PITUITARY HYPERPLASIA IN A MALE MOUSE AFTER THE ADMINISTRATION OF OESTRIN

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Several observers have noticed enlargement of the pituitary gland in animals subjected to oestrogens. This enlargement, as a rule, is distinctly less than that which follows castration. According to Wolfe and Phelps the changes caused by oestrin in the anterior lobe of the rat's pituitary are (1) a degranulation of the eosinophile and basophile cells, with a diminution of their total numbers, and (2) an increase in size and number of the chromophobe cells.

Cramer and Horning found pituitary changes in 11 among 12 mice which had been treated by cutaneous applications of oestrin; in three of them pituitary adenomata, consisting mainly of chromophobe cells, were present. Gardner, Strong and Smith have described a pituitary tumour, consisting chiefly of chromophobe cells, which developed spontaneously in an old breeding doe.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Description</th>
<th>Number</th>
<th>Pituitary Tumour Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Prolonged application of oestrogen</td>
<td>567</td>
<td>1</td>
</tr>
<tr>
<td>Male</td>
<td>Untreated controls to above</td>
<td>52</td>
<td>0</td>
</tr>
<tr>
<td>Female</td>
<td>Old untreated breeding does without mammary tumour</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Female</td>
<td>Old untreated breeding does with mammary tumour</td>
<td>50</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>679</td>
<td>1</td>
</tr>
</tbody>
</table>

Table I: Mice Examined for Pituitary Tumour

The writer has seen only one instance of pituitary enlargement, which might be described as a "tumour" among 679 stock mice, including 567 males which had been submitted to prolonged treatment with oestrogens (see Table I). The experimental history of the exceptional mouse is as follows.

Beginning in January 1935, when the mouse was six weeks old, cutaneous applications of oestrone (0.01 per cent) in benzene were made to the inter-
Fig. 1. Thyroid Adenoma. X 40

Fig. 2. Adrenal, showing lipoid accumulation (X) containing scattered nuclei and interposed between cortex and medulla. X 40
scapular region twice a week and continued, except for two short intervals, until death, 483 days later. On the 107th day of the experiment the tips of the left coagulating gland and seminal vesicle were excised and grafted subcutaneously in the right groin. From this graft a cyst formed containing at its maximum 4 c.c. of clear fluid, which was tested by Mr. F. L. Warren and found to be non-oestrogenic. When the administration of oestrone was stopped, the cyst shrank; when the applications were resumed, it expanded again. On April 27, 1936, the mouse, which had seemed in good health, was found dead. The post-mortem examination revealed, in addition to the cyst just mentioned, (1) a globular enlargement of the pituitary which measured $5 \times 5$ mm. in its two accessible diameters, (2) an adenoma of the left lobe of the thyroid, (3) pronounced changes in the adrenals, and (4) extensive mammary development (Figs. 1–3).

Serial sections of the pituitary tumour were stained with eosin and haematoxylin (Fig. 4). They show that the hyperplasia is limited to the anterior lobe of the pituitary: the posterior lobe, though enveloped, appearing normal. The gland consists almost entirely of cells of one type supported by a well differentiated vascular stroma. These cells have round or bluntly oval nuclei surrounded by a granular cytoplasm which in some instances is faintly coloured by haematoxylin and in others by eosin; they may be described as chromophobe. A few mitoses can be seen. No typical basophilic or eosinophilic cells are present. Hemorrhages are absent except for a few small extravasations in the neighbourhood of the posterior lobe, which are too minute to affect appreciably the bulk of the gland.

The thyroid tumour appears to be a simple adenoma (Fig. 1). The adrenal changes are of the kind previously described (Burrows) as occurring in male mice after prolonged applications of oestrogenic compounds. The change consists in the collection of round masses of cytoplasm containing much lipoid substance and scattered nuclei in the zona reticulata (Fig. 2). These masses appear to be formed by the coalescence of lipoid-laden cells derived from the inner part of the zona fasciculata. There is some evidence that a reconstituted X-zone may be a precedent to this adrenal change.

The mammae show an extensive development of acini, and resemble the breast of a pregnant female. The ducts are distended with secretion, and lactational changes are manifest in the alveoli of some, though not in all, regions of the breast (Figs. 3 and 5). The testes are normal in size, and

![Fig. 3. Mamma, showing advanced Gynaecomastia. × 12](image)
There is a copious round-cell infiltration.

Fig. 4. Pituitary, consisting entirely of chromophobe cells. X 500

Fig. 5. Mammary alveoli showing lactational changes. X 500
active spermatogenesis is in progress, though the spermatozoa are not completely developed (Fig. 6). There is a diminution rather than an increase of the interstitial gland cells, which are small and free from lipoid deposits. The epididymis contains large numbers of spermatozoa, some of which appear to be fully formed.

Features of interest in the case are the development of (1) an extensive chromophobe hyperplasia of the pituitary, (2) thyroid adenoma, and (3) gynaecomastia with lactation accompanied by spermatogenesis.

**SUMMARY**

Among 567 male mice submitted to prolonged applications of oestrogens, only one instance of great pituitary enlargement occurred. It was accompanied by a thyroid adenoma, changes in the adrenals, and extensive mammary development with lactational changes coincident with spermatogenesis.

**REFERENCES**


