.

The guinea pigs on the control diet consistently lost weight from the beginning of the experiment which was carried out over a period of 28 days. This is not typical of a negative control series of vitamin C.[3] One or both of 2 factors may have been responsible, the amount of vitamin C obtained from lettuce in the pre-experimental period may not have been optimal or the frequent injections, in animals made sensitive by vitamin C deficiency, may have influenced the appetite. However, all conditions were controlled throughout the experiment so that the curves are comparable.

A plausible explanation for the results obtained with the cortin-injected animals is that cortin aids in the utilization of the vitamin C still available in the body. In animals with one adrenal removed, the curve resembles that of the cortin-injected guinea pigs. This may indicate a greater production of cortin than normal. It is known that the remaining adrenal after a single adrenalectomy hypertrophies[4] in young animals. It might be possible that there was overcompensation in the production of cortin for a time. (The adrenalectomy was performed at the beginning of the pre-experimental period.) This interpretation receives added support in the improved resistance to scurvy of Group 5 over Group 2.

The question may be raised whether our extract contains hexu-

[3] Sherman, H. C., and Smith, S. L., The Vitamins, 1931, p. 171.

[4] MacKay, E. M., and MacKay, L. L., *J. Exp. Med.*, 1926, **43**, 395.

ronic acid. In preparation of the extract, ether was used for extraction. Hexuronic acid is insoluble in ether.

These results may indicate that the adrenal cortex through cortin aids in the utilization of vitamin C.

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Effect of Cyanide, Hydrogen Sulphide and Carbon Monoxide on Response of Smooth Muscle to Drugs.

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Attention has been called to the fact that cyanide in low concentration may reversibly inhibit the stimulating action of drugs on the smooth muscle of rabbit uteri and intestinal strips.[1] The usual procedure* was to produce a contracture by the addition of a certain amount of drug to the solution bathing the muscle in the Trendelenberg apparatus. After washing out the drug, a solution of neutralized, buffered M/2000 NaCN was added. Three to 5 minutes later the drug was again added in the original concentration. This almost invariably failed to produce any contracture whatever. Washing and again testing the tissue with the same concentration of drug produced a contracture similar to that first obtained.

Garry[2] noted that the response of smooth muscle to certain drugs may be abolished by oxygen lack, and that the normal tonus of the strips was decreased by small amounts of cyanide. We find that cyanide in concentrations as low as M/200,000 is capable of exerting an inhibiting action on the response of the strips to drugs. This suggests the possibility that the effect may depend upon a heavy metal catalytic system such as Warburg has demonstrated to be involved in biological oxidation. To test this possibility we have studied the effect of hydrogen sulphide and of carbon monoxide on this system. Hydrogen sulphide in a concentration of M/2,000, completely blocked the action of acetyl choline (2×10^{-6}) on intestinal strips. Furthermore, it was found that mixtures of carbon monoxide and oxygen inhibited the action of adrenalin on uterus and of

[1] Schmitt, F. O., and Nicoll, P. A., *Am. J. Physiol.*, 1932, **101**, 91.

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[2] Garry, R. C., *J. Physiol.*, 1928, **66**, 235.