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THE DEVELOPMENT OF THE HYPOPHYSIS OF THE ANURA

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EIGHTEEN FIGURES

Recent studies have shown that the epithelial portion of the hypophysis consists of three parts. It has been clearly demonstrated that these three parts are distinct both ontogenetically and histologically. Besides the anterior lobe proper and the pars intermedia previously recognized, Tilney ('13) has shown that a third epithelial part, the 'pars tuberalis' is to be distinguished in mammals and in birds. He gives a brief account of its development in the cat and in the chick. Woerdeman ('14) treats of early stages in the development of an homologous part, the 'lobulus bifurcatus,' in reptiles, birds, and mammals. Baumgartner ('16) traces the development of the 'pars tuberalis' in reptiles. Parker ('17) has described its ontogeny in the Marsupialia. In a recent paper ('18) the writer has given a detailed account of the development of the hypophysis of the rabbit and has followed the differentiation of the three epithelial parts until the time of birth.

The most striking feature in the development of the pars tuberalis is its paired origin. This is noted by all of the authors above enumerated. In the rabbit the pars tuberalis is discernible very early. From the thickened epithelium which lies in front of the early Rathke's pocket two thickened ridges are formed. These are the anlagen which fuse and form the 'pars tuberalis'—a thin lamina surrounding the infundibular neck and spreading out under the tuber cinereum.

The pars tuberalis is in many forms considerably more vascular than is the pars intermedia. It is further characterized by the tubular or acinar arrangement of its cells. Tilney states that the walls of these acini are composed of one or two layers of cells, while Parker and Atwell speak of them as being composed of one layer only.

Woerdeman ('14) draws an interesting homology between the pars tuberalis (which he terms the 'lobulus bifurcatus' following Bolk) and the inferior sacs of the Elasmobranch fishes, which, as is well known, have a paired origin. Woerdeman lacked material showing the development of the hypophysis in the higher fishes and in the Amphibia. On this account the writer felt that such an homology must be considered precarious until the ontogeny of the hypophysis had been studied for these remaining vertebrate classes (Atwell, '18).

The present study was undertaken for the purpose of ascertaining whether a homologue of the pars tuberalis is to be recognized in the amphibian hypophysis. In answering this question it was hoped that light would be shed on the question as to whether a lobe comparable to the pars tuberalis is constantly present in the hypophysis of all vertebrates.

THE DEVELOPMENT OF THE HYPOPHYSIS IN THE ANURA

The material for this study consists of some eighty series of sections of larvae of Rana pipiens, which range in length from 2 to 25 mm. This was augmented by the preparation of series of larval Rana clamitans obtained just preceding and during metamorphosis. For the hypophysis of the adult frog, specimens of R. pipiens and of R. catesbiana were used. For purposes of comparison several series of larvae of a toad (Bufo americana) were also prepared.

A series of wax-plate reconstructions was made from typical larval and adult stages to illustrate the morphogenesis of the hypophysis. The hypophysis of the adult frog was first studied in the gross and sketched at a low magnification, using the camera lucida. After sectioning, the same structures were identified and studied under higher powers. Graphic reconstructions were made and compared with the sketches obtained in the gross.

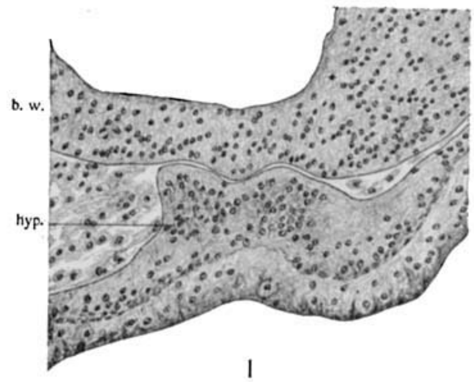
It is not the purpose of this study to treat at length the early appearance of the hypophysis. This has been done for the Amphibia by Goette ('75), Orr ('89), Haller ('97), and Corning ('99). Of the large number of series of sections studied only certain typical stages have been selected for description here.

3-mm. larva of Rana pipiens. At this stage the anlage of the hypophysis is already well formed. The ectoderm at the anterior end of the embryo is separated into two well-defined layers. It is from the inner of these that the hypophysis arises. In sagittal sections the hypophysial anlage shows as a wedge-shaped mass of cells lying between the neural tube and the wall of the foregut. The apex of the wedge is directed caudally. There is usually considerable separation between the two layers of ectoderm at the base of the wedge. The appearance given is that an attempt had been made at evaginating to form an hypophysial pocket.

A transverse section from near the anterior end of the hypophysis is presented in figure 1. It is seen that this part of the anlage shows a distinct bilaterality. Reconstructions of the entire hypophysis at this stage show that this bilaterality is confined to the anterior portion of the gland. Possibilities as to the significance of these appearances are discussed on a later page.

7-mm. larva of R. pipiens. A sagittal section of a 7-mm. larva is shown in figure 3. The oral plate is intact. The hypophysis, *hyp.*, extends caudally from its attachment to the inner layer of the ectoderm. It does not reach to the caudal end of the thin-walled infundibulum, *inf.* A reconstruction, from sagittal sections (fig. 5) shows that the hypophysis maintains its attachment to the ectoderm by a relatively broad band. Just caudal to the stalk the hypophysis is widened and shows a pair of thinner lateral shelves. It is believed that these give rise to the more definite lateral lobes of later stages.

8-mm. larva of R. pipiens (fig. 6). The hypophysis has recently lost its attachment to the ectoderm. It lies flattened out under the floor of the infundibulum and is now somewhat wider from side to side than nasocaudally. Its caudal end is now almost even with the caudal extremity of the infundibulum. The rather sudden breaking loose of the hypophysis from the ectoderm has resulted in a marked change in the shape of the gland. Before (fig. 5) it was much longer in a nasocaudal direction. Now (fig. 6)



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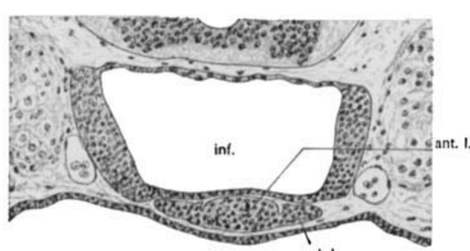

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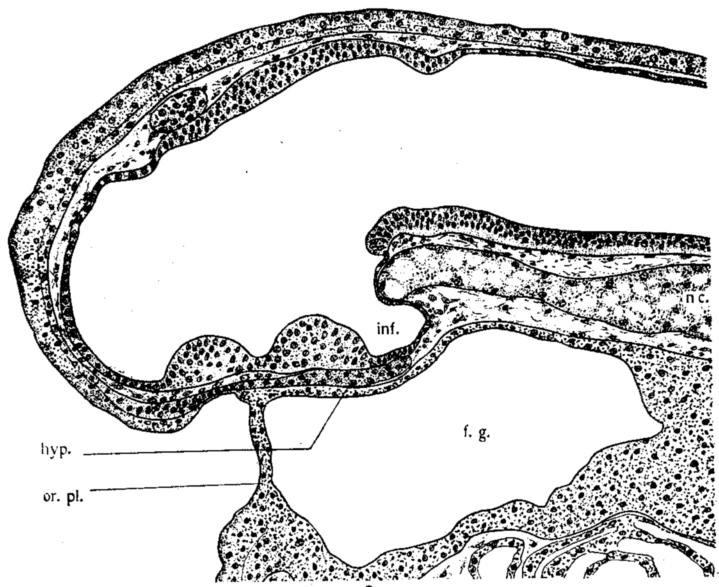
Fig. 1 Transverse section of anterior end of hypophysis of a 3-mm. larva of Rana pipiens, showing bilaterality of hypophysis anlage; *hyp.*, hypophysis; *b.w.*, brain wall. × 100.

Fig. 2 Transverse section of hypophysis region of a 12-mm. larva of R. pipiens. *l.l.*, lateral lobes; *ant. l.*, anterior lobe proper; *inf.*, infundibulum. × 100.

it is spread out from side to side. This rearrangement is a very disturbing factor in any attempt to follow the lateral lobes. They cannot be distinguished with certainty at this stage.

12-mm. larva of R. pipiens. A transverse section from an embryo of this length is shown in figure 2, a sagittal section in



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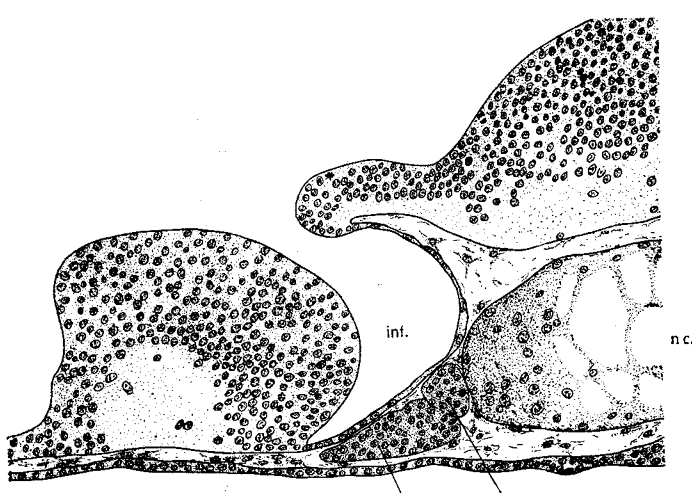

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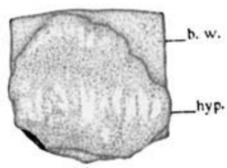
Fig. 3 Midsagittal section of head end of a 7-mm. larva of R. pipiens. *n.c.*, notochord; *inf.*, infundibulum; *f.g.*, foregut; *hyp.*, hypophysis; *or. pl.*, oral plate. × 75.

Fig. 4 Midsagittal section of hypophysis region of a 12-mm. larva of R. pipiens. *ant. l.*, anterior lobe proper; *p. int.*, pars intermedia; *inf.*, infundibulum; *nc.*, notochord. × 150.



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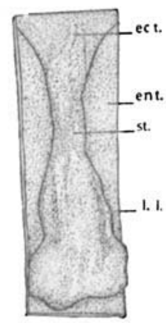

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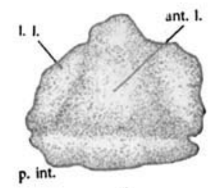

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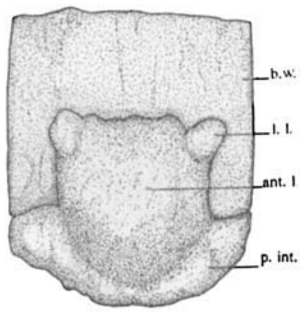

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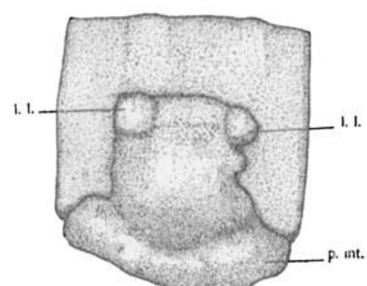

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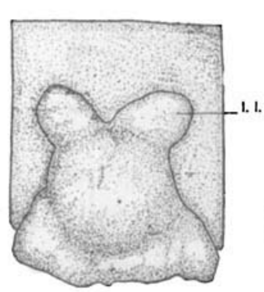

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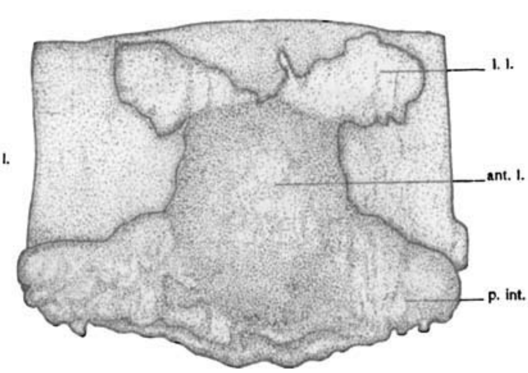

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Fig. 5 Reconstruction of hypophysis of a 7-mm. larva of R. pipens, viewed from the dorsal surface; caudal end at the bottom. *l.l.*, lateral lobe; *ent.*, entoderm; *ect.*, ectoderm; *st.*, epithelial stalk. × 100.

Fig. 6 Reconstruction of the hypophysis of an 8-mm. larva of R. pipiens, viewed from the ventral surface; caudal end is below. *hyp.*, hypophysis; *b.w.*, brain wall. × 100.

figure 4, and a dorsal view of a wax model of the epithelial hypophysis in figure 7. It will be seen that the hypophysis has its caudal end in close proximity to the anterior end of the notochord. The latter, in earlier stages, touched the dorsocaudal wall of the infundibulum, causing it to be indented (fig. 3). The hypophysis is already differentiated into three epithelial portions, one of which is paired. The anterior lobe proper is the thickened central portion of the gland. At its caudal end it is bounded by a bulging transverse ridge, the pars intermedia. From the sides a pair of thinner shelves or ledges (figs. 2 and 7) extend; these are the lateral lobes, the paired anlagen of the pars tuberalis.

18-mm. and 20-mm. larvae of R. pipiens. In these and all subsequent stages the morphological differentiation of the three epithelial portions is very distinct. In figures 8 and 9 models of these stages are viewed from the ventral surface, with the caudal end below. The anlagen of the pars tuberalis are visible as a pair of buds (*l.l.*) located at each side of the anterior end of the hypophysis. At the caudal end of the gland a curving transverse ridge, marked off by a groove, is the pars intermedia. This ridge is considerably longer than the width of the remainder of the gland.

A thickening at the caudal end of the infundibulum, corresponding to the extent of the pars intermedia, is the beginning of the neural lobe. It lies just dorsal to the pars intermedia and so is not visible in a ventral view of the reconstruction.

Fig. 7 Reconstruction of the epithelial hypophysis of a 12-mm. larva of R. pipiens, viewed from the dorsal surface. *l.l.*, lateral lobe; *p. int.*, pars intermedia; *ant. l.*, anterior lobe proper. × 100.

Fig. 8 Reconstruction of the hypophysis of an 18-mm. larva of R. pipiens, from ventral surface; caudal end below. *ant. l.*, anterior lobe proper; *p. int.*, pars intermedia; *l. l.*, lateral lobe; *b.w.*, brain wall. × 100.

Fig. 9 Model of hypophysis of a 20-mm. R. pipiens larva, from ventral surface; caudal end below. Abbreviations as for figure 8. × 100.

Fig. 10 Model of the hypophysis of a 22-mm. larva of R. pipiens, from the ventral surface. Caudal end below. Abbreviations as for figure 8. × 100.

Fig. 11 Model of the hypophysis of a 24-mm. larva of R. pipiens, from ventral surface. Abbreviations as for figure 8. × 100.

Already the two show evidences of coming into intimate relation with each other.

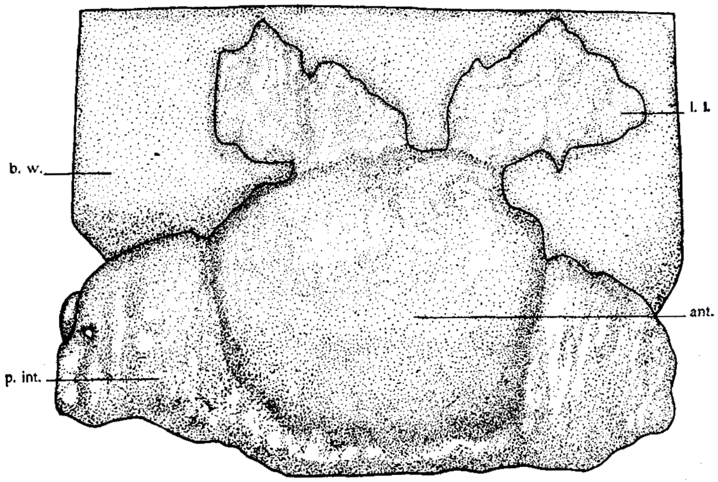
22-mm. and 24-mm. larvae of R. pipiens. Ventral views of wax-plate reconstructions made from these embryos are shown in figures 10 and 11. The lateral lobes, *l.l.*, which are the anlagen of the pars tuberalis, are larger and are flattened out under the infundibular floor. The pars intermedia conforms more closely to the shape of the neural lobe (fig. 11).

Larvae of R. clamitans and Bufo americana at metamorphosis. Very similar relations to the last are shown by a larva of R. clamitans possessing very short hind legs. A model from this embryo is shown in figure 12. That the spreading out of the lateral lobes under the infundibular floor is due to active growth is indicated by the irregularity in outline of the lateral lobes at these stages (figs. 11 and 12). Other larvae of R. clamitans obtained at later stages of metamorphosis show the lateral lobes in the process of separation from the anterior lobe.

A reconstruction from a toad (Bufo americana) which had just completed metamorphosis is presented in figure 13. The lateral lobes, *l.l.*, are seen to be joined. They are united to the anterior lobe proper by a single attenuated epithelial strand. The lateral lobes do not long remain united, however, for another toad of about the same age (not figured) shows one lobe entirely free, while the other is attached to the anterior lobe by a narrow strand.

From what has been observed in R. clamitans and B. americana it seems safe to assume that in general the lateral lobes become separated from the remainder of the epithelial hypophysis at the completion of metamorphosis or very soon thereafter.

Adults of R. pipiens and R. catesbiana. In the adult frog the pars tuberalis, derived from the two lateral lobes, is seen as a pair of epithelial plaques lying close under the 'infundibular' floor some distance in front of the remainder of the gland (figs. 14 to 18). Each plaque is approximately circular, but not infrequently shows a greater diameter from side to side. Each is 0.3 to 0.4 mm. in diameter and about one-fifth as thick. They



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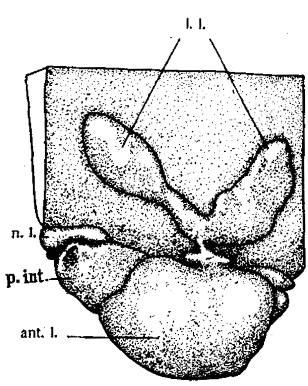

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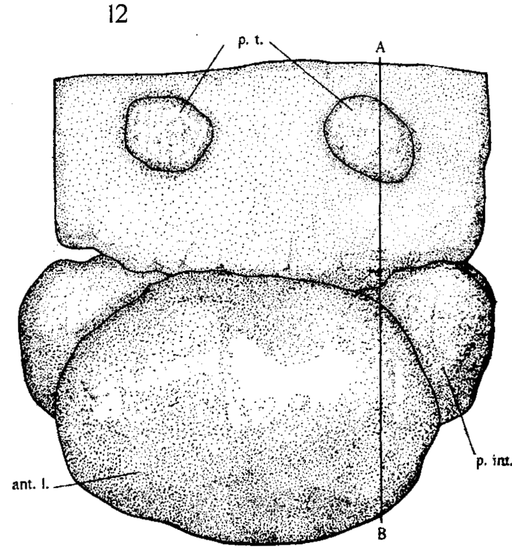

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Fig. 12 Ventral view of a model of the hypophysis of a larva of R. clamitans with small hind legs (legs 6 to 7 mm. long). *ant. l.*, anterior lobe proper; *p. int.*, pars intermedia; *l.l.*, lateral lobe; *b.w.*, brain wall. × 100.

Fig. 13 Ventral view of a model of the hypophysis of a toad (Bufo americana) which had just completed metamorphosis. *n.l.*, neural lobe; other abbreviations as for figure 12. × 100.

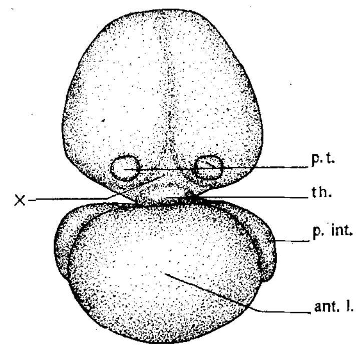
Fig. 14 Model of the hypophysis of an adult of R. pipiens, viewed from the ventral surface. *p.t.*, pars tuberalis; other abbreviations as for figure 12. *A–B*, plane of section shown in figure 18. × 35.

lie close to the brain wall, indenting but not invading it, figure 18, and are surrounded by the pia mater.

By a proper combination of dehydrating and clearing fluids the pars tuberalis may be seen in the gross, preferably with the aid of a binocular microscope or a low-power dissecting lens. Using a mixture of absolute alcohol, 60 parts, and xylol, 40 parts, it was possible to obtain the camera-lucida sketch shown in figure 15, which reproduces the ventral surface of the hypophysis of an adult bullfrog (R. catesbiana). Similarly the drawing from an adult specimen of R. pipiens presented in figure 16 A was obtained. To make sure that the parts observed in the gross were the same as those seen in sections, these two brains were later cut into transverse series. A graphic reconstruction of the caudal half of the so-called infundibulum and adjacent structures of one is shown in figure 16 B, and a single transverse section passing through the center of the pars tuberalis is presented in figure 17.

It will be seen that the two plaques composing the pars tuberalis lie under fairly thick lateral portions of the 'infundibular' floor. Between these thickenings and caudal to them the floor is very thin, X, Fig. 15. When observed in the gross this thin floor is almost transparent and this fact, no doubt, has given rise to the rather misleading description of the infundibulum as a "bilobed structure, emarginate posteriorly and divided by a median longitudinal groove" (Holmes, p. 294). Such relations are not evident from a ventral view of a reconstruction (Fig. 14). It seems to me doubtful whether the thickened 'bilobed' portion is properly to be considered as a part of the true infundibulum. I would restrict the name infundibulum to that portion possessing the very thin floor, *X*, figure 15, and exhibiting a single medial thickening at its caudal end, *th.*, figure 15 (see also fig. 16). Possibly the bilateral thickenings, from their more anterior position, are to be considered homologous with the tuber cinereum of the higher vertebrates.

Another feature of interest is the presence of small but well-marked depressions, one above each half of the pars tuberalis, figure 17. Whether these depressions are to be considered



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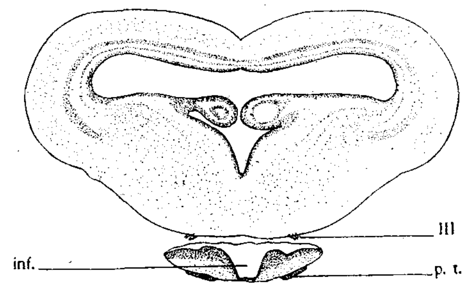

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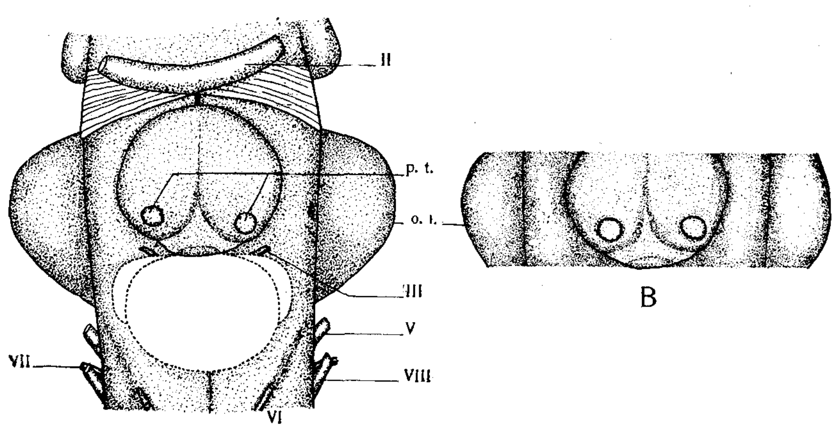

A B

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Fig. 15 Camera-lucida drawing of the 'infundibulum' and hypophysis of an adult of R. catesbiana, from the ventral surface. Caudal end is below. *ant. l.*, anterior lobe; *p. int.*, pars intermedia; *p.t.*, pars tuberalis; *th.*, thickening of infundibular floor; *X*, thin portion of infundibular floor. × 10.

Fig. 16 A Camera-lucida drawing showing a portion of the ventral surface of the brain of an adult R. pipiens. Main body of hypophysis had been removed; its approximate position is indicated in dotted outline. *p.t.*, pars tuberalis; *o.l.*, optic lobe; *II, III, V, VI, VII, VIII*, cranial nerves. × 10.

B Graphic reconstruction, from transverse sections, of portion adjacent in 'A'.

Fig. 17 Transverse section of the frog's brain shown in figure 16 A. *p.t.*, pars tuberalis; *III*, oculomotor nerve; *o.l.*, optic lobe; *inf.*, infundibulum. × 12.

homologous with the 'tuberal recesses' of higher vertebrates is uncertain.

The anterior lobe proper has become the most ventrocaudal portion of the gland. This lobe, then, does not deserve the name 'anterior' from its adult position in the frog, but from its very evident relation to the homologous lobe possessed by higher vertebrates. The lobe is oval in outline, being shorter in its nasocaudal dimension.

The pars intermedia is a long transverse ridge with bulging lateral terminations. It conforms in extent to the neural lobe which is definitely constricted from the infundibulum dorsally and at the sides. In handling, the hypophysis readily separates from the infundibulum, the break occurring at the narrow attachment of the neural lobe (fig. 18). In such a case the neural lobe, pars intermedia, and anterior lobe proper come loose as a unit. The pars tuberalis remains attached to the floor of the part interpreted as the tuber cinereum (fig. 16A).

In sagittal sections the neural lobe is cut in a direction transverse to its greatest length (fig. 18). As Stendell ('14) has noted, it presents in this section the form of a right-angled triangle with its hypotenuse lying against the pars intermedia.

The three epithelial lobes are histologically distinct. The anterior lobe proper, which has been so named from its resemblance to the anterior lobe of higher vertebrates, is very vascular and consists of cords of cells which are chromophilic and granular. The pars intermedia and the pars tuberalis may both be spoken of as chromophobic portions of the gland. There are, however, well-defined differences between the two. The pars intermedia of the frog, in contrast to the same lobe in mammals, for example, is traversed by numerous blood-vessels. The pars tuberalis, on the other hand, and this is also in contrast to the mammalian gland, is not invaded by vessels at all. This may in part be accounted for by its small size in the frog. Many of the cells of the pars intermedia (adult R. catesbiana) contain rounded hyalin bodies, considerably smaller than the nucleus. These seem to be more numerous in the neighborhood of the blood-vessels. Such hyalin bodies are not to be found in the pars tuberalis.

DISCUSSION

Entoderm. My observations bear out the assertion of Corning ('99) that entoderm does not enter into the development of the frog's hypophysis after the manner described by Kupffer ('94) and Valenti ('95). There is indeed a mass of cells, epithelial in appearance, in relation with the anterior end of the notochord in larvae of R. pipiens having a length of 2.5 to 3 mm. I am not able to find evidence that this mass becomes incorporated into the hypophysial anlage. That this epithelium-like mass is comparable with the 'protochordal plate' of other vertebrates, as suggested by Corning, Mrs. Gage, and more recently by Parker, seems to me not unlikely.

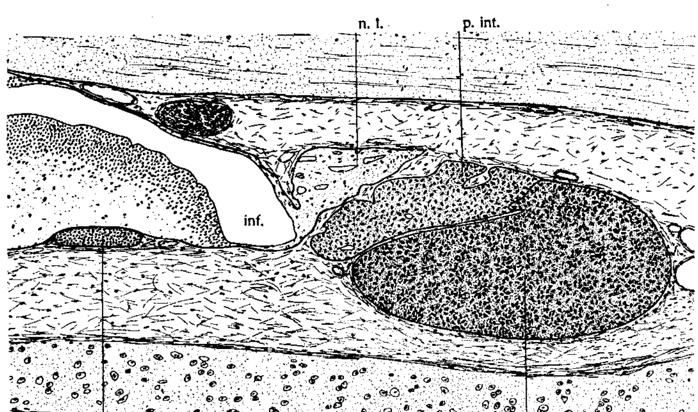

Fig. 18 Paramedian sagittal section of hypophysis of an adult frog (R. pipiens). Plane of section indicated by line A-B, figure 14. Nasal end is at the left. *inf.*, infundibulum; *p.t.*, pars tuberalis; *n.l.*, neural lobe; *p. int.*, pars intermedia; *ant., l.*, anterior lobe proper. × 50.

The pars tuberalis. A two-fold origin for the hypophysis of Ambylstoma has been recorded by Kingsley and Thyng. These observers believe that the bilaterality involves the entire gland and that the two parts soon fuse. The bilaterality observed in the frog's hypophysis seems, in certain stages at least, to be confined to the anterior portion of the anlage and does not extend to its caudal tip. I have never seen convincing evidence that the two parts come together and fuse in the frog.

It is with some difficulty that the two parts may be traced to the bud-like lateral lobes which later form the pars tuberalis.

When the hypophysis anlage breaks loose from its parent ectoderm, there is a very noticeable rearrangement in its shape, as has been noted. This is a disturbing factor in any attempt to trace the history of the lateral lobes. During the stages just preceding and following the separation, however, a somewhat thinner shelf is seen on each side of the anterior half of the anlage (figs. 5 and 7). These I have supposed to be the lateral lobes.

By the time the embryo has attained a length of 18 mm. the lateral lobes are definite bud-like structures at each side of the nasal end of the gland (fig. 8). The further development of the pars tuberalis consists in a spreading out of the lateral lobes under the brain floor and their subsequent detachment from the anterior lobe proper. This latter occurs, in Rana clamitans and Bufo americana at least, during the latter part of metamorphosis or very soon after its completion.

In the adult frog the pars tuberalis consists of a pair of epithelial plates, free from each other and from the remainder of the gland. The plates have been described by a few authors, but all have spoken of them as insignificant rudiments and none has considered them homologous with the lateral lobes seen during the development of the hypophysis of higher vertebrates.

The terminology for the various lobes of the hypophysis differs so much among writers that it is customary to gather into a table the names to be found in the literature. In the following table I have included only those authors who speak of three lobes of the Anuran hypophysis.

Terminology of the lobes of the Anuran hypophysis

OBSERVER	ANTERIOR LOBE PROPER	PARS INTERMEDIA	PARS TUBERALIS
Gaupp ('89)	Pars posterior	Pars anterior	Partes laterales
B. Haller ('97)	Hypophysis	Infundibulardrüse (Saccus vasculosus)	Vorderlappenpaares
Stendell ('14)	Haupt Lappen	Zwischen Lappen	Pars anterior or Pars chiasmatica
Atwell ('18)	Anterior lobe proper	Pars intermedia	Pars tuberalis

GENERAL CRITERIA FOR HOMOLOGIZING THE LOBES OF THE HYPOPHYSIS IN THE VARIOUS VERTEBRATE CLASSES

To homologize the lobes of the hypophysis throughout the vertebrate classes it is necessary to have clearly in mind both their developmental and their adult relations. I propose to enumerate some of the criteria by which they may be classified in the light of some of our recently acquired knowledge. It must be borne in mind that many of the points to be given are as yet supported by relatively few observations. However, it is hoped that their presentation in concise form may be found useful. The adult relations may first be considered.

Size. In general the anterior lobe proper is the largest of the three lobes, the pars intermedia the next smaller and the pars tuberalis the smallest. That these relations may not hold constant in all vertebrates is quite possible, but they are certainly true for the frog and for some mammals. Woerdeman ('14) believes that the pars tuberalis (his 'lobulus bifurcatus') becomes progressively less important as the vertebrate scale is ascended.

Form and position. The anterior lobe proper tends to maintain an approximately spherical or ovoid shape. It is not moulded to any marked degree by surrounding structures. It is not intimately attached to any tissue of nervous origin and in many forms does not even lie in contact with neural tissue. On this account Tilney ('13) has named this lobe the 'pars distalis.'

The pars intermedia is always conformed to the shape and extent of the neural lobe. In reptiles, birds, and mammals the pars intermedia is a thin epithelial layer applied to the neural lobe and derived from the superodorsal wall of Rathke's pocket. It more or less completely surrounds the neural lobe, which in these forms has its longest dimension in the sagittal direction. Later in life the pars intermedia invades the tissue of the neural lobe to a considerable extent. In the frog also the pars intermedia corresponds to the neural lobe in shape. Here the latter has its long axis extending from side to side. The pars intermedia has a very similar shape, with the exception that it is rounded and bulging where it protrudes beyond each side of the anterior lobe (figs. 14, 15, and 16).

The pars tuberalis likewise conforms to the shape of that part of the brain wall upon which it lies. It is essentially thin and lamina-like. In mammals it surrounds the infundibulum and spreads out under the tuber cinereum. Reconstructed and viewed separately, it may be described as 'saucer-shaped' (Tilney, '13) with a perforation for the infundibular neck. In reptiles thin bands and zones may be formed about the middle of the anterior lobe in addition to the thin plate which is spread out under the brain floor (Baumgartner, '16). In the Anura the pars tuberalis does not extend dorsal or caudal to the attachment of the neural lobe. It consists merely of a pair of small rounded plaques, located nasalward from the remainder of the gland.

It is important to note the relations of the pars tuberalis to the membranes of the brain. It lies in the pia mater in close relation to the brain floor, but does not appear to invade the neural tissue after the manner so characteristic for the pars intermedia.

Histology. Much remains to be worked out in regard to the normal histology of the hypophysis. It is my purpose merely to emphasize the fact that the three lobes may be readily distinguished by their histological characters. Tilney ('13) was first in attempting to classify the differences in structure of the three parts. This he did for a number of mammals and for the domestic fowl. According to Tilney, the three parts may be differentiated as to cell structure and vascularity. The pars tuberalis is more vascular than the pars intermedia and less vascular than the anterior lobe proper. Its cellular arrangement is that of cell masses with occasional small, relatively thick-walled acini. The cells are basophilic with rather scanty cytoplasm.

The histological features of the three parts of the reptilian hypophysis are thus summarized by Baumgartner ('16):

> The pars intermedia has a laminar arrangement of columnar clear-staining cells. The part derived from the lateral lobes are arranged

in columns (or sometimes acini) of clear-staining polyhedral cells. The anterior lobe proper is formed of columns or acini, with clear-staining and darkly-staining cells which may be acidophilic or basophilic. In general, the pars intermedia and the parts derived from the lateral buds may be considered the chromophobic and the anterior lobe the chromophilic part.

Parker ('17) has called attention to the tubular or acinar structure of the pars tuberalis of the hypophysis in marsupials.

In a recent paper the writer has emphasized the differences in structure in the several parts of the rabbit's hypophysis at birth. Of considerable interest in distinguishing between the pars intermedia and the pars tuberalis are the peculiar spindle-shaped and branching cells which have been observed in the former (Retzius, Herring, Trautmann, Atwell, and others). They have been called ependymal and neurogliar elements (Stendell). It is important to note that these cells have never been described for the pars tuberalis.

The frog forms an exception to some of the features found in the Amniota. In this form the pars intermedia is fairly vascular while the pars tuberalis is non-vascular. In the specimens studied (which were obtained in October and November) the pars tuberalis does not show a tubular or acinar arrangement of its cells. The pars intermedia is clearly in contrast to the pars tuberalis on account of the numerous hyalin bodies to be found in the former, but never in the latter (R. catesbiana).

It will thus be seen that there is very good agreement among the several vertebrate classes, so far as studied, as regards the main features of structure of the three epithelial lobes.

Development. It is by careful ontogenetic studies that the distinction between the three epithelial lobes is most strikingly brought out. Thus the pars intermedia, in those forms possessing a hollow hypophysis anlage, develops from the dorsal wall of Rathke's pouch. In those forms having a solid hypophysis fundament, as the frog, the pars intermedia is derived from the dorsal or caudal tip of the solid anlage. During development, in all forms, the pars intermedia becomes intimately united with the neural lobe.

The anterior lobe proper develops from the main body of the epithelial anlage. In the frog this is the middle and anterior part of the gland with the exception of the lateral lobes. In vertebrates higher than the Amphibia the anterior lobe is formed mainly from the anterior or ventral wall of Rathke's pocket.

The pars tuberalis has a paired origin, being derived from the lateral lobes, lateral buds, or 'tuberal processes.' It had been believed that for mammals the lateral lobes appear relatively late in development (Tilney, Miller), but the writer ('18) has shown that they are present very early in rabbit embryos. It seems likely that the 'bilateral origin' of the hypophysis observed in Ambylstoma by Kingsley and Thyng is an early appearance of the anlagen for the pars tuberalis. This, at least, is my interpretation of the bilateral conditions above recorded for very young embryos of R. pipiens.

The definite lateral lobes are, during development, attached close to the epithelial stalk at the ventral or nasal end of the gland. They may fuse with one another and form a single epithelial plate closely applied to the floor of the third ventricle (most Amniota). They may maintain their attachment to the anterior lobe proper or they may become detached as cell masses (certain reptiles), or as two epithelial plaques (frog). In snakes and in some lizards it is even stated that the lateral lobes disappear entirely (Baumgartner, '16).

SUMMARY

1. The hypophysis of the Anura consists of three epithelial lobes and a neural lobe. The lobes of epithelial origin are the anterior lobe proper, the pars intermedia, and the pars tuberalis.

2. From their development and their mature structure these lobes may be considered homologous with corresponding lobes of the hypophysis in all higher vertebrates.

3. The anterior lobe proper develops from the main central portion of the solid epithelial anlage. It comes to lie caudal and ventral to the other portions of the gland.

4. The pars intermedia develops from the caudal tip of the hypophysial anlage. It forms a long transverse structure conforming to the shape and extent of the neural lobe.

5. The pars tuberalis has its origin in the lateral lobes, which appear very early. These two lateral lobes spread out under the brain floor and become detached, forming two discrete, rounded plaques lying close under the brain floor in the pia mater.

6. The pars tuberalis is a constant structure, during development, in the hypophysis of amphibia and higher vertebrates. It is characterized by its paired origin (the two lobes appear relatively early and have their attachment near that of the epithelial stalk) by its laminar nature and by its adult location in the pia mater covering the tuber cinereum of the brain floor.

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