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Developmental Relationship between Epithelial Hypophysis and Infundibulum in *Triturus torosus.**

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Burch has presented evidence to show that the physiological differentiation of both the anterior and the intermediate lobes of the pituitary requires the contact of the epithelial hypophysis with nervous tissue, specifically the floor of the infundibulum.[1, 2] In experimental embryos of *Hyla regilla,* contact of hypophysis with infundibulum was prevented by early translocation of the infundibular anlage to a position in the hind brain. Such embryos developed into silvery-white tadpoles which failed to metamorphose. The "albinism" was shown to be caused by a lack of secretion of the *pars intermedia,* whereas the failure to metamorphose was attributed to lack of thyrotropic principle of the anterior lobe. Histological examination showed no evidence of differentiation in the hypophysis, a mass of deeply staining material occupying its normal position at the tip of the notochord, yet some distance away from the transplanted infundibulum. It was suggested by Burch that the infundibulum acts as an organizer upon the epithelial hypophysis.

I undertook experiments upon a urodele, *Triturus torosus,* to confirm Burch's findings. Using a method described earlier,[3, 4] gelatin was injected into 2 series of embryos in early tail-bud stage, namely, into the cavities of the brain of one series and into the foregut of the other. In the former series the ventricles of the brain, including the infundibular recess, were inordinately distended. In several instances the epithelial hypophysis failed to reach the floor of the infundibulum in its migration inward from the stomodeum, probably because of pressure exerted by the gelatin within the brain. These tadpoles exhibited without exception the syndrome of "albinism." The melanin in both epidermal and dermal melanophores was highly concentrated, whereas the pigment within the xantholeucophores was markedly dispersed. Histological examination disclosed the hypophysis as a mass of undifferentiated cells lying beneath the dien-

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1 Burch, A. B., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 608.

2 Burch, A. B., *Ibid.*, 1939, **40**, 341.

3 Eakin, R. M., *Univ. Calif. Publ. Zool.*, 1933, **39**, 191.

4 Eakin, R. M., *Ibid.*, 1938, **43**, 185.

cephalon and immediately anterior to the infundibular recess. As the larvae were sacrificed at the end of 5 weeks information regarding metamorphosis is not available.

In the second series, in which the foregut was maximally distended with gelatin, the hypophyseal anlage was recognizable at the time of injection as a patch of whitish cells in the region of the future stomodeum. In some specimens this cluster of cells remained entirely outside for 5 or 6 days after injection. As a result either of the enlargement of the buccal cavity through growth or of the partial liquefaction of the gelatin, the hypophysis was permitted eventually to migrate inward.

All larvae which were successfully maintained for 6 weeks showed normal pigmentation, except one. This one specimen exhibited the condition of "albinism" characteristic of hypophysectomized tadpoles of *Triturus*[5] and similar in all respects to the syndrome observed in the first series. Microscopic sections of the specimen showed the hypophysis as a block of undifferentiated material lying between the optic recess and the roof of the pharynx. In one place the cells of the hypophysis still formed a part of the pharyngeal epithelium. The gelatin had apparently prevented the epithelial hypophysis from reaching its normal position at the base of the infundibulum. Furthermore, large masses of cartilage, which evidently developed in response to the pressure exerted by the mass of gelatin within the foregut, imprisoned the hypophysis, thus precluding all possibility of its ever completing its inward migration. Although in contact dorsally with the optic recess, the hypophysis apparently induced no hyperplasia in the nervous tissue, as noted by other investigators.[1, 6]

The experimental larvae, other than the "albino" described above, were indistinguishable from the controls as regards pigmentation. Microscopic sections of each revealed, however, that the experimental procedure had not completely prevented the epithelial hypophysis from establishing contact with the infundibulum. In some instances it had succeeded in migrating to its normal definitive position at the posterior limit of the infundibular recess; in others it came to lie along the antero-ventral wall of the infundibulum. In one instance just a few posteriormost cells of the hypophysis reached infundibular tissue; for the most part the hypophyseal cells extended forward and ventrad through a foramen in the chondrocranium. Yet apparently this one point of contact was sufficient for the functional differentiation of the *pars intermedia,* at least. Since the larvae

[5] Miller, A. H., unpublished manuscript.

[6] Smith, P. E., *Am. Anat. Mem.*, **11**

of this series likewise were fixed prior to the time of metamorphosis, no information upon the functional differentiation of the anterior lobe is available.

Although the number of "albinos" in each series is very low, the evidence is so unmistakable that one may safely conclude that the developmental relationship between the epithelial hypophysis and infundibulum in urodeles is essentially as Burch has shown for *Hyla,* namely, that the functional differentiation of the former is dependent upon contact with the latter.

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Studies on the Cause of Increased Growth During Pregnancy.

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Slonaker,[1] Hain,[2] and Stein[3] have shown that pregnancy favorably affected the growth curve in rats over littermate virgin controls. Cole[4] observed that even in pregnant rats precociously matured with mare gonadotropic hormone there was an increased growth rate and this was confirmed by Cole and Hart.[5] The increased rate of growth was accompanied by increased food consumption starting as early as 48 hours after copulation. Lactation neither enhanced nor reduced this favorable effect. The data in this paper relate to the factors involved in this phenomenon.

Pseudopregnancy. Goss[6] and Slonaker[7] showed that a single pseudopregnancy increased growth in the rat though the effect of repeated pseudopregnancies was not determined. In our previous paper[5] one animal was cited having only 2 pregnancies followed by 13 periods of pseudopregnancy over a 9-month period. This animal continued to gain over her littermate control throughout this period and at autopsy this increase amounted to 119 g. We were, therefore, interested to ascertain if repeated pseudopregnancies would have as marked an effect as normal pregnancies had shown. This is im-

1 Slonaker, J. R., *Am. J. Physiol.*, 1927, **82**, 318.

2 Hain, A. M., *Quart. J. Exp. Physiol.*, 1932, **22**, 71.

3 Stein, S., *Endocrinology*, 1934, **18**, 721.

4 Cole, H. H., *Am. J. Physiol.*, 1937, **119**, 704.

5 Cole, H. H., and Hart, G. H., *Am. J. Physiol.*, 1938, **123**, 589.

6 Goss, H., *Anat. Rec.*, 1926, **32**, 232.

7 Slonaker, J. R., *Am. J. Physiol.*, 1929, **89**, 406.