HISTOPHYSIOLOGY OF THE PITUITARY CLEFT AND COLLOID CYSTS IN THE ADENOHYPOPHYSIS OF THE RAT. CHANGES AFTER GONADECTOMY AND ADRENALECTOMY

BY JAIME FERRER

From the Instituto de Investigaciones Medicas, Boul. Wilde 761, Rosario, Argentina

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SUMMARY

1. Pituitaries of normal, adrenalectomized and castrated male rats have been studied using the freeze-drying technique.

2. The pituitary cleft is surrounded anteriorly by an endothelioid fenestrated epithelium and posteriorly by a cubical or cylindrical epithelium. In the latter colloid droplets can be seen in the cytoplasm, and evaginations containing colloid droplets occur at the apical poles of the cells and project into the lumen of the cleft.

3. The histological picture suggests that the colloid contained in the cleft might be formed by: (a) destruction of the basophilic and eosinophilic cells of the pars distalis, (b) transudation of plasma from capillaries in the anterior wall of the cleft, (c) mucus discharged by goblet cells in the anterior epithelium, and (d) apocrine secretion and the secretion of colloid from the posterior epithelium.

4. Changes in the height, the amount of cytoplasmic colloid and the apocrine secretion of the posterior epithelium occur after adrenalectomy and castration.

5. There are two types of cyst in the adenohypophysis, one having a mucinous content and covered with a mucous epithelium, and the other a flattened epithelium and a colloid content. The latter, in addition to the pituitary cleft, might play some part in secretory processes.

The pituitary cleft in the rat is a space located between the pars distalis and pars intermedia; in shape it resembles a concavo-convex lens, the concavity of which is formed by the pars intermedia and the convexity by the pars distalis. Laterally, where the two lobes are united, it forms two pouches (Text-fig. 1).

The pituitary cleft is not only found in rodents, but also in other mammals and in man during childhood [Selye, 1943]. It is occupied by colloid, which can also be found in cysts in the pars distalis. In cattle the colloid-containing cavities may be lined either by cylindrical ciliated cells with some intervening goblet cells or by an endothelioid-type of epithelium [Bassett, 1951]. Selye [1943] found that intravenous injection of hypertonic sodium chloride solutions in rats results in an increase in the amount of colloid material, both in the pituitary cleft and in the small cystic cavities of the anterior lobe, but we have been unable to repeat this observation in our laboratory.

In order to determine the origin and significance of the colloid material and of the structures involved in its production, the pituitary glands of normal, adrenalectomized and gonadectomized male rats, previously treated by the Altmann–Gersh technique, have been studied.
MATERIALS AND METHODS

Preparation of tissues. Fourteen male rats were used, five normal, four adrenalectomized 10 days before death, and five castrated 30 days before death. The pituitaries were removed immediately after death, immersed in isopentane cooled in liquid air and afterwards dried in a vacuum at −30°C. The glands were denatured in absolute alcohol and embedded in paraffin; coronal sections 5µ thick were stained by the McManus–Hotchkiss (PAS) technique, a modification of Mallory's trichrome stain, Pap's method for reticular fibres and Mayer's mucicarmine.

Quantitative estimations. The epithelium lining the posterior wall of the cleft was studied quantitatively in nine rats (three normal, three adrenalectomized and three castrated). The projected image of this epithelium (×1000) was drawn on a long strip of uniformly thick paper and its length measured with a fine thread. The drawing was then cut out and its weight compared with that of a rectangular piece of the same paper of known area. The mean height of the epithelium could thus be established by simple arithmetic.

Two strips of this type were measured for each rat and the mean of the two estimations used to test, by analysis of variance, the effect of the experimental treatments on the height of the epithelium.

RESULTS

The appearance of the epithelium lining the pituitary cleft varied with its position, and that of the portion covering the pars intermedia, i.e. the posterior epithelium, with the experimental treatment.

The posterior epithelium in the normal rat is cubical, cylindrical or occasionally stratified, particularly in the angles of the lobes of the pars intermedia (Text-fig. 1).
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It always forms a continuous sheet, but is rarely uniform in height, being higher in some zones which alternate with others in which it is flattened. The cells occupying the former have, at their apical poles, evaginations which extend into the lumen (Plate, figs. 1, 2), a condition which was most evident in the adrenalectomized animals. In the cytoplasm of the epithelial cells are droplets which stained with the McManus–Hotchkiss’s technique and with the blue of the trichrome stain. There are regional variations in the amount of these droplets which are more plentiful in the zones where the epithelium is high than in those having a low epithelium (Plate, figs. 1, 2). The zones with the lowest epithelium have neither droplets nor evaginations (Plate, fig. 3). The amount of these droplets also varied with treatment, being greater in the hypophyses of the adrenalectomized animals than in those of the other two groups.

The appearance of the anterior epithelium, i.e. that covering the pars distalis, seems to depend on the amount of colloid present in the cleft. It is always very low, sometimes discontinuous, and when a large quantity of colloid is present this lining appears as a fenestrated endothelioid epithelium, lying upon a network of reticular fibres. Through the fenestrations basophilic and eosinophilic cells of the pars distalis and capillaries can be seen projecting into the lumen and in direct contact with the colloid of the cleft. In the anterior epithelium of some pituitaries are found small regions occupied by tall ciliated cells whose cytoplasm contains a considerable amount of mucus (Plate, fig. 4). The epithelium from the two pouches is always high and often stratified.

In the pars distalis there are two types of cyst: one with a mucous content and lined by a mucous epithelium (Plate, fig. 5), and the other containing colloid, lined by a flat epithelium similar to that forming the anterior lining of the cleft (Plate, fig. 6).

The pituitary cleft contains an inspissated colloid which stains from deep blue to yellow with Mallory’s stains and red by the McManus–Hotchkiss technique. Within this colloid are variable numbers of basophilic and eosinophilic cells in different degrees of disintegration and some erythrocytes. When a basophilic cell disintegrates it undergoes the following characteristic changes. At first the cell increases in size, its granulations swelling and later changing into large vacuoles with a homogeneous content; still later these structures coalesce to form one or two huge vacuoles, the substance of which has staining properties similar to those of the colloid itself, although

Table 1. Changes in the height of the pituitary epithelium following adrenalectomy and castration

<table>
<thead>
<tr>
<th>Treatments</th>
<th>n</th>
<th>Mean height of epithelium (μ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>3</td>
<td>6.46</td>
</tr>
<tr>
<td>Adrenalectomized</td>
<td>3</td>
<td>5.78</td>
</tr>
<tr>
<td>Castrated</td>
<td>3</td>
<td>4.14</td>
</tr>
</tbody>
</table>

n = number of rats for each treatment.

Analysis of variance

<table>
<thead>
<tr>
<th>Source of variation</th>
<th>Degrees of freedom</th>
<th>Sum of squares</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatments</td>
<td>2</td>
<td>17.14</td>
<td>6.03</td>
<td>0.05–0.02</td>
</tr>
<tr>
<td>Error (rats)</td>
<td>6</td>
<td>8.53</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
some are stained with the Orange G. Up to this time the cell membrane remains intact and the nucleus has a normal leptochromatic appearance. Later, however, the cellular membrane disappears and the cytoplasm, transformed into colloid, is incorporated into the colloid of the cleft. The nucleus gradually disappears by lysis, without any pyknosis or karyorrhexis. The basophilic cells lining the colloid cysts of the pars distalis undergo similar changes (Plate, fig. 6). The eosinophils, like the basophils, transform their granules into vacuoles that exhibit an affinity for Orange G.

The height of the posterior epithelium of normal, adrenalectomized and castrated rats is summarized in Table 1. This shows that no changes are induced by adrenalectomy, but that gonadectomy is associated with a significant flattening of this epithelium.

**DISCUSSION**

The histological picture of the two types of epithelium in the pituitary cleft of the rat and of the exfoliation of the chromophilic cells from the pars distalis implies that these structures may be connected with the production of the colloid.

The posterior epithelium seems to contribute both an apocrine and a colloid secretion. This contention is supported by the presence of colloid droplets inside the cytoplasmic evaginations which project into the lumen of the cleft (Plate, figs. 1, 2) for the alternative interpretation of this appearance, namely, that colloid is being reabsorbed by the cells of the posterior epithelium, seems unlikely. Further evidence that the posterior epithelium has an endocrine function is provided by the observation that the difference in the mean height of this epithelium between normal and castrated and between adrenalectomized and castrated rats was statistically significant, while there was no significant difference between normal and adrenalectomized animals. There was no correlation between the amount of colloid of the cleft and the height of this lining \((r = -0.09)\) from which it may be inferred that the changes in height were not passively induced.

The anterior epithelium would seem to contribute to the formation of colloid only through the mucus produced by its few goblet cells (Plate, fig. 4). The pars distalis may contribute to the formation of colloid by two different mechanisms: by the disintegration of chromophilic cells and by transudation of plasma from the capillaries near the cleft. Although Rasmussen [1927] described globules of colloid in blood vessels, we were unable to observe them, but theoretically colloid could be absorbed either through the capillaries or through the posterior epithelium.

The nature and functional significance of the colloid is far from clear. Rasmussen [1927] thought that it might play some part in the secretion of hormones from the pituitary gland, and although Bassett [1951] reported that tests for biological activity in colloid material taken from large cysts were negative, its derivation in part from the chromophilic cells of the pars distalis suggests that it must be of a hormonal character. In this connexion Catchpole [1949], Purves & Griesbach [1951, 1952] and Halmi [1952] believed that the granules of the basophilic cells might be the gonadotropic and thyrotrophic principles produced by the adenohypophysis, and Lewis, Lee & Astwood [1937] found intermedin in the colloid of the cleft. The morphological changes in the posterior epithelium which followed adrenalectomy and castration in the rat now favour the view that this epithelium also might participate in the
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mechanism of production of some hormones but not in others. Thus the material produced by the destruction of both types of chromophilic cells and the apocrine secretion and colloid in the posterior epithelium may possibly be mixed in the pituitary cleft in proportions which differ according to the treatment given.

The functional significance of the colloid cysts of the pars distalis is not yet thoroughly understood. They have colloid similar to that of the cleft, but contain more fluid; basophilic cells, similar to those of the pituitary cleft, are present, an observation which suggests that they might participate in the mechanism of secretion.

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DESCRIPTION OF PLATE

(All photomicrographs magnified × 600.)

Fig. 1. Posterior epithelium of the pituitary cleft (mean height marked by vertical line), of a normal male rat. Droplets of intracellular colloid may be seen at the apical poles, particularly in the evaginations of the upper part of the cytoplasm (PAS).

Fig. 2. Adrenalectomized male rat. Posterior epithelium of the pituitary cleft. (Mean height marked by a vertical line.) As in the normal rat this photomicrograph shows apocrine secretion and droplets of intracellular colloid (PAS).

Fig. 3. Castrated male rat. Posterior epithelium of the pituitary cleft (mean height marked by a vertical line). This lining is very thin, showing neither evaginations nor droplets (PAS).

Fig. 4. Goblet cells located in the anterior epithelium of the pituitary cleft. (Haematoxylin and mucicarmine.) a, pars intermedia; b, posterior epithelium; c, pituitary cleft; d, ciliated cylindrical cells of the anterior epithelium; e, pars distalis.

Fig. 5. Mucoid cyst located in the adenohypophysis. It is surrounded by ciliated cylindrical cells with goblet cells interspersed between them. (Haematoxylin and mucicarmine.)

Fig. 6. Colloid cyst of the rat’s adenohypophysis. It is lined by an endothelioid epithelium and contains colloid-like substance with two disintegrated basophilic cells.