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HYPOPHYSEAL DUCT TUMORS

A REPORT OF THREE CASES AND A FOURTH CASE OF CYST OF RATHKE'S POUCH

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Introduction.—In view of the very small number of squamous epithelial tumors of the hypophyseal region which have been reported in this country and their many points of interest, it seems permissible to call further attention to this group and to report in some detail a pathological study which has been made of three cases occurring in the surgical service of Professor Halsted of the Johns Hopkins Hospital.

The relative rarity of squamous epithelial tumors among hypophyseal neoplasms is suggested by the small number reported in the American literature. Among twenty-six hypophyseal tumors (certified histologically) reported by Cushing (1912), only two belong in this group. Jackson, in 1916, reported a case and referred only to the two of Cushing and another published by Dean Lewis (1910). To these should be added those of Farnell (1911) and Warthin (1916), as well as the three to be presented in the following paper. Erdheim (1904) observed at time of autopsy only two of these tumors, but pathologically resurrected five others which had been salvaged and preserved in the University of Vienna Museum between the years 1828 and 1883. In addition to these he collected about twenty cases from the literature which he decided belonged in the same group. Jackson (1916) tabulated thirty-eight examples, collected from the literature, to which I may add a full dozen, histologically certified tumors, reports of which I have found.

Classification.—Included among the squamous cell tumors of the hypophysis and infundibulum are tumors which range in structure from simple squamous epithelial-lined cysts to tumors which are often reported as teratomas, but which are probably "autochthonous teratoids developed by metaplasia from hypophyseal duct remnants" (Ewing). Case III of the present series and the case of D'Orsay Hecht (1909) appear to be examples of such "teratoids." Tridermal teratomas are rare, but instances have been reported by Wegelin, Rippmann (1865), and Kon. The entire group of squamous epithelial cell derived tumors belong to the general group of *heterogenous* hypophyseal tumors, the so-called *heterotopic* group

of Bonin, meaning that such tumors are composed of tissue foreign to the essential structure of the adult gland.

Embryology.—Although the embryology of this region is so well and generally known, it may help the reader to review briefly the salient features that have a bearing in the etiology of this special group of tumors.

Although Rathke first asserted in 1838 that the hypophysis developed from a diverticulum of the pharynx, it was not until 1875 that the essential points in its development were settled and clearly presented. At this time Goette and Mihalkovics demonstrated independently the ectodermal origin of the anterior lobe of the hypophysis. Milhalkovics' work, which was done on canine material, has received most attention and his findings confirmed by the work of subsequent observers.

Meantime, in 1860, Luschka had noted the presence of squamous epithelium in the *normal* hypophysis, but the pathological significance of this finding remained unappreciated for many years. Prior to Luschka squamous epithelial lined cysts had been observed (Zenker in 1857), and subsequently a number of such cases were put on record.

Erdheim (1903) in his studies on the structure of the normal thyroid had been interested in the occurrence of epithelial rests of the thyroglossal duct. Subsequently his observation of numerous squamous epithelial groups in a single "normal" hypophysis stimulated him to undertake a study of *serial sections* of thirteen adult normal hypophyses, in ten of which squamous epithelial cell rests were found (1904). This squamous epithelium occurred as small cell groups (in which intercellular bridges were demonstrable) located usually along the anterior surface of the infundibulum (the *processus lingualis* of the *pars intermedia* of Herring, 1908) or beneath the capsule of the upper surface of the anterior lobe. Turning to Mihalkovics' work, Erdheim found it already demonstrated that the rotation forward and upward of the developing anterior lobe carried the area of attachment of the hypophyseal duct to precisely the location of the *reliquii* (inclusions) of squamous epithelium found in a large majority (about 77 per cent.) of normal hypophyses.

Jackson's (1916) quotation to the effect that Erdheim "on careful examination of thirteen suitable fœtuses discovered that ten of them, or over 80 per cent, showed remains of buccal epithelium in the infundibular region," appears to be somewhat in error, since the thirteen hypophyses examined microscopically were those of adults. Erdheim discarded seven fœtal and new-born hypophyses because of the difficulty of recognizing squamous epithelial cell groups in the presence of incompletely differentiated hypophyseal parenchyma. This detail of Erdheim's work was correctly quoted by Dean Lewis (1910).

An anatomical point of importance in the consideration of the tumor producing potentialities of this region lies in the fact that the hypophyseal vesicle or sac, a later stage of Rathke's pouch, is composed of stratified cylindrical epithelium. Most of this tissue develops into the anterior lobe, but a single layer of cylindrical epithelium persists in the adult gland as the "*cleft*" ("Rathke's" cleft), separating the anterior and posterior lobes. On the contrary, the hypophyseal *duct* is composed of modified squamous epithelium which gradually passes over into the cubical epithelium of the buccal canal (Salzer, 1898). Furthermore, while the vesicle progresses, the duct retrogresses entirely, save for its cellular *reliquii.*

The following extract is of Erdheim's summary of Mihalkovics' illus-

trated explanation of the development of the hypophysis and the rôle of the hypophyseal duct.

In Fig. 1, "I," we see the *anlage* of the central nervous system, the fore (v), mid (m), and hind (h) brain vesicles, respectively. Between the ectodermal primary buccal cavity (n) and the entodermal foregut (f), stretches still the oral plate (pharyngeal membrane or "*rachenhaut*"). High above and at the same time behind, one finds a small depression (h) in the oral cavity, the "hypophysis angle" ("ch" in this and subsequent stages = chorda dorsalis). In Fig. 1, "II," the oral plate is ruptured and the pituitary anlage (h) deepened to a small cavity. At (i) the infundibulum has already begun to deepen. A further step (Fig. 1, "III,") shows that the small cavity has become the deep pituitary pouch ("h" = Rathke's pouch), "*which is lined by stratified cylindrical epithelium.*"

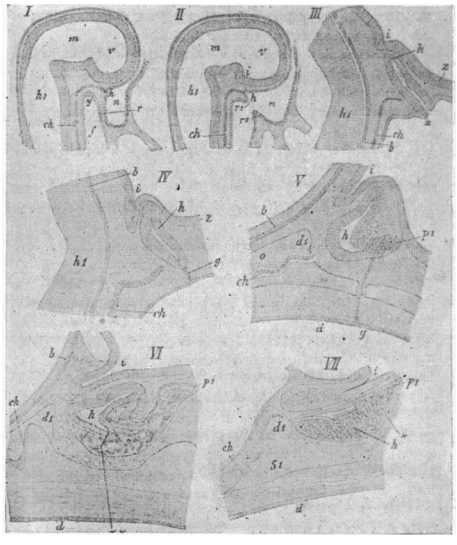

FIG. 1.—Illustrates the developmental cause of the suprasellar and upper sellar location of hypophyseal duct squamous-cell tumors. After the closure of Rathke's pouch (III, h) its connection (IV, g) with the pharynx is known as the hypophyseal duct. This is lined with modified squamous epithelium continuous with the pharyngeal mucosa. During the further development of the hypophysis the point of insertion of the hypophyseal duct (IV, g) is carried forward and upward (VII, x) by the rotation of the embryonic anterior lobe. This developmental fact correlates with the frequent occurrence in the mature gland of squamous epithelial inclusions along the infundibulum (in the processus lingualis of the pars intermedia), or near by beneath the capsule of the anterior lobe. The location of these inclusions corresponds with that of many squamous epithelial derived tumors. (After Mihalkovics.)

In "IV" the pocket in its upper part has developed into the thick-walled "*pituitary sac*" (h), composed of stratified cylindrical epithelium, while the under part has developed the small pituitary or hypophyseal duct (g) with a very narrow lumen (not shown in the figure) *lined by low cubical epithelium*. The differentiation of the hypophysis anlage into two totally different (*in both form and cell structure*) parts is an important fact. Whereas the pituitary sac develops into the anterior hypophyseal lobe, the pituitary duct disappears.

Already at this stage (Fig. 1, "IV") one sees that the pituitary sac is slightly curved. The infundibulum (i) has grown and lies on the posterior surface of the pituitary vesicle. In a further stage (Fig. 1, "V") one sees that the angular kinking of the pituitary sac ("H") has progressed and that the epithelial wall of the lower part of the sac at the place where it is connected with the canal (g) has developed a solid process (p_1) anteriorly and above. The lumen of the sac sends forward into the solid process a small cavity. The hypophyseal duct ("g") has lost its lumen and remains as a thin solid strand of epithelium which connects

the solid process of the primitive anterior lobe ("p_1") with the pharynx and runs between both sphenoidal bone cartilages (Fig. 1, "V").

In the further development of the glandular part of the hypophysis the solid process plays the cardinal rôle. In Fig. 1, "VI," one sees the *process* (p_1) already changed into a large number of solid glandular columns and that the lumen ("*h*") has come to lie somewhat eccentrically behind. Both sphenoid cartilages are united and the pituitary duct is no longer seen. The infundibulum (*i*) is still canalized. In the most mature stage (Fig. 1, "VII"), illustrated by Mihalkovics, one sees that the posterior part of the infundibulum ("*i*") has become the posterior lobe and now lies upon the anterior lobe ("*h*"). The lumen of the hypophyseal vesicle (about to become the "cleft" between the two lobes) is still present and still sends a small diverticulum into the glandular tissue. The glandular process (p_1) has been pushed forward and upward and lies below and along the anterior surface of the infundibulum. *The region of insertion of the erstwhile hypophyseal duct (Fig. 1, "VII, X") is carried upward, by the further rotation of the developing gland, to the anterior infundibular and upper pars anterior surfaces.*

It is in this locality that squamous epithelial cell groups have been commonly found and where the group of squamous epithelial neoplasms under consideration appear to have taken origin: either from the anterior surface of the infundibulum (Cushing, page 289), or from beneath the capsule of the anterior lobe (*cf.* Case I of the writer, in which the pars anterior was flattened cup-like below by a squamous epithelial cyst situated partly within and partly above the sella).

The Accessory Hypophyses.—A number of interesting researches have been concerned with the questions of patency of the craniopharyngeal canal and the finding of rests of the hypophyseal duct. Among the lower vertebrates it is well known (Jordan, D. S., 1896) that in *cyclostomata* the external pituitary opening remains patent throughout life. In *myxine* the pituitary opening extends into the pharynx and serves as a respiratory tube.

In human cranii Le Double in 1903 (cited by Arai, 1907) found the canal patent in 9 per cent. of newly born (aged one to three months). Arai found with considerable regularity on histological examination of canine and feline cranii three different bodies situated between the sella and the pharynx which, in addition to squamous epithelium, often contained elements similar to those of the anterior hypophyseal lobe. He designated these "*accessory hypophyses*" as: (1) *Hypophysis accessoria cranii* (later, 1911, independently found by Dandy in canine cranii and called the "*parahypophysis*"); (2) *hypophysis accessoria canalis craniopharyngei,* found in the body of the sphenoid bone; and (3) *hypophysis accessoria pharyngei,* the so-called pharyngeal hypophysis or *rachendachhypophyse* of other writers. Haberfeld (1909) found the pharyngeal hypophysis present in all of fifty-one pharynges examined, of all ages from infancy to senility.

It was larger in adults than infants, and often differentiated into tissue resembling anterior hypophyseal lobe. Haberfeld concluded that its function must be similar to that of the chief hypophysis. As an example of tumor formation in one of these accessory hypophyses may be mentioned the acidophile adenomatous tumor of Erdheim (1909) which in a case of acromegaly was found within the body of the sphenoid.

E. Christeller (1914), investigating the pharyngeal hypophysis in the human, made serial sections in thirty-one cases, and found the organ present in every case. In three cases in which functional disturbance of the chief hypophysis was diagnosed clinically he looked for possible histological changes in the pharyngeal organ. In one case of typical acromegaly associated with an acidophile adenoma of the chief hypophysis, the pharyngeal hypophysis existed only as groups of squamous epithelium. In the second case, one of *dystrophia adiposo-genitalis* associated with a basophile adenoma, only squamous epithelium was present in the pharyngeal accessory gland, but in the third case, similar to the case just cited, the "*rachendachhypophyse*" was substantially enlarged and composed largely of cells resembling eosinophile anterior lobe hypophyseal elements.

It seems evident that the entire region of the hypophysis from the pharynx to the *processus lingualis* of the *pars intermedia* is peculiarly rich in vestigial reliquii which may be considered as possessing both functional and tumor-producing possibilities. A study of four examples of cystic tumors arising in the region of the upper extremity of this chain of embryonic reliquii will be presented in the following paper.

CASE I.—*Intracystic squamous epithelial papilloma arising from a rest of the hypophyseal duct in the anterior lobe. Enlargement of sella and inclusion of hypophysis in wall of cyst. Headaches and visual disturbances (temporal hemianopsia and amaurosis). Treated for syphilis (positive Wassermann). Operation: evacuation of cyst (lateral intracranial approach); injury to internal carotid, ligation in neck. Exitus twelve days after operation. Autopsy.*

Abstract of J. H. H. Surgical History No. 38232. A white man, thirty-five years old, was transferred October 30, 1915, from the *medical* to the *surgical* service of Johns Hopkins Hospital with the persistent complaint of "blindness and headache." The family history was negative, and aside from typhoid fever at nineteen years of age, measles, mumps, and pertussis as a child, the only fact of importance in his past history was the occurrence of a Neisserian infection several years before. However, he denied all primary and secondary luetic stigmata. Beginning in July, 1914, he suffered with left frontal headaches, not severe enough to interfere with his work. Later the headaches became bi-parietal and more recently general in distribution, and usually started about 10 A.M. each day and ceased toward bedtime.

In November, 1914, visual disturbances began. He noticed distant vision was not as good in the left as in the right eye. The left

eye gradually failed. In the spring of 1915 Wassermann tests on the serum and spinal fluid were made at another clinic, and while there he received several injections of salvarsan. Several inunction treatments were given. This therapy is associated by the patient with a progression of visual disability. The right eye began to suffer about two months before admission (August, 1915) and rapidly failed, so that he can barely see to get about. There is only light perception in the left eye. He is practically totally blind.

He has lost forty pounds in the last year, now weighing 152 as compared with 192 a year ago. Thus at the onset of his illness he was fat and is said to have been a red-faced, healthy looking man. There has been no change in the skeletal structures. According to his statement his libido sexualis was perhaps a little below normal before the present illness. Since the latter there has been no *libido sexualis.*

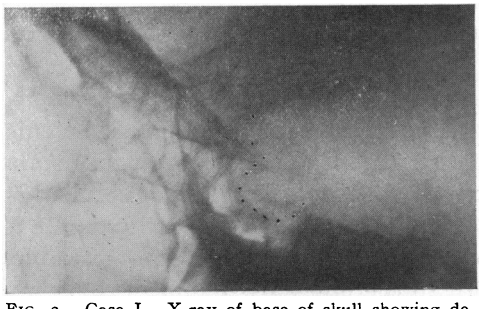

FIG. 2.—Case I. X-ray of base of skull showing destruction of clinoids, enlargement of sella and slight encroachment upon sphenoid space. This tumor, as subsequent pictures will indicate, originated in the upper surface of the anterior lobe below the dural diaphragma sellæ. Hence the enlargement of the sella in contrast to the two other cases in which the origin was suprasellar (cf. Figs. 10 and 13).

No nausea or vomiting.

Examination. — A well-developed man, rather pale.

Eyes: wide pupils, sluggish pupillary reaction to light on right; no reaction on left.

Fundi: showed marked pallor of temporal margins with swelling of nasal margins and fullness of vessels. Changes more in left fundus.

Visual acuity: left *nil;* right 6/200.

Course in hospital: While on the medical service a positive Wassermann test was present in the spinal fluid together with a luetic zone reaction in the colloidal gold test. He received salvarsanized serum intraspinously on two occasions.

X-ray report: October 15th (Dr. F. H. Baetjer). "Sella flattened out with destruction of posterior clinoids suggesting tumor" (Fig. 1).

Visual fields: Temporal hemianopsia on right, no vision in left eye.

Carbohydrate tolerance tests: No sugar in two specimens six and twenty-four hours after taking 100 grams of glucose.

Urine showed slight albumin with occasional granular casts, but repeated examinations were negative.

Operation.—October 30, 1915. Dr. G. J. Heuer. *Evacuation of hypophyseal cyst.* Usual lateral (left) approach as developed by the operator.

Findings: Unusually large collections of fluid in subarachnoid space, possibly related to recent salvarsanized serum injections.

The left optic nerve was stretched and dislocated outward. The tumor bulged forward between the two nerves. It was bluish and

apparently cystic. On puncture with a needle probably an ounce of brownish fluid escaped.

On attempting dissection of the cyst wall a hemorrhage occurred which could be controlled only by pressure and with the greatest difficulty. The left internal carotid artery evidently was seriously injured. This vessel was ligated in the neck just above the bifurcation of the common carotid. The cranial wound was then closed after placing rubber tissue drains down to the dura through the decompression opening.

Post-operative Course.—The patient apparently did very well until twelve days after operation, when there was sudden collapse, respirations ceasing. He was kept alive by artificial respiration for several hours, during which time there occurred a series of convulsions involving the left side particularly. Exitus.

The autopsy was made by Dr. A. B. Dayton, to whom I am indebted for the pathological material and use of the protocol.

Autopsy (No. 4508. November 12, 1915.—*Anatomical Diagnosis.*—" Squamous epithelial papillomatous cyst developing from a rest of Rathke's pouch." Operations: (1) lateral craniotomy and evacuation of cyst in hypophyseal region, (2) ligation of left internal carotid artery.

Bronchopneumonia. Pulmonary infarcts. Chronic appendicitis. Phleboliths of spleen and liver.

Body.—Is that of a white man 176 cm. (5 ft. 10 in.) in length. The skin is of smooth texture and the pubic hair is rather scanty, but has the normal masculine arrangement. It is also scanty on the face and in the axillæ. The pupils are regular, the left measuring 4 mm. and the right 5 mm. The scleræ are clear. The nose and ears present nothing of note. The teeth are in good condition. The genitalia are apparently normal. Just below the left angle of the jaw there is a horizontal scar of a recent operation about 4 cm. in length. On the scalp there is the wound of the usual temporal flap operation, which exposes the left frontal and temporal lobes. This, likewise, has healed *per primam.* There is very little, if any, bulging.

Though the patient is not very obese, there is considerable subcutaneous and retroperitoneal fat. There is no excess of peritoneal fluid and the surfaces are everywhere smooth and glistening. The appendix is about 9 cm. in length. Its serous surface is greatly injected, looks swollen and œdematous, is club-shaped, and at its extremity it has a diameter of about 1 cm. There is one delicate, fibrous adhesion. The other abdominal viscera seem normally disposed. The mesenteric lymph glands are not enlarged.

The left pleural cavity is free of fluid and its surfaces are everywhere smooth and glistening. The right pleural cavity is free of fluid. There are a few delicate fibrinous tags binding the edge of the lower lobe down to the diaphragm. There is considerable fat in the anterior mediastinum, and in picking this to pieces it is thought that there is some thymus tissue present. Roughly estimated, the latter amounts to 15–20 grams. The pericardial sac contains 10 c.c. of lemon-yellow fluid. Its surfaces are everywhere smooth and glistening.

Thyroid: Weight 31 grams, soft in consistency and of normal appearance. Parathyroids: Two were dissected out, of normal size and appearance. Adrenals: Together weigh 10 grams. Normal. Testicles: Are of normal size, consistency and gross appearance on section. Heart: Weighs 350 grams,

otherwise normal. Spleen: Weighs 150 grams. Acute splenic tumor. Subcapsular phleboliths. Pancreas: Weighs 110 grams. Normal. Liver: Weighs 1900 grams. Phleboliths similar to those of the spleen.

The left internal carotid after dissection showed a double silk ligature just above its point of origin from the common carotid. An antemortem thrombus was present.

Gall-bladder, neck organs and aorta normal.

Examination of Tumor, Brain, and Skull by the Writer.—After the routine injection of the brain *in situ* with 10 per cent. formalin it was removed with the tumor intact. This left the sella (Fig. 4) practically bare. The latter measured 3 x 3 cm. in its antero-posterior and transverse diameters, and was about 1.5 cm. in depth. There was no defect in its floor, which seemed thinned, but the lateral and posterior walls were greatly affected. Poth posterior clinoids were destroyed and the residuum of the dorsum sellæ was only about 1 mm. thick. The left postero-lateral wall showed a gross defect (*A*) corresponding with the prominent pole of the tumor (Fig. 3, *A*) of the same side. The relative uninvolvement of the left anterior clinoid process probably explains why no destruction of the anterior clinoids was apparent in the lateral röntgenogram view of the sella made before operation. The base of the sella showed no defect.

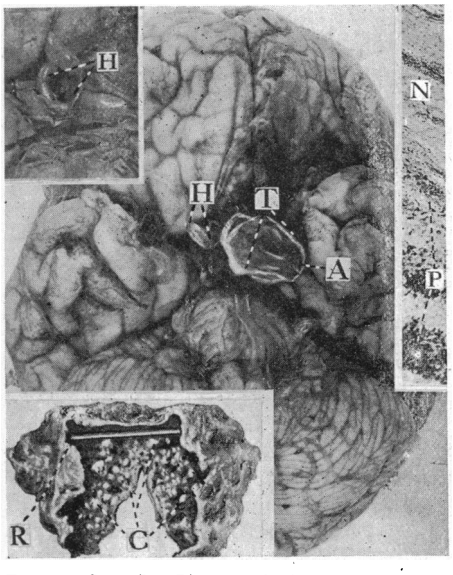

FIG. 3.—Case I. Photograph (reduced) showing tumor (*T*) at base of brain (removed after fixation *in situ* by injection of 10 per cent. formalin). The left lower insert is a retouched print to show the cauliflower-like intracystic papillomatous mass (*C*) on the superior inner surface of the cyst. The lower half of the cyst wall shows a mass (*R*) consisting largely of anterior lobe hypophyseal elements (cf. Figs. 6 and 7). The accessory mass (*H*), enlarged after incision in left upper insert, proved to be a hemorrhage in the right optic nerve. The upper right insert is a low-power photomicrograph of a segment of the nerve bordering the hemorrhage. *P*= large phagocytes laden with blood-derived pigment. *N*=perivascular round-cell infiltration.

The brain showed only slight flattening of the convolutions over the convexity, but a fairly well-marked compression ring at the base of the cerebellum gave evidence of a moderate degree of herniation through the foramen magnum.

At the time of the autopsy the left hemisphere was quite soft, the ligation of the internal carotid evidently having interfered considerably with its injection with formalin. The corresponding cerebral vessels on the left, the anterior cerebral, likewise the main cortical vessels and the superior sagittal sinus, were full of postmortem blood clot. The right internal carotid was normal. Both posterior communicating arteries seemed abnormally large, measuring about 1.5 mm. in diameter. The left was considerably stretched by the tumor. The left internal carotid for a short distance was surrounded by tumor and contained a dense clot, which seemed in the gross to be of antemortem character. The optic chiasm was dislocated far to the left and somewhat backward. The right optic nerve appeared rather slender and showed "a small cystic tumor mass" (Fig. 3, *H*) .8 x .7 cm. in diameter at a point about 1.5 cm. from where the nerve left the chiasm this mass seemed to be in the sheath of the nerve. There was no subsequent note concerning this local metastasis

(?) in the protocol. Examination by the writer finds a circumscribed brown to yellow-colored *hemorrhage* in the location of the above-described "tumor mass" (Fig. 3, *H*). The entire small mass in the right optic nerve is excised for microscopic confirmation.

Coronal section of the brain showed some diffuse hemorrhage in the left parietal lobe. Possibly most of this was caused at operation in exposing the hypophyseal region, but ligation of the internal carotid with possible subsequent softening may be a factor in the changes here.

The cranial nerves are normal save for the above referred to optic nerves and slight traumatism to the left olfactory nerve.

The tumor (Fig. 3) was an irregular spherical cystic mass, which measured 3 x 3 x 2.5 cm. in diameter, situated in the hypophyseal region. The hypophysis as a separate organ could not be located. After removal of the brain with cyst attached, the sella (Fig. 4) was left quite bare. Any residuum of the hypophysis must obviously be incorporated in the tumor. Neither was any trace of the infundibulum found at the time of the autopsy. Exami-

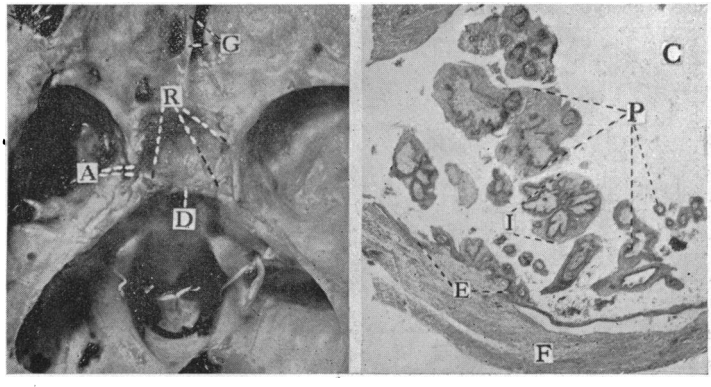

FIG. 4.—Case I. Photograph (reduced) at left of base of skull showing dilated sella. Clinoids (*R*) largely destroyed. Dorsum sellæ (*D*) thinned. Postero-lateral wall shows an erosion (*A*) corresponding with the prominent pole of the tumor (Fig. 3, *A*). *G*=crista galli. The picture at the right is a low-power photomicrograph of an upper angle of the collapsed cyst showing the strikingly papillomatous intracystic growth (*P*) composed of squamous epithelium. Lining the fibrous wall (*F*) is a layer of similar epithelium which shows sessile papillomatous masses in places (*E*). The papillomatous mass (*I*) is shown further enlarged in Fig. 5. *C*=cyst cavity.

nation at the present time of the base of the brain discloses no evidence of the infundibulum in the region of the tuber cinereum. Instead this locality appears to have been in close relation with the wall of the tumor mass. The floor of the third ventricle is intact, the ventricle not dilated. The choroid plexus of this and the other ventricles is normal in appearance. The pineal is normal in gross appearance. The region of the tuber cinereum shows some yellow-brown discoloration, apparently hemorrhagic in character.

The tumor then had replaced the infundibulum and largely obliterated the hypophysis, filled the sella and extended above, closely involving the surrounding structures and being in close relation with the floor of the third ventricle.

At the time of removal of the brain the cyst ruptured and "a degenerated portion of the tumor" measuring 2 x 1 x 1 cm. was extruded. It seems probable that this was part of the papillomatous intracystic mass, although it may possibly have been coagulated serum.

Fig. 3 (lower insert) shows the cyst after detachment from the brain. It has been incised and spread open. The wall is seen to vary greatly in

thickness, and it seems likely, in view of the microscopic findings, that this is due largely to the presence of hypophyseal tissue in the basal portion (Fig. 3, *R*) of the tumor wall. On the interior of the wall may be seen numerous small raised papillomatous masses (Fig. 3, *C*), having a somewhat cauliflower appearance, but the greater part of the cyst contents are lost.

Microscopic Examination.—The Tumor: The cyst wall (Fig. 4, *F*) varies in thickness from 1 to 6 mm. It is composed largely of fibrous tissue, with considerable hyalinization. Lining the interior of the cyst is a zone of stratified squamous epithelium (Fig. 4, *E*) with typical intercellular bridges, but no horny layer. In the cyst cavity lie cross sections of papilloma masses (Fig. 4, *P*) covered with similar epithelium. Of the latter, the more deeply staining layer of basal cells (Fig. 5, *B*) is sharply differentiated from the connective-tissue framework of the villous-like processes. This central framework (Fig. 5, *C*) is composed of a fairly loose connective tissue, which carries the nutrient blood-vessels (Fig. 5, *S*). Where the papillary contents of the cyst have not been lost they loosely fill the cavity (Fig. 4, *C*) of the cyst. The papillary masses are mostly of a pedunculated character, relatively

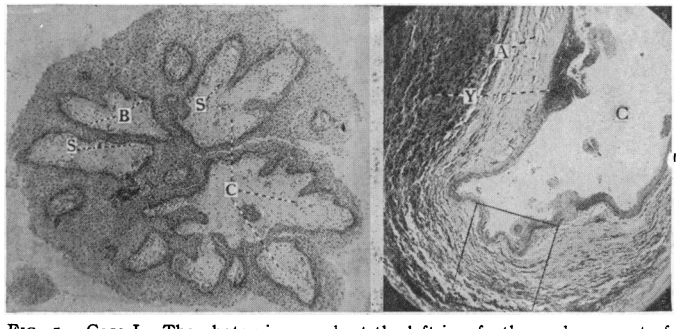

FIG. 5.—Case I. The photomicrograph at the left is a further enlargement of one of the papillomatous processes (Fig. 4, *I*). The squamous epithelial character of it is distinctly shown. *B*=basal layer of epithelium. *S*=blood-vessels which lie in a fibrous stroma (*C*). At the right is a very low-power photomicrograph of a segment of the cyst wall from which the papillary ingrowth is largely lost. *C*=cyst cavity. *Y*=areas of hemorrhage. The squared area is further enlarged in Fig. 6.

few processes of sessile appearance being found (Fig. 4, *S*). The stalks of the pedunculated processes are rarely to be seen anywhere, so that the absence or presence of these in other parts of the cyst where the contents have disappeared cannot be used as a criterion in determining whether the intracystic papilloma arose equally from all parts of the lining or only in the region where they are still to be seen. It seems probable that the cyst was equally filled throughout with growth similar to that shown in the photographs, and that the mass extruded at autopsy and subsequently lost probably consisted largely of these papillary masses. In the latter the basal layer of cells is everywhere intact. No invasion of the underlying stroma or other malignant criteria are present. The squamous epithelial lining of the cyst in these large sections occasionally sends short processes into the wall, but nowhere do these have a malignant appearance.

The wall of the cyst is well preserved in several microscopic sections. Two blocks for study were taken through nearly the whole circumference of the cyst near the mid-line, and a third, of similar extent but away from the mid-line, consequently of much smaller dimensions. The fibrous tissue of the wall is mostly of a dense type. Extensive areas of hyalinization are present, some of which possess a marked lamellated appearance. This,

together with the sinuous outline of the tissue, causes in certain areas a resemblance to an arteriosclerotic *aortic* wall. Numerous areas of hemorrhage (Fig. 5, *Y*; Fig. 6, *H*) are present throughout the wall. Some of these are large and show no attempt at organization. Other smaller ones show fibroblasts extending throughout the clot, while a rich granulation tissue may encompass the periphery of such areas.

Anterior lobe hypophyseal tissue is present in the wall of the cyst (Fig. 6, *A*). In one section strands of anterior-lobe epithelium extend for a distance of about 3.5 cm. Much of this consists of only a few strands of cells in thickness, but over an extent of about 1 cm. there is a thickness of about 12 to 15 strands or cords of anterior-lobe cells, and for a similar extent tissue of about half this thickness is present. These cells are well preserved (Fig. 7, *A*), showing perfectly differentiated eosinophile, basophile and chromophobe cells (the last few in number). In a certain area a recent hemorrhage has widely separated the strands of anterior-lobe tissue, and here the cytoplasm of such cells tends to stain less strongly, although the nuclei still take the stain well and the great majority of cells are apparently still viable. The granules of the eosinophiles are sharply stained (hæmatoxylin and eosin stained celloidin and paraffin preparations). In addition to strands of cells there are fairly large areas, 1 mm. or more in diameter, in which the flattening of the cell groups is not so marked, and they are arranged in characteristic acini. The intimate blood supply of the strands, columns, and acini of anterior-lobe elements is quite well preserved in spite of the fact that such tissue often lies in a fairly dense fibrous wall. Capillaries in most instances lie adjacent to strands or tubules, and in some cases the anterior-lobe cells delicately line these endothelial spaces. Most of the acinar areas are composed of well-stained cells, but areas are found where such is not the case. One of the latter areas is somewhat detached from the external surface of the cyst wall, and its cells are beginning to undergo necrosis. There is considerable hemorrhage in this area, and the base of it shows a mass of granulation tissue growing into it from the wall of the cyst. None of the cells of this degenerating mass appear to be of the eosinophilic type.

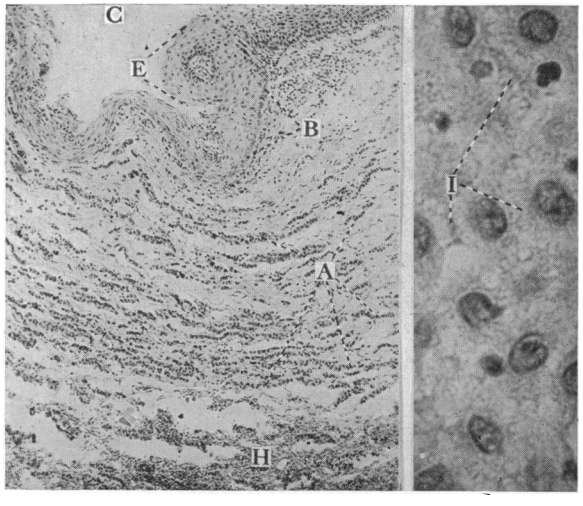

FIG. 6.—Case I. At the left is shown a medium-power enlargement of the squared area in Fig. 5. Strands of anterior lobe hypophyseal cells (*A*) lie in the fibrous wall. *E*-sessile projection from squamous epithelial lining of cyst. *B*=basal layer. *C*=cyst cavity. *H*=zone of hemorrhage. At the right is a photomicrograph (oil immersion magnification) showing the presence of intracellular bridges (*I*) in the squamous epithelium of the tumor.

In the large microscopic preparation, which comprises practically the whole median circumference of the cyst wall, is found a large area of necrosis (cf. Fig. 3, *R*), about 3 x 4 mm. in diameter. This is composed of

anterior-lobe elements, most of which show a definite acinar arrangement. It occupies almost the whole thickness of the cyst wall at this point, and throughout most of its circumference is surrounded by a vascular granulation tissue. In the latter zone are found isolated anterior-lobe elements, as well as entire acini lined by cells or filled with detached cells, which are in various stages of degeneration (Fig. 7, *N*, *R*). Many of these cells show the characteristic granulation of eosinophilic anterior-lobe elements. Indeed such granulation is seen in some cells in the necrotic mass whose nuclei do not take the stain.

Throughout the latter area, but more especially at the periphery, one sees numbers of colloid-like accumulations, some of which are quite homogeneous and refractile, others of which still show a fine granulation. Some of these are several times the size of a large eosinophilic anterior-lobe cell. A few of these hyaline accumulations lie in the meshes of the wall adjacent to the cyst cavity, which at this place has lost (desquamation or trauma?) its epithelial lining. The smaller of these masses resemble the *hyaline*

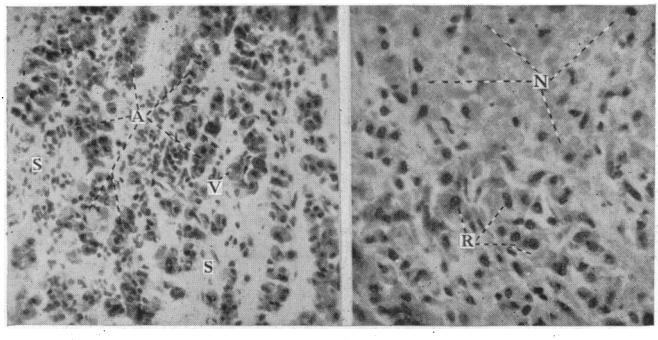

FIG. 7.—Case I. At the left is a photomicrograph showing an area in the wall of the cyst where clumps of anterior lobe hypophyseal elements (*A*) are thickly scattered through the stroma (*S*) of the cyst wall. The photomicrograph at the right is of a section taken through the area *R* of Fig. 3, where a large amount of anterior lobe tissue was present with very little stroma. Much of the area had undergone necrosis and the photomicrograph is taken through the edge of the necrotic tissue. At *N* are necrotic cells, while at *R* are cells the cytoplasm of which stains faintly but the nuclei take the stain well

bodies of the pars nervosa described by Herring. (Concerning the latter, it it not clear whether they are the secretion product of epithelial cells of the *pars intermedia,* which may have penetrated the pars nervosa, or whether they may result from the degeneration of single epithelial cells. The occurrence of numbers of similar bodies in close relation to a mass of anterior-lobe tissue undergoing extensive necrosis would seem to favor the view that such material may possibly result from a degeneration of cells in bulk, rather than an accumulated secretion of one or more cells. However, the analogy is not complete, since the hyaline bodies of Herring arise presumably from the intermedia epithelium, whereas the tissue here described is apparently solely anterior lobe.) As to the causation of this necrosis, it would seem most likely due to interference with the blood supply, possibly owing to the operative procedures. It is evidently a comparatively recent affair.

There is evidence also of the presence of *pars intermedia* elements in the wall of the cyst. This consists of a number of epithelial glands lined by cubical or columnar epithelium, and either flattened out, appearing as tubules, or else larger and ovoid in outline. In the latter case they may contain material of a colloid-like appearance, taking the pink stain well. Usually

they have been flattened out by the pressure of the cyst, and their long axes lie parallel with the circumference of the cyst wall. There is no apparent evidence of these glands discharging any secretion into the cyst cavity.

No posterior-lobe tissue could be identified, although there was almost similar appearing connective tissue in places.

Polymorphonuclear leucocytes are scattered through the cyst wall, and in fewer numbers occur throughout the structure of the papillomatous processes, both through the stroma and in the epithelial covering.

Numbers of foreign body giant cells lie in the wall of the cyst, usually associated with the absorption of blood pigment, but in places found at the periphery of clear spaces (Fig. 5, *A*), from which cholesterin crystals have been dissolved out by the process of fixation of the tissue.

Section through the *mass* (Fig. 3, *H*) in the *right optic nerve* shows a large (1 cm.) recent hæmatoma. This has expanded the nerve to a thin shell. In the wall one sees great numbers of large mononuclear phagocytes (Fig. 3, *P*), similar to the "compound granular cells," loaded with black hæmatogenous pigment. Occasional small hemorrhages and œdematous areas have further disturbed the remaining nerve substance. A striking feature is the presence of focal areas (Fig. 3, *N*) of small mononuclears. These areas are usually perivascular in arrangement and are largest in the sheath of the nerve, extending thence inward along the vascular spaces. It is barely possible that these may be unrelated to the hæmatoma, and of a more chronic significance, related to the syphilitic infection (*vide infra*). The blood-cells composing the hemorrhage are well preserved and show no organization. The bright yellow color which was seen in the gross has persisted and appears as a light yellow to brown, finely granular pigment, comparable to bile pigment under similar (fixation and staining) conditions.

Section through the base of the brain and the aqueduct of Sylvius shows two small (¼ to ½ mm.) isolated hemorrhages. Compound granular cells are very numerous. The aqueduct is patent.

The *pineal* shows no microscopic abnormality.

Thyroid.—Acini normal or perhaps below normal in size. Colloid fills practically all of the vesicles, a few of which are distended, with flattened epithelial lining. A small amount of fetal tissue is present here and there between the acini, but no typical adenoma formation is present; no encapsulation of these small areas. The epithelial lining throughout is of low cuboidal, nearly flat, or more rarely low columnar type. The latter, however, is of such small amount in comparison with the flat type as to be practically within normal limits. The gland appears as a whole to be of normal structure.

Parathyroid.—About 2.5 x 1.5 mm. in size, lying near the above described thyroid section in the loose extracapsular fibrous tissue. Essentially of normal appearance; composed of closely packed columns of cells, with here and there a definite acinar arrangement, occasionally with a small lumen. A small bit of colloid-appearing substance was present in one acinus. The cells show what seems to be a neutrophilic staining affinity, with here and there a slight pink variation.

Testicle.—Despite the recorded (protocol) gross normality, the microscopic examination finds a serious alteration of the normal structure (Fig. 8). Spermatogenesis has practically ceased. The seminiferous tubules, for the most part, are lined by one (Fig. 8, *S*) or two layers of cells, which, in striking contrast to the normal, exhibit no mitotic figures. None of the cells have advanced beyond the stage of secondary spermatocyte. No spermatozoa or spermatids are found. The tunica propria (Fig. 8, *T*) is hyalinized and con-

siderably thickened. A few tubules are seen, in which the epithelial cells have lost all resemblance to spermatocytes and look like fibroblasts. The *tunica propria* of such tubules show a marked fibrous increase.

The interstitial tissue (Fig. 8, *M*) shows a moderate increase in connective tissue, both diffusely and in strands and patches, the latter of which are 1 mm. or more in diameter. Much of this connective tissue shows well-formed fibrils and elongated flattened nuclei, evidently a connective tissue of not very recent formation. However, most of it is rather loosely meshed, apparently due to œdema. Occasional small areas of round-cell infiltration were found. No miliary gummata were found.

Dr. R. B. Mills, who has recently (1919) made a special study of the testicle, was kind enough to examine sections from this testicle. In his opinion, the cessation of spermatogenesis is complete; practically only Sertoli (supporting) cells remain in the tubules. The interstitial cells of Leydig he found to be present in normal numbers. As to the causation of the changes he gave no opinion.

Thymus.—Isolated, irregular branching clumps and strands of lymphoid tissue lie scattered through a fatty framework. The Hassell's corpuscles show no proliferative changes, but, on the contrary, a number of them are hyalinized with non-staining nuclei. Some of these corpuscles apparently are being phagocytosed by large foreign-body giant-cells. The capsule of the gland is 1 mm. thick and composed of hyalinized fibrous tissue. Fairly large vessels lie here and there throughout the fatty meshwork, but the vascularization of the lymphoid areas is not striking. Regressive changes in the gland seem predominant.

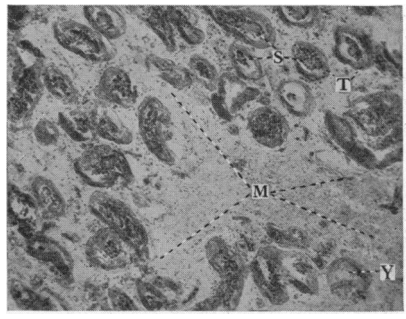

FIG. 8.—Case I. Photomicrograph (low magnification) of the testicle. Spermatogenesis has ceased. The single layer of cells (*S*) present in most of the tubules is composed of Sertoli cells. The basement membrane (*T*) is thickened and occasional tubules devoid of epithelium (*Y*) are found. At *M* is a patch of loose fibrous tissue. A slight increase in stroma is present elsewhere.

Pancreas.—The islands are numerous and showed no hyalinization. Elsewhere no fibrosis was made out. A special study was not made of the gland, but in the hæmatoxylin and eosin stained preparations nothing abnormal was found.

Appendix.—Shows a marked grade of chronic appendicitis. In places the wall is 4 mm. thick. The mucosa is lost in some places, whereas in others fibrous changes have occurred. The thick fibrous wall is infiltrated with small mononuclears and eosinophilic polymorphonuclears.

Adrenals.—Show no striking changes.

Liver and Spleen.—Normal save for a few uncalcified phleboliths.

Lung.—Purulent bronchitis, section from upper lobe; also a small fibrous-encapsulated calcified area.

The lower lobe—the sections show an infarct, small areas of broncho-pneumonia, and large areas of hemorrhagic broncho-pneumonia.

Summary of Case I.—A previously healthy white man, thirty-five years old, began rather abruptly to suffer with severe headaches, progressive diminution of vision, and loss of libido sexualis. In different clinics, although he denied luetic infection, positive Wassermann tests

resulted in anti-luetic therapy. Later the diagnosis of tumor in the hypophyseal region was made by means of radiography. The visual fields showed a bitemporal hemianopsia. The exploratory craniotomy was complicated by unusual hemorrhage; however, the cyst presenting above the sella and between the optic nerves was evacuated, and the patient recovered from the immediate effects of the operation, but died twelve days later with symptoms indicating failure of the medullary centres (about one and one-half years after the onset of symptoms).

At the autopsy of this slightly obese man a squamous epithelial intracystic papilloma was found presenting above the enlarged sella with remains of the anterior hypophyseal lobe and traces of pars intermedia preserved in the basal sector of the cyst wall. Death apparently was caused by increased intracranial pressure (cerebral œdema). Testes showed histologically a marked atrophy. Thymus was retrogressive. Other glands of internal secretion showed no definite changes. Changes of subsidiary interest were found in the lung (broncho-pneumonia, pulmonary infarcts) and appendix. *Diagnosis: benign squamous epithelial intracystic papilloma arising from a rest of the hypophyseal duct in the upper surface of the anterior lobe.*

CASE II.—*Cystic suprasellar tumor with adamantinoma characters developing from an infundibular squamous epithelial rest of the hypophyseal duct in a child aged eleven years. Headaches for five years. Excrescence of sex features since age of nine, no marked adiposity. Progressive failure of vision for one year. Projectile vomiting for eight months. Other general pressure symptoms. Operation: Evacuation of cyst and partial removal of cyst wall (lateral operation). Death.*

Abstract of J. H. H. Surgical History No. 42460. A small white girl, eleven years old, was admitted April 20, 1917, to the Surgical Service of the Johns Hopkins Hospital, *complaining* of "headaches," impairment of vision, and difficulty in walking. For at least five or six years, according to the parents, the child has complained of headaches, general in character, but perhaps worse in front than behind. These have gradually increased in frequency until the past three or four weeks, since when they have been almost constant. Within twelve months the vision of both eyes has gradually but progressively failed. This has become so marked that she cannot recognize faces or objects at table. There has been occasional abrupt and forcible vomiting for eight months. During the last six weeks there has been considerable weakness, finally so much that she cannot stand. Gradual impairment of hearing in last year, during which time she has complained of noises in the head. The child was born after a normal labor. The mother is somewhat robust and masculine looking.

Developmental Phenomena.—Following tonsillectomy two years ago for chronic tonsillitis, with "some arthritis," there occurred marked somatic changes. She increased very rapidly in weight. The hair of the head grew much longer and richer. A moderate growth of pubic hair has appeared (see Fig. 9), but the menses are

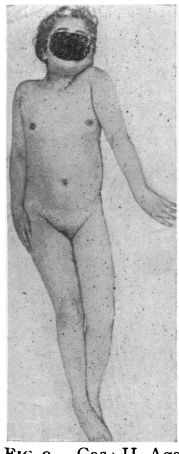

FIG. 9.—Case II. Age eleven years. Growth of pubic hair. Apparent beginning development of breasts. No obesity.

still absent. No distinct increased appetite for sweets, but there is a definite history of polyuria (recent incontinence).

The child was brought in chiefly because of increase in headaches and stupor and visual impairment. Slight increase in size of head.

Examination.—A docile, quiet, rather torpid child. Rich, dark curly hair, well-developed mammary tissue with slight pigmentation of the nipples. The bony pelvis has begun to assume some of the proportions of maturity. Bowing of the femoræ is present.

Hirsuties: Well-developed pubic and axillary hair.

Fingers long and tapering, nails curve and are well kept. No prognathism; teeth normal with no abnormal spacing.

Skin: Somewhat dry and harsh.

General physical aside from above facts is negative.

Visual fields could not be taken.

Grip equal on the two sides. Bilateral optic atrophy with choked disk and proliferative changes. Clonus of legs and equivocal Oppenheim and Gordon signs.

X-ray Report (Dr. F. H. Baetjer).—Marked separation of the sutures, partial destruction of posterior clinoids with calcification just above it, suggesting a suprasellar tumor (Fig 10).

Operation (April 24, 1917, Dr. G. J. Heuer).—*Evacuation of hypophyseal cyst with extirpation of lining of cyst. Lateral approach.*

Findings.—The cyst appeared over the chiasm which was pushed forward. On puncture of the cyst 30 c.c. of thick, peculiar, reddish-brown fluid was obtained. On microscopic examination it showed numerous red blood-cells, a few cholesterin crystals, and some curious rosette-like clusters of small cells, squamous epithelial, apparently. After aspirating this fluid the lining membrane in which were numerous small calcified patches could be stripped away.

NOTE.—Preliminary ven-

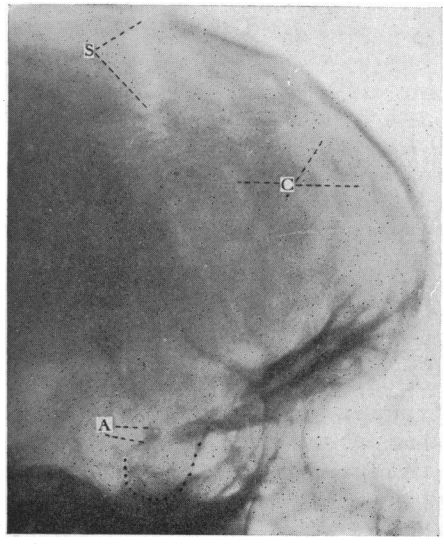

FIG. 10.—Case II. Unretouched print from lateral X-ray plate showing suprasellar calcified mass at *A*. *S*=separation of fronto-parietal sutures. *C*=frontal convolutional atrophy. The latter changes make an internal hydrocephalus probable, due most likely to blocking of the ventricular foramina or the iter by the upward growth of the tumor. The heavy calcified mass above *A* is too far forward to be pineal.

tricular puncture has shown a high grade of internal hydrocephalus; 120 c.c. of fluid which spurted for a height of six or eight inches.

Died on evening of same day apparently of cerebral œdema. Temperature rose to 105°. Autopsy not obtained.

Microscopic Examination.—The tissue removed at operation (part of the lining membrane of the cyst) consisted of a few small bits of tissue too small to photograph. The tissue was hardened in formalin and embedded in celloidin in three separate blocks.

Examination of sections (Fig. 11) from one block shows a predominance of squamous epithelium, present in masses or processes, or strands which line cystic areas, or constitute the periphery of areas of myxomatous connective tissue (Fig. 11, *M*).

The individual larger mass (Fig. 11, *Y*) is made up of stratified epithelium with peripheral convoluted processes which are covered by a sharply staining basal layer of columnar epithelium (Fig. 11, *E*). The nuclei of the latter are oval or slightly flattened, and occupy the greater part of the cell length save for approximately the distal one-third, which is of clear pale pink cytoplasm. The distal periphery of these cells is capped in certain areas by a thin layer of "membrana propria" (Fig. 11, *P*), which shows an occasional dark flat (shrunken) nucleus, which lies at right angles to those of the basal layer. Similarly the cells of the latter are at right angles to the subjacent epithelial cells.

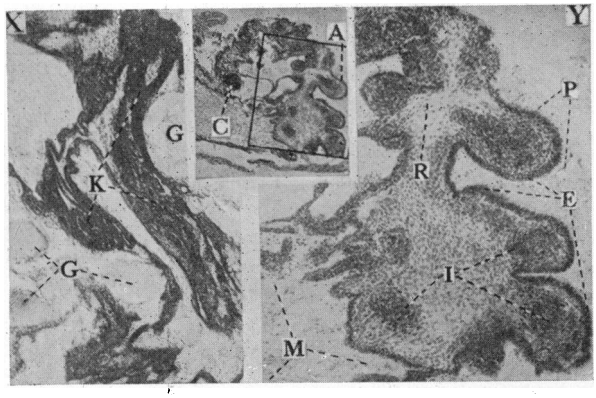

FIG. 11.—Case II. Photomicrographs of tissue removed at operation. The enclosed area in the upper central insert is from the wall of the cyst and presents the adamantinoma picture which is more clearly seen in the enlargement at the right (*Y*). The mass of stratified epithelium borders a connective tissue area (*M*). Its peripheral layer of columnar epithelial cells (*E*) is situated at right angles to the underlying zone of epithelium which shows tendencies to whorl formation (*I*). The central zone (*R*) is not strikingly differentiated (*cf.* Fig. 17, *Y* and *U*). Note the delicate elevated membrana propria at *P*. The insert (*X*) at the left shows an unusual basal cell epithelioma-like differentiation present in another block of tissue of the same tumor. *K* = columns of deeply blue staining epithelial cells which lie next to dead masses (*G*) of keratinized epithelium. This basal cell picture was found in one small area in tissue from this case only.

The cells beneath the basal layer (the intermediate zone) have larger oval or nearly round, more lightly staining, nuclei, which tend to stain less strongly as the centre of the mass or process is approached. The cell bodies of this intermediate zone are somewhat flattened, with small but varying amounts of cytoplasm. In the central zone intercellular bridges are visible with the high power or else a varying degree of reticulation has taken place. In the latter case the cells consist of almost bare nuclei with thin protoplasmic processes, which stretch out and join similar ones of adjacent cells, often resulting in a "stellate" appearance of such individual cells. In case no reticulation exists, the cytoplasm is larger in amount, giving polygonal outlines to the cells. Such cells show clearly the intercellular spiculæ or bridges.

Concentric-layered epithelial nodules (Fig. 11, *I*) lie in the convoluted processes of the mass or elsewhere in the intermediate zone below the basal

layer of cells. These appear to be the precursors of epithelial pearls, but show no keratinization. Their peripheral layers tend to be flattened, with dark nuclei, the cells centralwards becoming larger, with round, more lightly staining nuclei.

The epithelium which borders the large myxomatous area (Fig. 11, *M*) is a direct continuation of the peripheral basal layer of the above-described processes, but quickly loses its characteristic appearance and comes to consist of a double layer of cells which are flatter and contain much less cytoplasm than the typical basal cells. Also the basal layer of epithelial processes which extend into underlying fibrous or myxomatous tissue tend to lose their typical appearance and become flatter. The myxomatous tissue shows a very loose structure, with fibroblasts and thin-walled capillaries. Besides there is a small amount of adult connective tissue present. Small cystic areas below the main epithelial mass are lined by flat epithelium, which in places extends across open spaces in a single layer of cells.

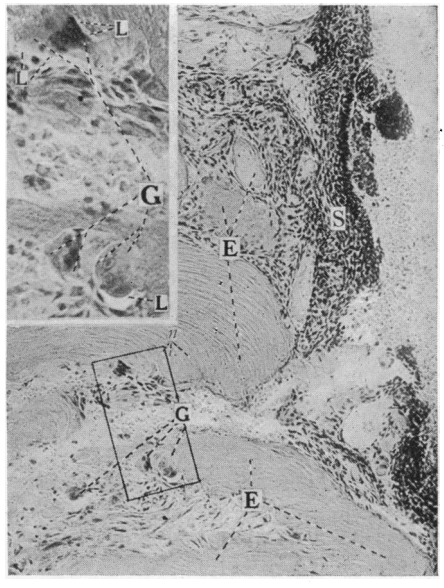

FIG. 12.—Case II. Showing phagocytosis of keratinized epithelium (*E*). *G* = foreign body giant-cells. Those lying within the squared area are shown enlarged in the insert above. Note that the giant cells (*G*) have penetrated the masses of dead epithelium and lie within lacunæ. The phagocyte at the lower right corner of the insert is close applied to the dead tissue, a free space separating it from connective tissue cells whose nuclei take the stain. *S* = viable modified squamous epithelium showing neither typical adamantinoma nor basal cell characters. *n* = clear spaces of dead nuclei.

A single calcified vessel (Fig. 11, *C*) is present in the sections from this block. The wall shows a diffuse infiltration with lime salts. The lumen is filled with a homogeneous material in which the individual elements are fused.

Sections from the other blocks show quite a different variation of the structure above described, with a predominance of degenerative changes. Sections are made up largely of nests and processes of keratinized necrotic stratified epithelium (Fig. 11, *G*, and Fig. 12, *E*), in which a relatively slight but varying amount of calcification has occurred. When present the calcium salts deposit involves alone or more intensely the outer layers of dead epithelium. No ossification is present. A few larger nests or processes composed of viable squamous epithelium, resembling in their essentials those found in the preceding block, are present, but much of the live epithelium is present as attenuated processes (Fig. 11, *K*), which ring the periphery of dead epithelial masses. Only a suggestion is found of the sharply differentiated cylindrical basal cells, and these in no place assume the tall columnar character (Fig. 11, *E*) which is pictured above. Instead, much of the still viable epithelium shows as dense staining solid processes (Fig. 11, *K*) and nests which resemble the familiar picture of a typical basal cell epithelioma of the skin.

Lying in lacunæ (Fig. 12, *G*) formed in the periphery of the dead tissue, closely rimming the contour of the same, or occasionally lying between the dead masses in the midst of the granulation tissue which fills such spaces, are large, irregularly shaped, foreign-body giant cells (Fig. 12, *G*). In the

case of giant cells closely applied to the dead epithelium, either on the surface or lying in lacunæ, a concave surface is usually presented toward the dead tissue, small particles of which may be seen detached from the main mass and about to be enclosed by the encircling cytoplasm of the phagocyte. Other masses of dead epithelium surrounded by giant cells show a disappearance of a dust-like zone of calcification in the immediate vicinity of the phagocytes. This is striking, since calcification in undisturbed necrotic masses is usually more intense at the periphery of the mass. The latter calcified masses are usually surrounded by live epithelium, and no giant cells or fibrous tissue are in proximity to them.

The third and last block contains a small amount of the cyst lining with areas of calcification, large areas of recent hemorrhage, which show, owing to the formalin fixation, much hæmosiderin pigment change. But besides there is a more important small area about 0.4 in diameter composed of obvious hypophyseal anterior lobe element derivatives. These consist of chromophobe and eosinophile cells and a relatively normal amount of connective tissue. Chromophobe cells predominate. In general, traces of the normal structure are to be found in the fairly well-formed acini with delicate fibrous stroma. Marked pressure effects are to be seen in the flattening and convolution of such acini. The latter show no colloid, but in a few a lumen is present. In considerable areas no acini are to be made out, and the picture is of larger masses of cells, such as may be seen in anterior-lobe adenomata.

Summary of Case II.—A female child eleven years old, who had suffered with headaches of increasing frequency for five years, progressive failure of vision for one year, and occasional projectile vomiting for eight months, was brought to the hospital because of increasing disability and the recent appearance of stupor. Instead of retardation of sexual characters, there was perhaps slight exaggeration of same. Radiography showed a suprasellar nodular shadow, due to calcification; partial destruction of posterior clinoids, and separation of the fronto-parietal sutures suggesting a secondary hydrocephalus. At the exploratory craniotomy a suprasellar cyst containing 30 c.c. of fluid was evacuated and partly extirpated. Histological examination of tissue from the wall of the cyst showed definite squamous epithelial cell derivatives presenting the picture of adamantinoma. Death apparently from cerebral œdema. No autopsy.

(*To be continued.*)