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THE ASCORBIC ACID CONTENT OF THE PITUITARY GLAND IN RELATION TO STRESS AND ADRENALECTOMY

BY

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It has been generally recognized that the stimulation of the adrenal glands by either endogenous or exogenous ACTH causes a depletion of ascorbic acid in these glands (Long, 1947, Sayers et al., 1945).

The adrenals, however, are not the only organs which respond in such a manner. Stimulation of the gonads by gonadotrophic hormones causes similar changes in the ascorbic acid content of the ovary (Pincus & Berkman, 1937, Claesson et al., 1949). According to the above mentioned paper of Pincus & Berkman the uterus reacts in the same way as does the ovary and in the discussion of a paper by Long, Pincus mentions a release of ascorbic acid from the pituitary gland of rabbits following copulation.

The impression is obtained that acutely enhanced activity is connected with decrease of the ascorbic acid content of several organs. It is not clear whether a relation can also be found with the release or production of hormones, or with a generally increased cell metabolism.

If increased activity is maintained for some time the ascorbic acid content returns to normal or even rises above normal values. This is true both for the gonads stimulated by gonado-
trophic hormones (pregnancy) and for the adrenals stimulated by ACTH.

Experiments by Poumeau-Delille (1949) which appear to belong to this latter class stimulated us to perform the investigation described in this paper.

Poumeau-Delille showed that in partially adrenalectomized rats the ascorbic acid content of the pituitary gland rose, whereas in totally adrenalectomized rats the ascorbic acid content was decreased. These experiments give no clue as to what happens after a single stimulation as for instance under conditions of acute stress. Moreover, shortly after adrenalectomy (24 hours) the pituitary gland appears to be very rich in ACTH, as the implanted gland causes a very marked decrease of the ascorbic content of the adrenals (Sayers & Chi-Ping-Cheng, 1949). The same authors show that stress causes a moderate decrease of the ACTH content of the pituitary gland.

The following experiments were therefore planned:
1. Determination of the ascorbic acid content of the pituitary gland of rats at various times after a stress stimulus.
2. Determination of the ascorbic acid content of the pituitary gland of rats 24 hours after adrenalectomy.

Method.

Female albino rats weighing 175—275 grams were used except in a pilot experiment in which male rats of the same weight were used. The concentration of ascorbic acid was practically the same but the weight of the pituitary glands of the females was much higher than that of the males (average 5.14 mg./100 gm. rat against 3.02 mg./100 gm. rat), so that the total content per gland was correspondingly higher. For this reason 5 »male« glands were pooled for each determination and only 3 »female« glands. The glands were immediately frozen in dry ice and stored in a Dewar vessel until the determinations were performed. The adrenals were then homogenized in metaphosphoric acid and the ascorbic acid determined colorimetrically by the method of Loeffler & Ponting (1949). The ascorbic acid content was expressed in mg./100 gm. wet
gland, as was done by Poumeau-Delille. The values obtained were only slightly higher than her values for normal rats (abt. 140 mg./100 gm.).

**Experimental results.**

In a first experiment 0.5 ml. of a 4 per cent formalin solution injected subcutaneously was used as a stress agent. This type of stress has been used extensively by Selye and others and has, in our experience regularly produced a marked decrease of the lymphocytes and eosinophils in rats. There was no change in the weight of the pituitary glands so that these figures as well as the body weights, which were about 200 gm., have been omitted from the tables for the sake of brevity. Table 1 shows the effect of formalin on the ascorbic acid content of the pituitary glands at various times after the injection. The data after 1 and 2 hours and the corresponding control value were obtained by pooling 5 glands, the other data by pooling 3 glands.

**Table 1.**

Ascorbic acid mg./100 gm. gland in the pituitary glands of rats 0, 1, 2, 4 and 6 hours after a sube. injection of 0.5 ml. 4 per cent formalin.

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Average: 142 145 139 142 145

It is evident that formalin stress which must have resulted in acute pituitary activity as shown by previous observations, did not alter the ascorbic acid content of the pituitary gland.
A second series of experiments was concerned with the effect of adrenalectomy. 12 female rats, weighing abt. 200 gm. were adrenalectomized, 12 control rats were subjected to a sham operation and treated in the same way. Two other groups of 12, one adrenalectomized and one sham operated, received subcutaneous injections of 20 mg. ascorbic acid immediately following operation in order to compensate for the endogenous ascorbic acid. All rats were killed 24 hours after operation, the pituitary glands pooled in groups of three and the ascorbic acid determined in the usual manner. Again no difference was found in the weights of the pituitary glands. Table 2 gives the data obtained.

The Roman figures refer to the various groups:
I — adrenalectomized,
II — adrenalectomized + ascorbic acid,
III — sham operated,
IV — sham operated + ascorbic acid.

Table 2.
Ascorbic acid mg./100 gm. gland in the pituitary glands of adrenalectomized and sham operated rats c. q. treated with ascorbic acid.

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As in the case of stress, adrenalectomy did not affect the ascorbic acid content of the pituitary glands. The average values appear to be somewhat lower than in the sham operated groups, but the variation in the individual values make it quite clear that these differences are not significant. Moreover, the values are not significantly different from those of Table 1, which indicates that the operations considered as stress did not influence the ascorbic acid content (at least not 24 hours after the operation).
DISCUSSION

The above mentioned results show that increased corticotrophic activity of the pituitary gland is not reflected in its ascorbic acid content. In this respect the pituitary gland behaves differently from the adrenals and the ovaries. It is possible that the situation is different with regard to the gonadotrophic activity (Pincus, 1947) and to the corticotrophic activity in subacute experiments (Poumeau-Delille, 1949).

At the present time it is not possible to give any explanation for this different behaviour, as we know nothing at all about the significance of ascorbic acid either in the synthesis of hormones in, or of their release from these glands. We do not even know if its presence is necessary for the synthesis of hormones, as its occurrence in endocrine glands might suggest, or if its absence is essential, as the decrease in ascorbic acid content in adrenals and ovaries under conditions of hyperactivity suggests.

This latter possibility appears to be of interest since Booker et al. (1950) showed that the excretion of ascorbic acid in the urine increases under conditions of stress, and this does not suggest that it is used up during steroid synthesis.

When the role of ascorbic acid in this respect has been elucidated a simple solution will probably be found for the behaviour of the pituitary gland ascorbic acid.

SUMMARY

The ascorbic acid content of the pituitary gland of rats under conditions of acute corticotrophic hyperactivity (formalin stress, resp. 24 hours after adrenalectomy) appeared to remain unchanged.

REFERENCES