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Vascularity of the environs of the human pharyngeal hypophysis as a possible indication of the mechanism of its control

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INTRODUCTION

The control of the sellar adenohypophysis by neurohormones carried in the hypothalamo-hypophysial portal blood and by target organ hormones circulating in the systemic blood is well established (Catt, 1970). One might assume that similar vascular mechanisms are involved in the control of the extrasellar collection of active adenohypophysial tissue known as the human pharyngeal hypophysis. In the absence of an experimental animal, data on the human pharyngeal hypophysis are derived from studies on post-mortem material. It is agreed among investigators that the pharyngeal hypophysis has a profuse systemic blood supply at all ages but opinions differ on the presence of direct vascular association between the hypothalamus and the pharyngeal hypophysis (Boyd, 1956; Hachmeister, 1967). It has been suggested (McGrath, 1971) that the vascularity of the environs of the pharyngeal hypophysis is indicative of the mechanisms involved in its control. The purpose of the present paper is to present in detail the data on which this suggestion is based.

MATERIALS AND METHODS

One hundred and thirty-three specimens of the human pharyngeal hypophysis prepared for volume studies (McGrath, 1971) were available for histological examination in serial section. The larger sphenoidal part of the pharyngeal hypophysis was studied over its full extent. Those specimens in which the pharyngeal hypophysis came into close proximity with numerous venous sinuses were placed in a 'vascular environs' group. Those specimens in which the pharyngeal hypophysis was surrounded throughout its extent by a band of fibrous tissue were placed in a 'fibrous environs' group. The specimens were considered in age/sex groups based on the age of 50 years.

Five *en bloc* specimens were available for the study of the relationship between the pharyngeal hypophysis and the overlying vomerosphenoidal fossa, formed by the posterior articulation of the vomer and sphenoid. These specimens had been removed from one male and four female cadavers aged over 50 years.

Ink flow studies were performed on 14 dried bases of skull and 74 bodies of sphenoid removed at autopsy. In 70 specimens the dorsum sellae had been damaged. A well of Silastic (Silastic 732 RTV, Dow Corning Pty. Ltd.) was formed about the hypophysial fossa in the 18 intact specimens and about the vomerosphenoidal fossa

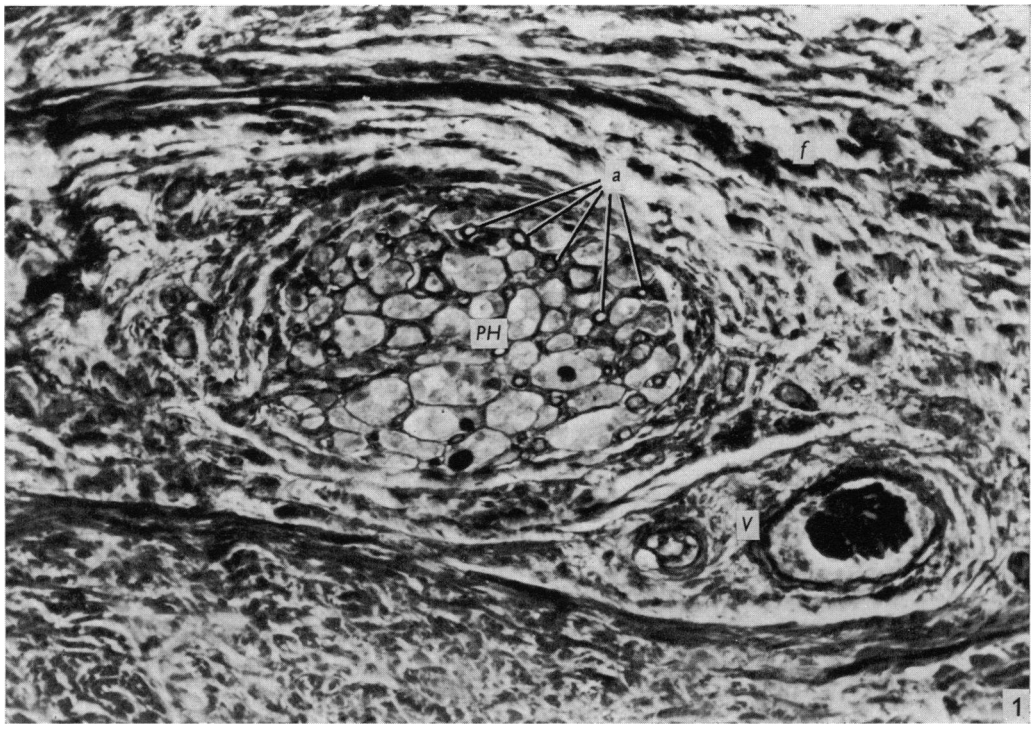

Fig. 1. Coronal section through the more posterior part of the pharyngeal hypophysis from a female aged 31 years. The pharyngeal hypophysis (*PH*) presents as a compact cellular mass within the fibrous layer (*f*) of the mucoperiosteum. A well-defined vascular bundle (*V*) is evident. Within the pharyngeal hypophysis numerous arterioles (*a*) can be seen between the cell clusters. PAS–orange G. × 125.

in the remainder. The well was filled with green drawing ink and the trans-sphenoidal ink flow was observed macroscopically. In the autopsy specimens the route of ink flow was dissected under low-power magnification. In a further series, India ink or pigmented latex was injected into the sellar hypophysis in the undissected base of skull of 24 cadavers aged over 50 years. Following this injection, each body of sphenoid was removed *en bloc* and examined macroscopically. The mucoperiosteal segment underlying the vomerosphenoidal fossa was removed and sectioned. The presence of injected pigment in the venous sinuses related to the pharyngeal hypophysis was then sought microscopically.

RESULTS

A constant feature of the mucoperiosteal segments examined in serial section in the present investigation was the presence of a well-defined vascular bundle running in the sagittal plane in the vicinity of the pharyngeal hypophysis. This bundle ran in the fibrous layer of the mucoperiosteal segment and formed part of the profuse blood supply to the roof of the pharynx from the maxillary vessels. A marked histological

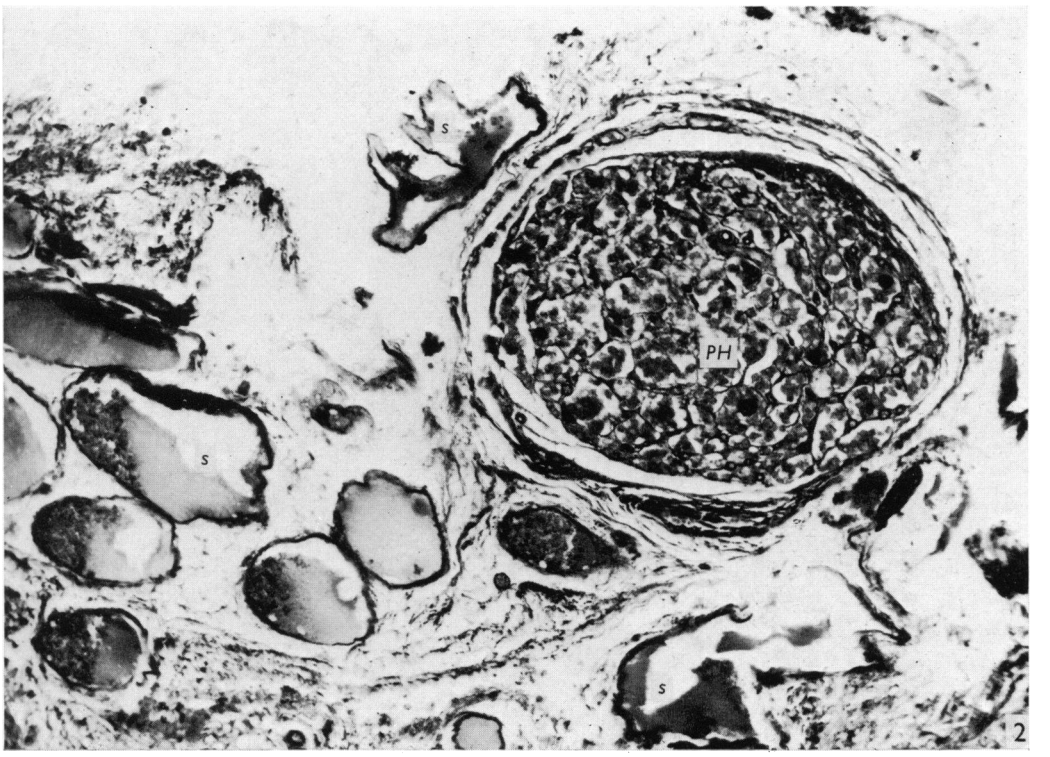

Fig. 2. Coronal section through the more posterior part of the pharyngeal hypophysis from a female aged 65 years. The pharyngeal hypophysis (*PH*) has extended into the vascular pedicle and is surrounded by numerous venous sinuses (*s*) bound together with loose areolar tissue. PAS–orange G. × 80.

Table 1. *Incidence of vascular and fibrous environs of the human pharyngeal hypophysis in* 133 *subjects from* 14 *to* 95 *years*

Sex	Age (years)	Vascular environs	Fibrous environs
Male	< 50	3 (20 %)	12 (80 %)
Male	> 50	47 (67 %)	23 (33 %)
Female	< 50	4 (27 %)	11 (73 %)
Female	> 50	29 (87 %)	4 (13 %)
Total	< 50	7 (23 %)	23 (77 %)
Total	> 50	76 (74 %)	27 (26 %)

feature of the pharyngeal hypophysis, particularly in the younger group of subjects, was the presence of numerous arterioles between the cell clusters. Communications between the vascular bundle and the vessels within the pharyngeal hypophysis were common (Fig. 1).

Examination of the full extent of the environs of the pharyngeal hypophysis re-

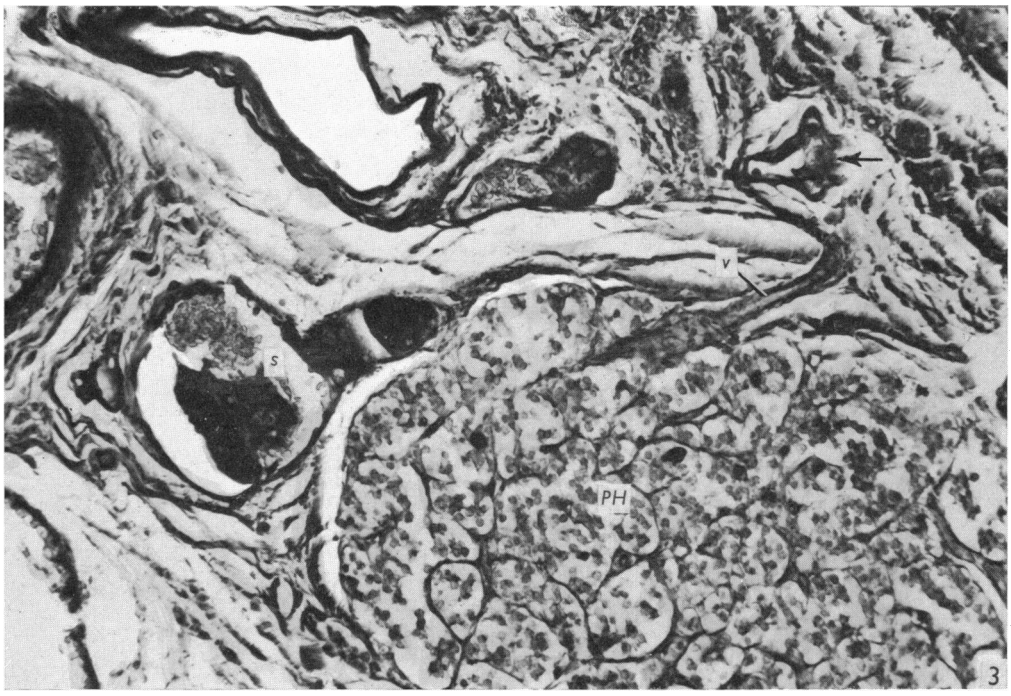

Fig. 3. Coronal section through the more posterior part of the pharyngeal hypophysis from a female aged 65 years. The pharyngeal hypophysis has extended into the vascular pedicle deep to the plane of the mucoperiosteum. The vessel seen extending from the venous sinus (*s*) through the capsule of the pharyngeal hypophysis could be followed in serial section to vascular trabeculae between the cell clusters. The vessel (*v*) passing through the capsule above extended to the vessel (arrow) immediately adjacent to the capsule. The cells of the pharyngeal hypophysis show a marked shrinkage effect. PAS–orange G. ×125.

vealed marked differences in the vascularity of the tissue immediately surrounding the more posterior part of the organ. In the 'fibrous environs' group this tissue retained its fibrous nature (Fig. 1), but in the 'vascular environs' group the more posterior part of the pharyngeal hypophysis was invested by numerous thin-walled venous sinuses held together with loose areolar tissue (Fig. 2). This finding was common in the older age group in both sexes, and in this group the incidence was appreciably higher in females. In the younger subjects the finding was uncommon and the incidence was about equal in both sexes (Table 1).

Within the older age group there was no apparent association between the age of the subject and the vascularity of the environs of the pharyngeal hypophysis. In the younger group two of the three males and the four females in the 'vascular environs' group were aged over 40 years.

During serial examination of the specimens it was noted that in the 'vascular environs' group the venous sinuses closely related to the pharyngeal hypophysis were not in the plane of the mucoperiosteum, but formed a vascular pedicle attached to the deep surface of the sphenoidal part of the mucoperiosteal segment. This vascular pedicle was present in all specimens in both age groups. In the older age group

Fig. 4. Sagittal section through the body of the sphenoid from a female aged 61 years. Hypophysial fossa (arrow), dorsum sellae (*ds*), intersinusoidal septum (*st*). Cancellous bone (*c*) is evident around the posterior boundary of the sphenoidal air sinus. The anterior pin (*a*) is between the mucoperiosteum of the roof of the pharynx and the posterior border of the vomer (*Vm*). The posterior pin (*p*) is between the mucoperiosteum and the inferior surface of the sphenoid (*Sp*). The fixation of the pharyngeal mucoperiosteum to the posterior vomero-sphenoidal articulation is evident. ×2.

93 % of the pharyngeal hypophyses extended deeply into the vascular pedicle and, in the majority, a close relationship with the venous sinuses was established. In the younger group the pharyngeal hypophyses with vascular environs extended into the vascular pedicle and all came into close proximity with the venous sinuses, but the pharyngeal hypophyses with fibrous environs remained in the plane of the mucoperiosteum and did not extend deeply beyond the base of the pedicle. Communication between the vessels within the pharyngeal hypophysis and the venous sinuses forming the pedicle were common in the 'vascular environs' group (Fig. 3), but such communication did not occur in the 'fibrous environs' group.

In the five *en bloc* specimens sectioned in the sagittal plane the vascular pedicle was seen to extend anteriorly between the vomer and the sphenoid and superiorly to the inferior surface of the sphenoid (Figs. 4, 5). Within the pedicle, thin-walled venous sinuses closely related to the sphenoidal part of the pharyngeal hypophysis opened

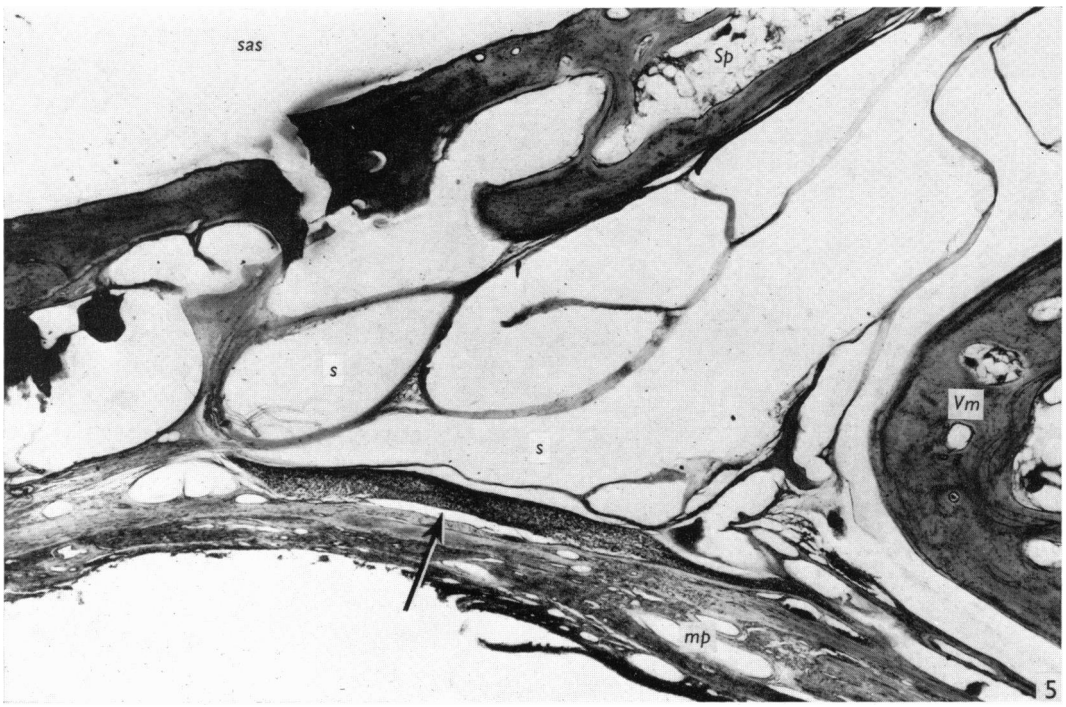

Fig. 5. Sagittal section through the posterior articulation of the vomer (*Vm*) with the sphenoid (*Sp*), from a female aged 73 years, The cavity of the sphenoidal air sinus (*sas*) is above. Large thin-walled venous sinuses (*s*) fill the vomerosphenoidal fossa and extend to the sphenoid above and between the sphenoid and the vomer anteriorly. The sphenoidal part of the pharyngeal hypophysis (arrow) presents as an elongated cellular body deep to the pharyngeal mucoperiosteum (*mp*). The close association between the pharyngeal hypophysis and the venous sinuses of the vomero-sphenoidal fossa is evident. Haematoxylin and eosin. × 20.

into large veins between the vomer and the sphenoid and into vascular spaces in the sphenoid.

Direct trans-sphenoidal ink flow between the hypophysial and vomerosphenoidal fossae was readily demonstrated in 8 (57 %) dried bases of skull and in 32 (43 %) autopsy specimens of body of sphenoid (Fig. 6). In the remaining specimens the ink spread diffusely through the specimen or failed to penetrate the floor of the fossa. In the autopsy specimens the intersinusoidal septum was attached to both the roof and the floor of the sphenoidal air sinus in 58 (78 %) specimens. Ink flow across such septa was along canals in the compact bone. On transverse section the canals were found to be filled with a core of fibrous tissue and two or three veins running in parallel. Trans-sphenoidal ink flow also occurred through the cancellous bone immediately adjacent to the posterior boundaries of the sphenoidal air sinus. In every autopsy specimen cancellous bone was found in continuity between the hypophysial and vomerosphenoidal fossae (Fig. 4). In the more extensive type of sphenoidal air sinus the cancellous bone, and hence the ink flow, was restricted to the posterior part of the roof, the posterolateral angles, and the floor of the sphenoidal air sinus.

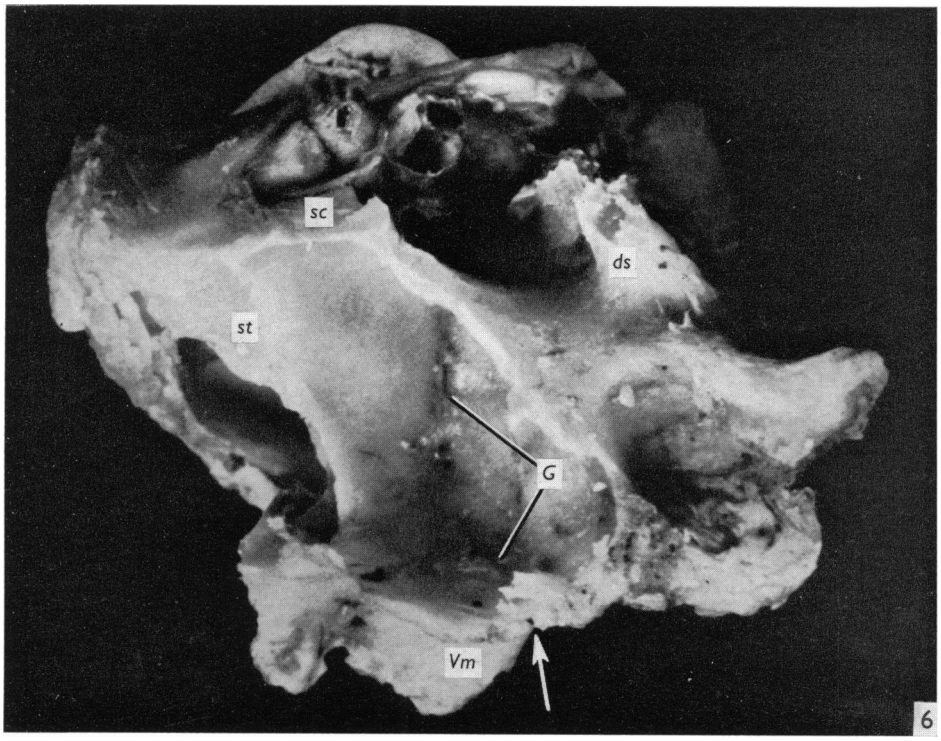

Fig. 6. Sagittal section of the body of the sphenoid from a male aged 82 years, after the application of green ink over the vomerosphenoidal fossa (arrow). The dorsum sellae (*ds*) has been damaged. The intersinusoidal septum (*st*) is to the right of the median plane. The outer wall of the left sphenoidal air sinus and the antero-inferior part of the intersinusoidal septum have been removed. Sulcus chiasmatis (*sc*), vomer (*Vm*). The flow of ink (*G*) can be traced to the right in the floor of the left air sinus and thence in the septum to the hypophysial fossa. × 3.

The trans-sphenoidal flow of pigmented material from within the capsule of the sellar hypophysis to the vomerosphenoidal fossa was demonstrated in 11 (46%) of the cadaver specimens. However, further flow of the pigment into the pharyngeal hypophysis was not demonstrated conclusively, as the distribution of the pigment in the mucoperiosteum removed from the vomerosphenoidal fossa was not restricted to the venous sinuses adjacent to the pharyngeal hypophysis, and contamination during processing could not be excluded.

DISCUSSION

The capacity of adenohypophysial tissue, grafted to a site remote from the hypothalamus, to respond to factors circulating in the systemic blood has been demonstrated by a number of investigators (Purves & Sirett, 1967; Peng, Pi & Wu, 1969). In his study of the human pharyngeal hypophysis in the fetus and the newborn, Boyd (1956) observed that the pharyngeal hypophysis has a profuse systemic blood supply but that vascular communication between the hypothalamus and the pharyngeal

hypophysis was unlikely. In the present series it is evident that at all ages the pharyngeal hypophysis continues to receive an excellent blood supply from systemic vessels which run in close proximity to it in the plane of the mucoperiosteum. In the present series it is also evident that in subjects up to the fifth decade the pharyngeal hypophysis remains throughout its extent within the plane of the mucoperiosteum. In these subjects histological data indicate that the vascular connexions of the pharyngeal hypophysis are restricted to the systemic system. It therefore appears that the active pharyngeal hypophysis in the younger subject functions in the manner of an isolated graft of adenohypophysial tissue responding to factors circulating in the systemic blood. It is of interest that in this younger age group the volume of the pharyngeal hypophysis in the female is significantly smaller than that in the male (McGrath, 1971).

In the present series marked changes in the vascular relations of the more posterior part of the pharyngeal hypophysis become evident in the fifth decade and are common over the age of 50 years. In this age group the pharyngeal hypophysis extends deep to the plane of the mucoperiosteum and communication between the venous sinuses of the pharyngeal hypophysis and those of the overlying vomerosphenoidal fossa is established. In the *en bloc* specimens communications between the latter sinuses and intrasphenoidal vessels are evident. Similar communications have been described by Romeis (1940) and Müller (1958). Ink flow studies in the present investigation confirmed the findings of Arey (1950) on trans-sphenoidal blood flow. Arey, in his investigation into the craniopharyngeal canal in the human, found that the vascular pattern of the body of the sphenoid resembled that of a vertebral body and that free trans-sphenoidal venous flow between the hypophysial and vomerosphenoidal fossae was a constant feature. Data arising in the present investigation following on injection of ink into the sellar hypophysis *in situ* supported the findings of Hachmeister (1967). This worker investigated the pharyngeal hypophysis from 29 subjects aged from the fifth decade and from 3 younger subjects. In some specimens ink injected into the sellar hypophysis was followed macroscopically across the sphenoid and microscopically into the pharyngeal hypophysis. The ages of the subjects of the ink-flow specimens were not noted.

From the above it appears that a trans-sphenoidal extension of the hypothalamo-hypophysial portal system to include the pharyngeal hypophysis is possible in an appreciable number of subjects. If such an extension does exist, neurohormones could be transmitted to the pharyngeal hypophysis, bringing it under hypothalamic control. As the presence of active adenohypophysial tissue in the pharynx is peculiar to the human, the likelihood of obtaining direct evidence of trans-sphenoidal transmission of neurohormones is remote. However, Hachmeister (1967) in his series of pharyngeal hypophyses, predominantly from older subjects, concluded that data from cytological, immunohistochemical and ink flow studies established the human pharyngeal hypophysis as part of the hypothalamo-hypophysial system. Additional data based on the present investigation suggest that inclusion of the pharyngeal hypophysis in such a system involving direct hypothalamic control is delayed until the fifth decade. In this regard it is of interest that in the older age group there is a significant increase in the volume of the pharyngeal hypophysis in the female but not in the male (McGrath, 1971).

SUMMARY

The control of the human pharyngeal hypophysis is unknown and the possibility of obtaining direct evidence on the mechanisms involved is remote in the absence of an experimental animal. Data based on histological studies of post-mortem material indicate that up to the fifth decade direct vascular communication between the hypothalamus and the human pharyngeal hypophysis is unlikely. It is concluded that in this age group the pharyngeal hypophysis functions as an isolated graft of adenohypophysial tissue responding to factors circulating in the systemic blood. From the fifth decade, and particularly after the age of fifty years, histological studies indicate a marked increase in the vascularity of the environs of the pharyngeal hypophysis and the establishment of vascular connexions which could faciliate direct transsphenoidal hypothalamic control of the human pharyngeal hypophysis.

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