THE EVOLUTION OF THE PITUITARY.*

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The interest and importance of the pituitary for the physiologist needs no emphasising. From the point of view of comparative anatomy and evolution it is no less interesting. The ductless glands as a group seem to be characterised by peculiarities in their histories; some of these are of course well known, such as that of the thyroid originating from the endostyle of low chordates or of the pineal derived from the parietal eye.

Attempts to trace the history of the pituitary have been many, but few can be regarded as satisfactory. In this study I shall attack the subject by beginning with a description of the structure of the pituitary in the mammal as a type. Its development will be outlined; and lastly, an attempt will be made to sketch out the phylogeny of the pituitary as far as is possible from the data at our disposal.

1. The Mammalian Pituitary.

The *pituitary body* (glandula pituitaria, hypophysis cerebri, hirnanhang) is a complex organ lying immediately ventral to the forebrain in all craniates. It is composed of tissue derived from two sources—from the forebrain itself and from the superficial ectoderm of the under surface of the head; that from the brain is the *infundibulum*, that from the superficial ectoderm the *hypophysis*. The infundibulum contains an extension of the cavity of the third ventricle, the

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infundibular cavity. Where the infundibulum comes into contact with the hypophysial tissues it is specialised, containing a mass of neuroglia cells, and is known as the *pars nervosa.* The hypophysial tissues are sometimes called pars buccalis.

The hypophysial tissues fall under three headings:—*pars anterior*, *pars intermedia*, and *pars tuberalis*, all three glandular. For cytological details of these parts, see Bailey (1921).

The *pars anterior* (Hauptlappen, pars distalis) is a compact gland composed of chromophil (acidophil and basophil) cells arranged in cords.

The *pars intermedia* (Zwischen lappen, pars infundibularis) is a gland of chromophobe faintly basophil cells in dense layers, which is closely pressed against the pars nervosa. It is almost non-vascular and its secretion is supposed to make its way through the pars nervosa into the lumen of the infundibulum, and thus to reach the general circulation by means of the cerebro-spinal fluid (Herring, Edinger, 1911).

Between the pars anterior and the pars intermedia is a cleft (which may be absent in some forms), the *hypophysial cavity.* It is a closed sac and apparently functionless, but it is of importance in connection with the development of the pituitary. Morphologically it separates the pars anterior from the pars intermedia.

The *pars tuberalis* (Zungenförmige fortsatz, lobulæ laterales, lobulus bifurcatus, pars chiasmatica) is a vascular structure pressed against the floor of the brain (eminentia saccularis of the tuber cinereum) and lying dorsal and anterior to the pars anterior. Its cells are basophil, and arranged in tubular acini. The pars tuberalis is in contact with the pars intermedia in some forms, but not in others. It may lap back round each side of the infundibular stalk and the two processes meet behind it. The relations of the pituitary as described are shown in fig. 1. In the vertebrate series, however, these relations may be modified in many ways. In some the pars anterior is not anterior in position to the pars intermedia but ventral or postero-ventral; the hypophysial cavity may be absent, the pars tuberalis may be not only distant but actually separated from the rest of the organ; the infundibular cavity may be very much reduced and not extend down the infundibulum to the pars nervosa; the infundibulum may be long so that the glands are distant from the brain, or short.

In view of the divergence and variation in structure and position of parts, it is not surprising that there should be considerable differences in nomenclature. Some systems are based on relative position (anterior, intermedia), others on relation to neighbouring structures (tuberalis, infundibularis), or on origin (nervosa), or on relative size (hauptlappen). Quite often the pituitary is spoken of as divided into anterior and posterior lobes. It is not my intention to add to the confusion by proposing new terms, but to select those which are the least inappropriate morphologically as well as physiologically. A classification based only on function of the hormone secreted would in the present state of knowledge be premature.

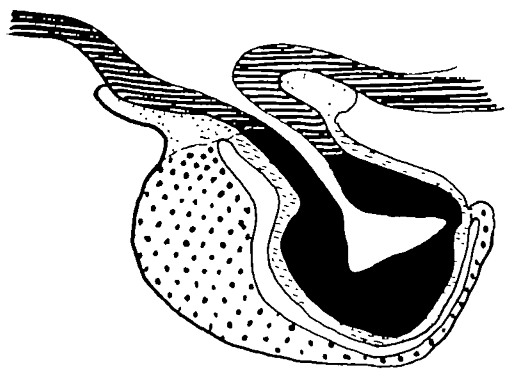

FIG. 1.—Sagittal section through the pituitary complex of the adult cat. In this and all following figures the head of the animal is to the left. Large dots, pars anterior; small dots, pars tuberalis; horizontal broken lines, pars intermedia; black, pars nervosa; thick horizontal lines, floor of third ventricle (infundibulum and tuber cinereum).

The pars anterior is well defined morphologically; it is never closely associated with any other part of the organ (though it may be joined to the pars intermedia when the cleft is absent). Its histological characters are constant, its cells stain deeply, and it is highly vascular. Its activity probably influences the development of long bones and sexual maturity. Although not always the most anterior in position it is usually and as will be seen later primitively so, and the term pars anterior is sufficiently well recognised to remain. Its method of secretion has been studied by Stewart, 1922.

The pars intermedia is also well marked. It is always closely apposed to the pars nervosa (except in Myxine), its cells are faintly basophil, its vascularity is negligible. Some of its cells migrate into the pars nervosa, and into the edge of the pars anterior (Herring, 1908). As to its secretion, there is not yet agreement. It is probable that the discordant results may be due to the fact that many investigators do not distinguish between the pars intermedia and the pars tuberalis. In older accounts of the pituitary these two parts are dealt with together as the pars intermedia. The secretion of the pars intermedia sensu stricto probably produces melanophore expansion in Amphibia and oxytocic and galactagogue effects in mammals. The name intermedia is derived from the position of this part between the pars anterior and the pars nervosa, and as these relations are constant the term may be accepted. Wulzen (1914) describes a curious structure in the intermedia of the ox, the significance of which is obscure.

The pars tuberalis has only recently been recognised. Tilney (1913) in a paper giving admirable descriptions of the part in several forms gave it the name tuberalis from the fact that it is closely associated with the eminentia saccularis of the tuber cinereum. Staderini (1909) termed it lobus chiasmaticus. By other authors it has been given other names (see Woerdeman, 1914; Stendell, 1914 *b*; Herring, 1908; Bolk, 1910; Joris, 1907; and Mihalkovic, 1874). Those who do not recognise its distinctness usually call it a tongue-like process (Zungenförmige fortsatz). Parker (1917) suggests the identity of the tongue-like process with the pars tuberalis. Tilney (1913) groups the infundibularis and tuberalis together as pars juxtaneuralis.

Its relations appear to be variable: in mammals it sits like a collar round the stalk of the infundibulum and may completely encircle it; in frogs it remains separate in two parts which lie anterior to and distinct from the rest of the organ (Atwell). In fish the dorsal portion of the pars anterior (*i.e.* that nearest the brain) is modified, and its cells are chromophobe. This portion Stendell (1914) calls the *übergangsteil*, and it probably represents the pars tuberalis: de Beer (1923) has suggested that the "übergangsteil" of Petromyzon ("middle lobe," Gentes, 1907) is probably the homologue of the tuberalis. This point will be dealt with later.

Although not very dissimilar from the intermedia, the pars tuberalis differs from it in being well supplied with blood vessels. The effect of its secretion is probably pressor.

Of all the names this part has been called, most, with the exception of tuberalis which will be retained here, are comparatively unknown.

The hypophysial cavity when present separates the pars anterior from the pars intermedia, except in Cyclostomes (see p. 281). In no form is it in connection with the exterior in the adult (in development it appears as Rathke's pocket), except in Cyclostomes and the fish Polypterus and Calamoichthys.

The cells of the pars anterior, where it touches the cleft, form an epithelium and so differ from the cells of the centre of the pars anterior with its rich supply of capillaries. This denser strip lining the cleft would thus bear a superficial resemblance to the tissue of the pars intermedia. The point is of physiological importance, for if there were a strip of intermedia cells between the anterior and the cleft, an extract from the "anterior lobe" (*i.e.* that part of the organ lying anterior to the cleft) would not be pure. (*Cf.* Swale Vincent, 1922.)

Furthermore, there is the possibility that the intermedia substance may diffuse across the hypophysial cleft and so contaminate the pars anterior. This possibility must be avoided in preparing a pure extract.

The study of development, however, apart from other evidence, appears to show definitely that whenever the cleft is present it must separate the anterior and neuro-intermediate lobes (see p. 278).

The terminology of the neural elements of the pituitary is less satisfactory. The pars nervosa is recognised as the specialised region in connection with the pars intermedia; but the term "infundibulum" is rather vague. Often loosely described as a "downgrowth from the forebrain," it is sometimes used to mean the cavity, *e.g.* "a funnel-shaped extension of the third ventricle" (Herrick, 1922). Is the pars nervosa contained in the infundibulum, and if so, what term must be applied to that portion of the infundibulum which is not pars nervosa? These are questions which immediately arise.

In development there is no doubt that the pars nervosa is part of the infundibulum, but in the adult it is simpler to regard it as separate. The infundibulum is the floor of the third ventricle behind the optic chiasma, which may project downwards more or less. Perhaps *primary infundibulum* may be used to denote the outgrowth from the floor of the brain in the embryo, which, when it meets the hypophysis becomes specialised into *pars nervosa* and *infundibulum.*

In Petromyzon there is a pars nervosa, and the infundibulum scarcely projects downwards at all. In Man the pars nervosa is carried at the end of a stalk. The extension of the cavity of the third ventricle into the infundibulum is of course the infundibular cavity.

It is a question, then, as to whether the infundibulum is to be included in the pituitary body. We may perhaps best use the term *pituitary body* to denote the well-defined anatomical unit consisting of the four parts above described —anterior, intermedia, tuberalis, and nervosa. In all higher forms it is furthermore enclosed in a fibrous capsule and lodged in the sella turcica. The other structures, such as infundibulum, and possibly also the tuber cinereum, can be grouped with the pituitary body as a functional unit best styled the *pituitary complex.* The tuber cinereum is that region of the floor of the forebrain situated behind the optic chiasma and in front of the corpora mamillaria.

In the older literature the pituitary body is divided into anterior and posterior lobes. The anterior lobe comprises only the pars anterior, and as such is well defined. But the posterior lobe, which always contains the pars nervosa and pars intermedia, may or may not also contain the pars tuberalis. Sometimes middle lobe is used to denote the pars intermedia.

It is useful to have a term which will comprise the pars nervosa and pars intermedia only, since they are always in the closest morphological association and are physiologically connected also. To serve this purpose the term "*neuro-intermediate* lobe" may be suggested. This is a well-marked functional unit in the adult although it is developmentally of double origin (like many other endocrine organs, *e.g.* adrenal).

These terms may be conveniently enumerated here in diagrammatic form:—

Adult				Embryo		
Pituitary complex	Pituitary body	Anterior lobe (Pars anterior)		from Hypophysis.		Epithelial portion.
		Pars tuberalis				
		Neuro-intermediate lobe	Pars intermedia			
			Pars nervosa	Primary infundibulum	from floor of 3rd ventricle.	Neural portion.
	Infundibulum					
	Tuber cinereum					

The older view that the pituitary derived some of its tissues from the endoderm may be said to have been dropped. (But see Atwell, 1916, and Parker, 1917.)

2. The Development of the Mammalian Pituitary.

(The cat, see Herring, 1908 *b*.)

The ectoderm of the head in the depression of the stomodæum becomes invaginated to form a little pit, Rathke's pocket or hypophysis. It lies just anterior to the tip of the notochord and is directed towards the floor of the forebrain, which at this stage is bent downwards owing to the marked cranial flexure (fig. 2). The floor of the forebrain is evaginated slightly to form the down-growing primary infundibulum, and infundibulum and hypophysis come into contact (fig. 3).

The cavity of Rathke's pocket becomes closed by the disappearance of the lumen in the stalk connecting it with the stomodæum. It is now the hypophysial cavity. The infundibular evagination is more marked.

The wall of the hypophysial cavity which touches the stalk and dorsal to the anterior lobe. Two lateral horns next grow back round the infundibular stalk and fuse behind it, so that the pars tuberalis encircles the infundibular stalk like a collar (see Tilney, 1913; Woerdeman, 1914; Parker, 1917; Atwell, 1918).

3. Phylogeny.

(*a*) Amphioxus.

The structures in the head region of Amphioxus have been discussed almost *ad nauseam*. Briefly the structures of interest here are:—*Kölliker's pit*; *Hatschek's pit*, and the *preoral pit* (fig. 5).

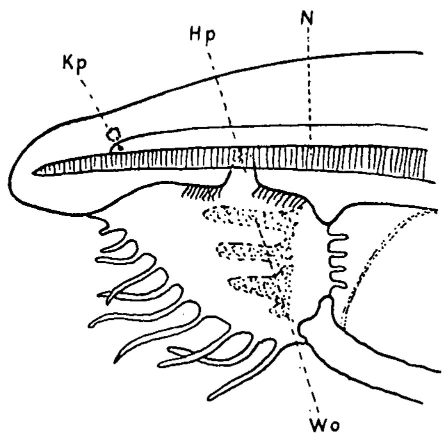

FIG. 5.—Amphioxus showing: W.o., wheel organ (formed from preoral pit); H.p., Hatschek's pit; K.p., Kölliker's pit; N., notochord (from Goodrich).

Kölliker's pit, which lies on the left side of the head, represents the neuropore. It remains in proximity to the brain, but its cavity is not continuous with that of the central vesicle in the adult. To it is ascribed an olfactory function. There are not wanting theories which homologise it, and consequently the neuropore with the hypophysis of higher vertebrates (Stendell, 1914). But since in these higher forms the neuropore exists quite separate from the hypophysis this homology is improbable. The most satisfactory suggestion is that of Goodrich (1917), who sees the homologue of the hypophysis in the preoral pit, a depression in the superficial ectoderm of the undersurface of the head in front of the mouth in the young Amphioxus.

In this preoral pit one of the head cavities (the left) comes to acquire at an early stage an opening to the exterior. This opening is represented in the adult by Hatschek's pit, the connection with the head cavity having been lost.

Later in development the preoral pit gets carried into the buccal cavity and it gives rise to the ciliated organ of Müller. Now the relations between the anterior head cavity and preoral pit of Amphioxus are comparable to those existing between the hypophysis and premandibular somite in some higher forms. In Torpedo and Raia the premandibular somites and the hypophysis are connected by a tube, and in the reptiles Phrynocephalus and Gongylus, and in the duck, by a strand of tissue. (See Goodrich, 1917.)

The homology of the preoral pit of Amphioxus with the hypophysis is, therefore, supported by tangible evidence.

Thus in the adult Amphioxus the hypophysis is in all probability represented by a ciliated organ whose function is to create a current of water. Of the neural portion of the pituitary complex of higher forms there is no trace. Kupffer's "infundibulum" is not a depression containing a cavity, but a patch of modified cells on the floor of the brain vesicle.

(*b*) The pituitary in adult Cyclostomes.

The Cyclostomes, which are the most primitive known Craniates, show features of great interest in connection with the pituitary. The organ is characterised by the feeble development of the pars nervosa, the fact that the hypophysial cavity remains open to the exterior, and that the glands of the organ do not form a compact mass but are stretched out in a line.

In Petromyzon (fig. 6) the pars intermedia is closely pressed against the pars nervosa. The infundibulum is very feebly indicated and the pars nervosa lies horizontal, parallel with the long axis of the animal. The pars anterior is well marked, consisting of a gland of chromophil cells, and between it and the pars intermedia is a portion which has been called übergangsteil (Stendell, 1914) or middle lobe (Gentes, 1907). This portion is vascular and composed of chromophobe cells, so that its histological characters suggest

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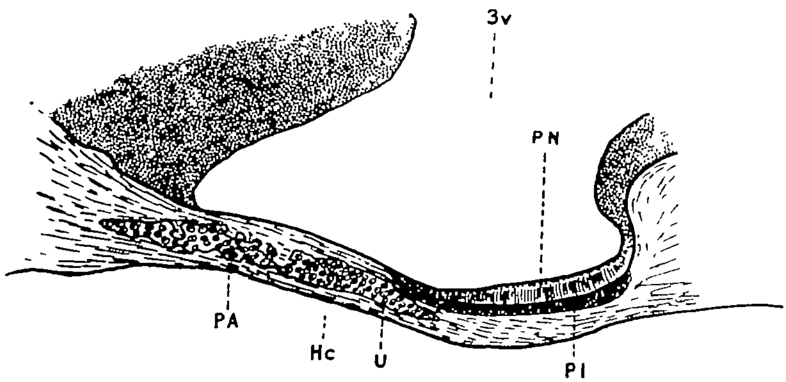

FIG. 6.—Sagittal section through the pituitary of Petromyzon. P.A., pars anterior; P.I., pars intermedia; U., übergangsteil; P.N., pars nervosa; 3v., cavity of third ventricle; H.c., hypophysial cavity.

to have records of the weights of the different parts of the organ in the different forms.

The hypophysial cavity is separated from the glands in the adult by connective tissue, and does not separate the pars anterior from the intermedia; it is open permanently to the exterior on the dorsal side of the head, as the so-called nostril.

In Myxine (fig. 7) the pituitary is only represented by a single glandular portion and a shallow infundibular portion, but they are not in contact with one another, being separated by a layer of connective tissue. The pars nervosa contains neuroglia fibres. The hypophysial gland consists of slightly basophil cells in little groups, separated by septa of connective tissue. It is separated from the hypophysial cavity (which here has a posterior aperture into the gut as well as to the nostril) by connective tissue. Stendell (1914 *b*) calls it pars intermedia, but considers the possibility that it may not be the homologue of only the pars intermedia of higher forms. It may represent the generalised gland from which in higher forms the different parts have become specialised. The pituitary of Myxine is therefore the simplest known. Until its development has been followed it is scarcely safe to say whether it is primitive or degenerate.

(*c*) Development of the pituitary in Petromyzon.

The hypophysis arises as an inpushing of superficial ectoderm just anterior to the mouth and posterior to the

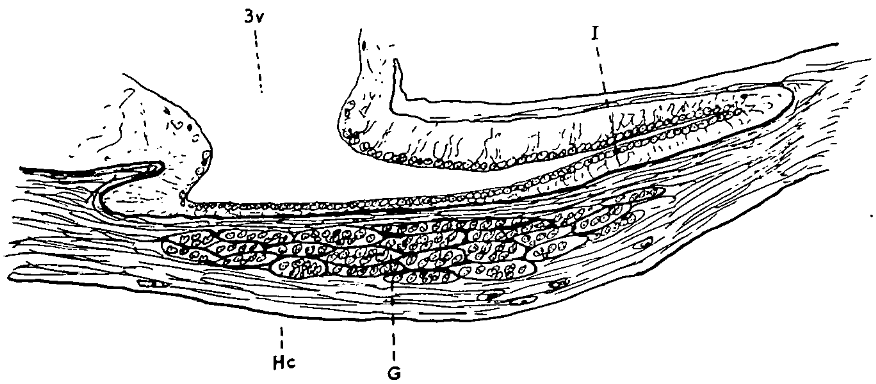

FIG. 7.—Sagittal section through pituitary of Myxine. I., infundibulum ; G., gland (hypophysial portion) ; 3v., cavity of third ventricle ; H.c., hypophysial cavity (naso-pharyngeal canal).

olfactory invagination. As development proceeds, the upper lip by its great expansion carries the olfactory organ and hypophysis round dorsally, and causes them to lie sunk in a depression which opens to the exterior by a single median dorsal pore, the nostril.

The hypophysial tissue, a solid ingrowth, extends backwards almost to the tip of the notochord beneath the brain. In the region beneath the optic chiasma a gland begins to differentiate from the dorsal side of the strand of tissue, and then a cavity appears in it below the glandular portion, of which the gland forms the dorsal wall. The gland becomes marked out into pars anterior, übergangsteil, and pars intermedia, which last becomes apposed to the pars nervosa. The hypophysial cavity becomes separated from the glands by the ingrowth of connective tissue. At the same time it extends both backwards and forwards: backwards to form the well-known hypophysial sac and forwards to open to the exterior by means of the hypophysis olfactory depression and the median dorsal pore, see fig. 8 (de Beer, 1923).

(*d*) The subneural gland of Urochorda.

The Ascidians possess a gland immediately ventral to the nerve ganglion, connected with the pharynx by means of a duct (which in some forms may become subdivided into many).

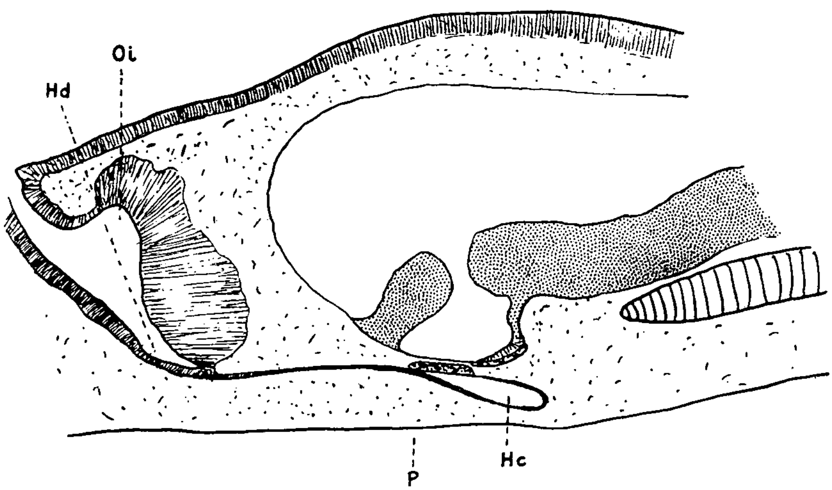

FIG. 8.—Sagittal section through developing Petromyzon showing the formation of the hypophysial cavity and its separation from the glands. H.c., hypophysial cavity; H.d., hypophysis depression; O.i., olfactory invagination; P., pharynx.

The gland secretes cells which pass down the lumen of the duct into the pharynx where it opens just behind the papillary zone in the dorsal tubercle (fig. 9).

On comparing this structure with the pituitary of higher Chordates, it is at first sight natural to conclude that the two are homologous. Such, however, cannot be the case, as is shown by a study of the development (Stendell, 1914*a*). For the gland arises not from the hypophysial tissue but from the degenerated cerebral vesicle of the larva; it is met by one or more inpushings from the buccal cavity. It is thus possible that these latter may be homologised with the hypophysis; but the gland proper cannot represent the pituitary body of higher forms. The only portion to which it might be compared is the pars nervosa, since both are derived from the

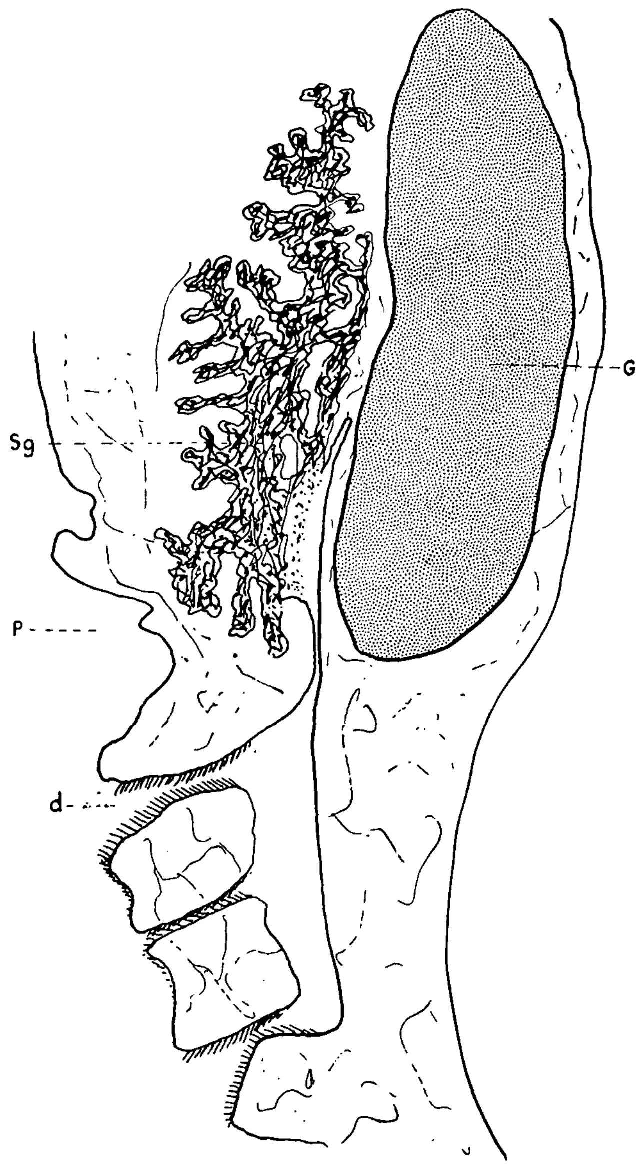

FIG. 9.—Sagittal section through the subneural organ of Ciona intestinalis. S.g., subneural gland; G., ganglion; d., apertures of ducts; P., pharynx.

nervous system. But the differences between them histologically, embryologically, and functionally are so great that one is compelled to assume that the subneural gland is a structure peculiar to the Ascidians. In confirmation of this, extracts from it do not produce the effects obtained from extracts of the pituitary of all Craniates so far tested (see Hogben and Winton, 1922).

(*e*) The pituitary of other Chordates.

In the other groups the main relations of the parts of the pituitary body are fairly similar to those described for the Mammalia.

The pars nervosa and the pars intermedia are always present and in mutual contact, so that the neuro-intermediate lobe is a constant feature in all Craniates with the exception of Myxine. In Elasmobranchs the pars nervosa is only very slightly developed.

The pars anterior is always large and vascular, but it may be ventral to the remainder of the organ, as in Amphibia. The hypophysial cavity may or may not be present. It has already been mentioned that typically the hypophysial cavity separates the pars anterior from the pars intermedia. This it does, when present, in all Craniates except Cyclostomes. In Petromyzon while the cavity is in contact with the glands in the young form, before the ingrowth of connective tissue separating them occurs, the glands lie dorsal to it in a straight line and form its dorsal wall. This is probably due to the fact that in the development of Petromyzon, the hypophysial tissue grows backwards from the front of the head beneath the brain and develops the glands on the side towards the brain and the cavity on the side of the mouth. The floor of the brain is here almost flat and the hypophysial cavity extends horizontally parallel with it; the glands therefore lie in a straight line between the brain and the cavity. The large extension of the hypophysial cavity on the ventral side renders it necessary that the glands should only develop on the dorsal side if they are to have any relation with the brain, which at least is certain in the case of the pars intermedia.

In the remainder of the Craniates the infundibulum projects a considerable distance ventrally, pressing down the posterior portion of the hypophysial tissue (pars intermedia). At the same time the hypophysis approaches the brain at an angle. That part which will give rise to the pars anterior is thus at an angle to that which will become pars intermedia (see fig. 3). When the hypophysial cavity becomes nipped off from the stomodæum it is small and contained between the rudiments of the pars anterior and the pars intermedia, which in this manner it separates from one another.

The hypophysis of Selachians and Amniota arises as a hollow invagination, Rathke's pocket, which is situated within the stomodæal depression (see fig. 2). In Petromyzon,

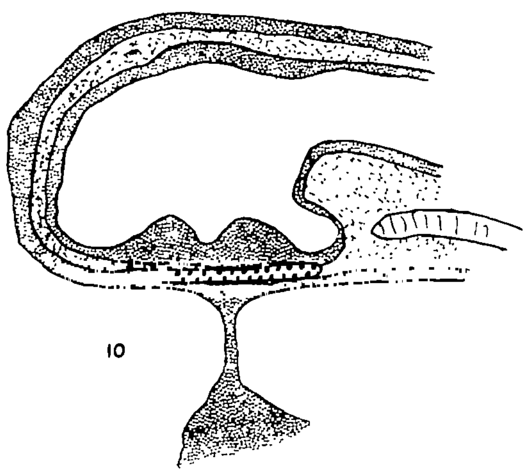

FIG. 10.—Sagittal section through developing frog showing the origin of the hypophysis (large dots) as a solid ingrowth from in front of the mouth (from Atwell).

Teleostei, and Amphibia, however, the hypophysis arises as a solid inpushing of tissue from just in front of the stomodæum (fig. 10). It is probable that this is the primitive position, without connection with either mouth or nose (Scott, 1883), and that in the Selachians and Amniotes the great size of the forebrain and marked cranial flexure causes the rudiment of the hypophysis to be displaced backwards into the stomodæal depression. This is in agreement with the supposed homology with the preoral pit of Amphioxus, which is of course in front of the mouth.

When the hypophysis arises as a Rathke's pocket, the cavity of the invagination becomes nipped off as the hypophysial cavity. In those forms where the ingrowth is solid,

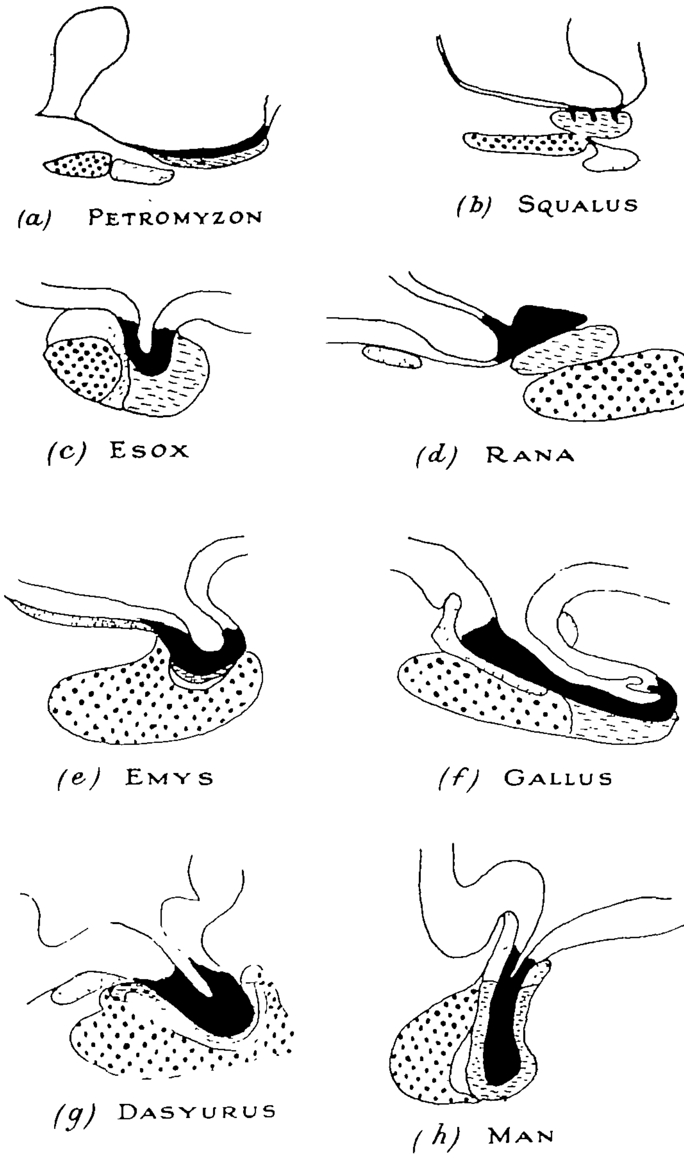

FIG. 11.—Diagrammatic representation of the relations of the pituitary in the different groups of Craniates. Large dots, pars anterior; horizontal broken lines, pars intermedia; small dots, pars tuberalis (übergangsteil); black, pars nervosa; modified (*c*) and (*e*) from Stendell, (*d*) from Atwell, (*f*) and (*h*) from Tilney, (*g*) from Parker. The anterior end is to the left in each case.

the hypophysial cavity arises later by hollowing out. The actual method holding in any form is probably determined by embryonic developmental conditions.

The pars tuberalis has already been described in the mammal (see Tilney, 1913; Parker, 1917; Atwell, 1918; and Atwell and Marinus, 1918). In the bird its relations are not very dissimilar (see Tilney, 1913; Atwell and Sitler, 1919; Stendell, 1914, under "Zungenförmige Fortsatz"). In reptiles, Baumgartner (1916) has shown that it is a well-defined element of the pituitary. In Urodela (Atwell, 1921), the pars tuberalis is present as a pair of processes which stretch forwards under the brain. In Anura (Atwell, 1919) these processes become completely detached from the rest of the hypophysis at metamorphosis.

In the cases described the pars tuberalis is always in contact with the tuber cinereum in the adult, though it arises from the lateral buds from the sides of the hypophysial tissue (see Tilney, 1913; Baumgartner, 1916; Atwell, 1918).

In Teleostei, Herring (1908) showed that the pars anterior is associated with a portion which lies dorsal to it and which is composed of chromophobe cells. Stendell (1914 *b*) terms this portion übergangsteil. It is possible that this represents the pars tuberalis in these forms.

In Selachians (Stendell, 1913; Woerdeman, 1914; Baumgartner, 1915) there are a pair of so-called "inferior lobes" attached to the pars anterior. In Squalus the whole organ undergoes rotation during development, but the inferior lobes, which Woerdeman homologises with the lobuli laterales, are in a condition which could be derived from the übergangsteil of Petromyzon if its lateral extensions were to become constricted and to assume a more ventral position. Against this, however, must be set the fact that Herring could not find any pressor principle in the pituitary of the Elasmobranch. The pars nervosa in the Selachian is only very feebly developed, and consists of processes from the floor of the infundibular depression projecting into the pars intermedia.

In fig. 11 the relations of the parts of the pituitary in the chief groups are diagrammatically represented.

4. Conclusion.

Having now surveyed the pituitary in the forms in which it occurs, and the possible homologues of its parts in other forms, an attempt may be made to sketch its evolutionary history.

The hypophysial constituent appears to have been evolved earlier in phylogeny than the infundibular. In Amphioxus there is a representative of the hypophysis but not of the infundibulum; and in the ontogeny of Craniates, the hypophysis appears before the development of the infundibulum. From Smith's work (1915) it would appear that the differentiation of the pars nervosa is dependent on the presence of the hypophysial tissues; which by this fact of dependent differentiation helps to confirm the belief that it is a phylogenetically younger structure, but the matter is obscured by an observed case of an infundibulum without any hypophysis at all in a pig fœtus (see Holt, 1922).

In its earliest appearance the hypophysial tissue forms a ciliated organ (Amphioxus). Later it sank beneath the surface of the ectoderm and was probably in communication with the exterior by means of a duct. For the significance of Rathke's pocket and the hypophysial cavity (which is functionless since it is closed and the glands are endocrine; in Cyclostomes it is separated from the glands) must be that they represent a condition in which the hypophysis formed an externally secreting gland with a duct, possibly before any relations with the brain were established.

With the acquisition of the endocrine mode of secretion and of the connection with the infundibulum for the evacuation of the secretion of the pars intermedia, the hypophysial cavity lost its primary function. In Myxine it has acquired a secondary posterior connection and serves to admit water to the gut. In Petromyzon it remains open to the exterior, but blind; its function here is unknown. In all other forms it is closed (except Polypterus and Calamoichthys) or absent altogether. In the development of the Ammocoete there is a well-formed pituitary at a stage when the endostyle has not yet formed the thyroid. If this ontogenetical priority represents a priority of phylogeny, the pituitary may be older than the thyroid qua gland.

It is interesting to note that the operative evidence from Amphibia goes to show that presence of the anterior lobe is necessary for correct functioning of the thyroid, and that thyroidectomy is accompanied by compensatory hypertrophy of the anterior lobe (see Uhlenhuth, 1921). Herring's (1920) results showing the absence of effect on the post-pituitary substance of thyroid feeding or thyroidectomy may be mentioned in this connection.

In concluding this survey from the morphological point of view of the present state of knowledge regarding the pituitary, it remains for me to express my gratitude to Professor Goodrich, Dr Hogben, and Mr Huxley, with whom I have discussed the terminology, and to whom I am indebted for advice.

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