

Relationship of the Pituitary to the X zone of the Mouse Adrenal.*

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The relationship of the X zone of the mouse adrenal¹⁻³ to the pituitary is not known. It was considered that the use of the technic of hypophysectomy might produce results of help in the elucidation of this problem.

Material and Methods. Virgin female "Swiss albino" mice, aged 40-42 days at the commencement of the experiment, were used. The adrenal X zone is well developed at this age. Hypophysectomy was performed by the parapharyngeal approach. Injection of the hormones noted below was started 24 hours after the operation (except that the chorionic gonadotropin injections were commenced 48 hours after operation) and the animals killed 24 hours after the last injection. The mice were grouped as follows:

1. Twelve intact untreated animals killed at 54-58 days of age.
2. Eleven animals hypophysectomized for 12 days and 8 for 14 days and then killed.
3. Nine hypophysectomized animals injected with a pituitary preparation, principally adrenocorticotropin‡ in nature, 1 mg per day divided into three intraperitoneal in-

jections, for 12 days.

4. Nine hypophysectomized animals injected subcutaneously with 1 mg of pituitary gonadotropin, principally LH‡ in nature, for 10 days.

5. Five hypophysectomized animals injected subcutaneously with 1 mg per day of pituitary gonadotropin, principally FSH‡ in nature, for 10 days.

6. Six hypophysectomized animals injected intraperitoneally with 11 I.U. of human chorionic gonadotropin ("Korotrin") per day for 10 days.

The right adrenal was treated routinely after fixation in Bouin's and stained in Harris' haematoxylin and eosin or Heidenhain's Azan. The left adrenals were fixed for histochemical studies and are not being reported upon here. The thymus, uterus and ovaries were weighed; the ovaries were then treated as for the right adrenal. The completeness of hypophysectomy was judged by the examination of serial sections of the appropriate area in 2 cases from each group; in the remainder the success of the operation was judged by the examination of the sella turcica region under binoculars (x 15). Added confirmation was given by the weight of the animal and, where relevant, by the weights of the uterus and ovaries and the histological condition of the ovaries and adrenals.

Results. The intact untreated animals showed a well-developed X zone with deep eosinophilia of the cytoplasm and large vesicular basophil nuclei. After 12 to 14 days of hypophysectomy the X zone became more compact,[§] the cytoplasm of the cells had

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¹ Howard-Miller, E., *Am. J. Anat.*, 1927, **40**, 25.

² Parkes, A. S., *Phys. Rev.*, 1945, **25**, 203.

³ Jones, I. Chester, *Q.J.M.S.*, 1948, **89**, 53.

‡ The author is very grateful to the Armour Company for the ACTH and LH preparations and to the Schering Corporation for the FSH. The ACTH used was lot 42B about 36% potency of the Armour La-1-A standard; see Forsham, P. H., *et al.*, *J. Clin. End.*, 1948, **8**, 15, for discussion of this and of the type of contaminants. The LH type of gonadotropin was Lot FW-234, the main contaminants being posterior lobe hormones; there was slight FSH activity. The FSH type of gonadotropin ("Synergist") produced good follicle development in the ovaries of hypophysectomized mice with some luteinization.

§ Leblond, C. P., and Nelson, W. O., (*Bull. Hist. Appl.*, 1937, **14**, 181), note the disappearance of the X zone after hypophysectomy but their data include only four mice which would have had an X zone at the time of operation and the length of time for which these were hypophysectomized is not made clear. The "brown degeneration" occurring in another series⁴ did not appear in the hypophysectomized animals in this experiment.

shrunk and stained only faintly with eosin; the nuclei were irregular and stained deeply with haemotoxylin (remains of the X zone can be seen up to 100 days after hypophysectomy⁴). The zona fasciculata showed the atrophy characteristic of the adrenals of other animals after hypophysectomy;⁵ the zona glomerulosa showed no change in the routine histological preparations. In the ACTH injected animals the X zone was unaffected but the rest of the cortex resembled that of the normal animal. In the LH injected animals the X zone was maintained in a condition similar to that of the normal animal; the zona fasciculata was unaffected and showed the atrophy characteristically appearing after hypophysectomy; the zona glomerulosa was not affected. In the FSH injected animals the X zone had not degenerated as far as in the hypophysectomised controls but the degree of maintenance was much less than in the LH injected animals; the rest of the cortex had an appearance typical of that of the hypophysectomised animal. In the animals injected with chorionic gonadotropin the X zone had disappeared and a medullary connective tissue capsule had formed; the remainder of the cortex was unaffected by the hormone.

Discussion. The X zone depends upon the pituitary for the maintenance of its normal histological structure and a pituitary gonado-

tropin seems to be the maintaining factor. This gonadotropin is possibly LH, the effect of the FSH preparation then being due to the contaminating LH. The rich LH secretion of castrate animals^{6,7} would account for the persistence and growth of the X zone of the prepuberally castrated male mouse and for the evocation of a "secondary X zone" in the mouse castrated when adult.

The chorionic gonadotropin, which has some physiological properties in common with LH, swept the X zone away, paralleling its action in the intact animal.⁸ It is equivalent in its results to the direct action of testosterone on the X zone of the *hypophysectomised* prepuberally castrated male mouse.⁹ In normal animals, then, it may be that the maintaining factor of the pituitary is overridden, in the male at puberty by the direct action of androgens on the X zone and in the female early in first pregnancy by an "anterior pituitary-like" hormone arising from the conceptus or the endometrium.¹⁰ The X zone seems to be independent of ACTH which indeed may be concerned mainly with the zona fasciculata.⁵ The results require confirmation by the use of chemically pure pituitary factors when these are available.

⁶ Hellbaum, A. A., and Greep, R. O., *Am. J. Anat.*, 1940, **67**, 287.

⁷ Greep, R. O., *PROC. SOC. EXP. BIOL. AND MED.*, 1940, **44**, 214.

⁸ Takewaki, K., *J. Facult. Sci.*, Tokyo, 1935, **4**, 83.

⁹ Jones, I. Chester, 1948, in preparation.

¹⁰ Rowlands, I. W., *J. Endocrinology*, 1947, **5** (3), Supp. p. xx.

⁴ Jones, I. Chester, *Anat. Rec.*, 1948, **100**, (4) Supp., p. 49 and unpublished.

⁵ Deane, H. W., and Greep, R. O., *Am. J. Anat.*, 1946, **79**, 117.