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ADAMANTINOMA OF THE CRANIOPHARYNGEAL DUCT *

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In the files in the neurosurgical clinic of the University of Pennsylvania are 244 cases of sellar and parasellar lesions, and of this number we have classified 14 as adamantinoma. Of these, 11 have been definitely identified histologically; in 2 the histologic picture is suggestive, and in 1 the diagnosis is based on the presence in a child of a large calcified suprasellar cyst.

Erdheim [1] first suggested that the squamous epithelial cells were remnants of the craniopharyngeal duct and that tumors composed of these cells were in fact duct tumors (Hypophysenganggeschwülste). Since Erdheim's contribution, in 1904, others have followed, recording isolated cases or series of cases, but there is still much uncertainty and lack of agreement as to how these duct tumors should be classified. The following classification seems to us the most satisfying: (1) adamantinomas or, preferably, ameloblastomas; (2) Rathke's pouch tumors; (3) carcinomas; (4) teratomas.

The identification of the lesion as an adamantinoma before operation is not free from difficulties. Variations in the exact location of the lesion between the third ventricle above and the pituitary fossa below, variations in the field distortions, variations in the roentgenograms, variations in the endocrine picture and discrepancies in the age of the patient are such that one may well hesitate before operation to speak of the nature of the lesion with much assurance.

There have been many contributions to the literature on duct tumors since Erdheim's paper in 1904, but the student interested exclusively

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1. Erdheim: Sitzungsb. d. k. Akad. d. Wissenschaft. Math.-naturw. Cl. **113**:537, 1904.

in adamantinomas I would refer to the more recent articles by Critchley and Ironside,[2] to Peet[3] and to Beckmann and Kubie.[4] The first includes a series of 12 cases, the second 3 and the third 7. These three groups, with the 14 cases of this series, comprise a total of 36 tumors of this type. Contrary to what seems to be the prevailing opinion, we believe that of the 2 duct tumors, the adamantinomatous and the Rathke pouch tumors, the former are relatively much more frequent.

PART I. ABSTRACTS OF HISTORIES

CASE 1.—*A boy, aged 7, after four years of headache was admitted to the hospital with an enlarged sella turcica and bitemporal hemianopia. Thirteen years after a transsphenoidal operation and seven years after a transfrontal evacuation of a cyst, the patient was still alive and mentally alert, though a dwarf and blind.*

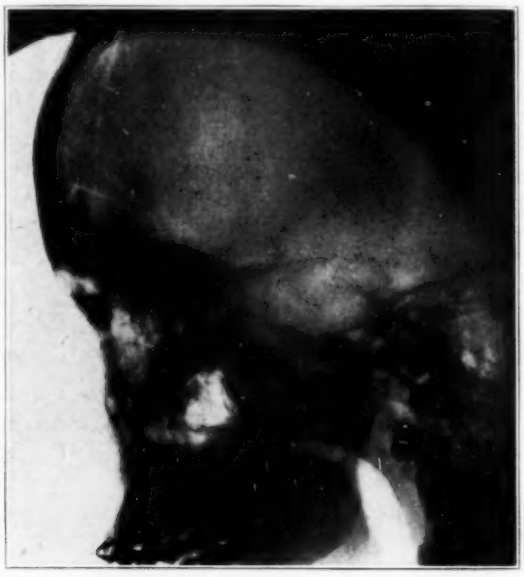

Fig. 1 (case 1).—Roentgenogram, showing moderate atrophy of the dorsum sellae, with marked enlargement of the pituitary fossa, and evidence of calcification between the anterior and posterior clinoid processes; slight convolutional atrophy.

Clinical History.—J. F. G., a boy, aged 7, was referred to the neurosurgical service of the University Hospital by Dr. George E. de Schweinitz, on April 11, 1918. When 3 years of age he began to have headaches, which increased in severity and frequency until his sixth year. During this period, the child was sullen and difficult to manage. He had an attack of jaundice, hay fever and

2. Critchley, M., and Ironside, R. N.: Brain **49**:437, 1926.
3. Peet, M. M.: Pituitary Adamantinomas, Arch. Surg. **15**:829 (Dec.) 1927.
4. Beckmann, J. W., and Kubie, L. S.: Brain **52**:127, 1929.

bilateral mastoiditis. The tonsils and adenoids were removed. About a year before admission, the headaches ceased, suggesting a spontaneous decompression. Eighteen days before admission, the mother discovered for the first time that he had lost the sight of the left eye. On the following day, Dr. de Schweinitz found a bitemporal hemianopia, and roentgen examination revealed enlargement of his sella turcica (figs. 1 and 2).

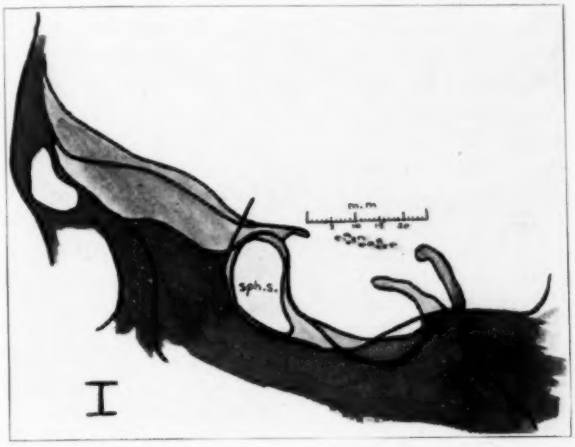

Fig. 2 (case 1).—A sketch of the roentgenogram (fig. 1), drawn to scale.

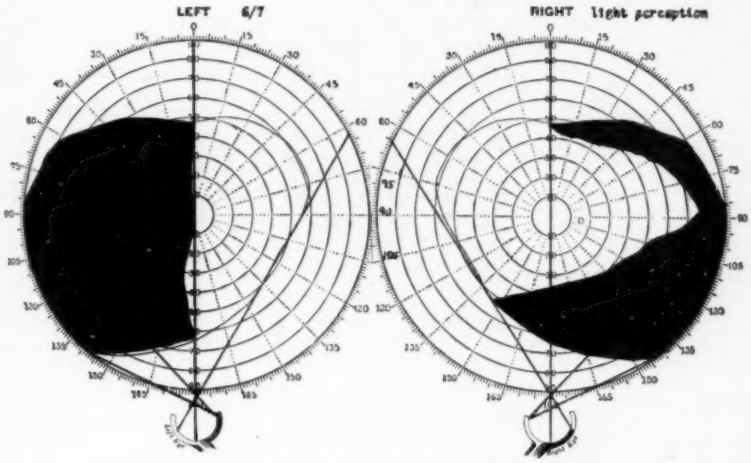

Fig. 3 (case 1).—Bitemporal hemianopia; incomplete in the right eye. Vision in the right eye was limited to light perception; in the left eye, 6/7.

Examination.—On admission to the University Hospital, examination revealed that vision in the right eye was reduced to light perception; in the left eye it was 6/7 (fig. 3). The pituitary fossa showed a considerable increase in both the antero-posterior and the vertical measurements. A brother, though two years younger, was several inches taller.

Transsphenoidal Operation.—On April 16, by our usual technic, the nasal septum was resected, the sphenoid sinus opened and the bluish wall of a cyst presented. On incision of the cyst wall, a yellowish, oily fluid escaped. Following the evacuation of the cyst the wound was closed.

Immediate Result.—The immediate result was recorded as a recovery.

Postoperative Course.—Following the operation there was a striking improvement in the patient's general condition, the temporal hemianopia disappeared, and there was complete restoration of vision in the left eye. This improvement continued for seven years; then it was noticed that vision was not as acute as it had been, and arrangements were made for readmission to the hospital.

Second Admission.—On March 9, 1925, the patient again had a complete hemianopia of the right eye and complete loss of vision in the left eye. The dimensions of the sella turcica had increased considerably since the examination seven years before. During this time he had grown only 4 inches (10.16 cm.), and his stature was that of a boy aged 7.

Transfrontal Craniotomy.—On March 10, under local anesthesia, a transfrontal craniotomy was performed on the left side. On elevating the frontal lobe, the cyst wall presented between the optic nerves. After evacuation of the cyst, some calcareous deposits were found in the cavity and removed. The cyst wall, isolated from the optic nerves and chiasm and from the anterior wall of the pituitary fossa, collapsed. The cavity was swabbed with a 2.5 per cent solution of tincture of iodine. The wound was closed.

Immediate Result.—The immediate result was again recorded as a recovery.

Subsequent Course.—After the second, as after the first, operation there was a decided improvement in vision. This was maintained for over a year. From that time on, sight again began to fail, until at the time of writing this article the patient was totally blind, thirteen years after the first operation, seventeen years since the first headache. Despite a prolonged course of glandular feeding, the patient, now 20 years of age, was dwarfed. In every respect except stature and vision he seemed in perfect health, and was in attendance at a preparatory school.

Pathologic Report.—There were a few scattered epithelial cells, some of which were calcareous and others of which looked as if they were arranged in stratified fashion. Calcification and degeneration were widespread.

CASE 2.—*A girl, aged 8, had had daily headaches for years; in the past month vision had almost failed, and for eight days headache had been intense and vomiting incessant. A large calcified tumor was found and in part removed. The patient was discharged twelve days after operation.*

Clinical History.—L. E. H., a girl, aged 8, was referred to the neurosurgical clinic by Dr. J. L. McKee, on Nov. 13, 1925. She was an only child, of normal birth, and had had measles, chickenpox and whooping cough. Her father died of tuberculosis. The mother said that the child had had a headache every day since she could talk. The attacks lasted about an hour and a half, and little attention was paid to them. But for the eight days preceding admission the headache had been intense and vomiting incessant. For a month vision had been failing, until at the time of admission the child could not recognize her playmates.

Neurologic Status.—Apart from an abortive ankle clonus on both sides, there were no neurologic signs except those to be recorded.

Pituitary Stigmas: There was a tendency to adiposity, protruding abdomen (fig. 4), prominent breasts and tapering fingers. The basal metabolic rate was —6.

Ocular Disturbances: The left eye showed temporal hemianopia; vision was limited to counting fingers. The right eye was blind. The disks had the appearance of a subsiding choking, with atrophy; they were gray with blurred margins (fig. 5).

Roentgen Observations.—There were destruction of the clinoid processes, erosion of the floor of the sella and some enlargement of the sella. A large calcareous deposit was seen extending backward and upward; it was about 4 cm. in diameter (figs. 6 and 7).

Diagnosis.—A preliminary diagnosis of calcified tumor of Rathke's pouch was made and exploration advised.

Craniotomy.—On Jan. 13, 1926, a transfrontal craniotomy was performed on the left side. On reflection of the flap, the dura was exceedingly tense, but for-

Fig. 4 (case 2).—Photograph of the patient at the age of 8 years; she had had headaches for years. In the past month vision had almost failed; headaches were intense, and vomiting was incessant. There was temporal hemianopia in the left eye; the right eye was blind. There was destruction of the clinoid processes, and some enlargement of the sella. The roentgen shadow showed a large calcareous deposit 4 cm. in diameter. A transfrontal craniotomy was performed, with removal of a large calcareous tumor. The pathologic diagnosis was adamantinoma of the craniopharyngeal duct.

tunately a dilated ventricle was found and with its evacuation the pressure was entirely relieved, so much so that the frontal lobe of its own weight fell away sufficiently to expose the region of the chiasm.

The tumor was readily seen, presenting prechiasmally. The left optic nerve, first seen, was on the stretch and ribbon-like. The center of the tumor seemed cystic, and about 1 cc. of fluid was evacuated. Through a capsular opening the cavity was curetted, but little tissue was recovered. The capsule was then freed

from the chiasm and optic nerves, and as much as could be easily detached was removed. When finished, there presented in the sella a cavity, measuring approximately 2 by 2.5 cm. in diameter. This cavity was tamponed with cotton pledgets, saturated with epinephrine (1:1,000) and swabbed with a 3 per cent solution of

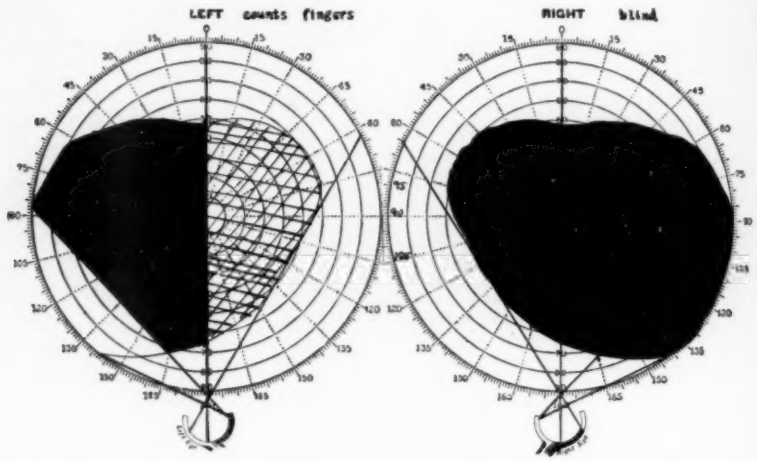

Fig. 5 (case 2).—The fields before operation. There was temporal hemianopia of the left eye; vision was limited to the counting of fingers. The right eye was blind.

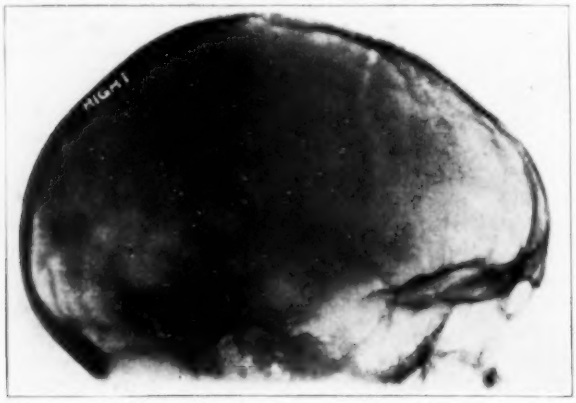

Fig. 6 (case 2).—Roentgenogram, showing marked atrophy of the dorsum sellae, complete disappearance of the posterior clinoid processes, marked enlargement of the pituitary fossa and evidence of calcification above and behind the dorsum sellae.

tincture of iodine. The operation was extraordinarily free from any difficulties; the patient was given 325 cc. of citrated blood; the systolic pressure rose to 85, and the pulse rate dropped 20 points. At the conclusion of the operation, the patient was conscious.

Postoperative Course.—In the convalescent period vomiting persisted. The child did not react well. The general condition was not especially satisfactory, and on January 25, twelve days after the operation, the child was taken home. The asthenia continued, and the child died on February 1.

Histologic Report.—The tumor was composed of the typical anastomosing epithelial columns. In the sections the stroma was considerably more abundant than the epithelial portion of the tumor. The latter was lined with a basal layer of ameloblasts, above which were the typical stellate cells arranged in a loose, spongy, syncytium-like manner. Between these cells and the basal layer of columnar cells there was a layer, two or three cells thick, which lay at right angles to the columnar layer. Papillary projections were sent out by the epithelial columns. Nests, pearls and tooth-budlike projections were rarely seen in this tumor. It was extremely interesting to note how widely the different tumors varied in this respect. In some these elements were numerous, in others few, and in still others scarce or even rare.

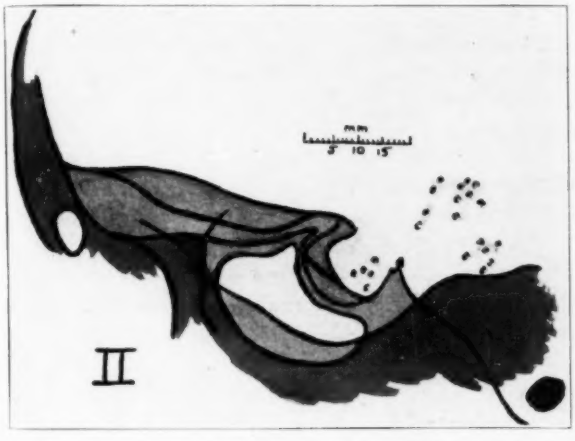

Fig. 7 (case 2).—A sketch of the roentgenogram (fig. 6), drawn to scale.

The stroma was a prominent part of the specimen. It was composed of a fibrillar tissue in which were scattered a good many cells. The structure of the stroma varied rather strikingly. In some regions it was composed of dense areas of fibrous tissue and fibroglia fibrils among which were scattered relatively few cells. In other areas it was a loose, almost myxomatous tissue. Cyst formation was not prominent in the sections studied, but there were numerous areas within the stroma that gave evidence of degeneration. These areas were composed of accumulations of cells that had swollen and undergone hydropic degeneration, probably later to coalesce and form an area of cystic degeneration. These swollen round cells within the stroma were numerous. They had a very small, darkly staining nucleus, which was often eccentric. Their nature was not clear, though they looked much like markedly swollen gitter cells.

Calcification was fairly abundant in the tumor. Most of it occurred in the stroma, but some was found within the epithelial columns. In the latter areas the calcification appeared to occur in a group of stellate cells. Calcium in the stroma was laid down as granules, or as concentric deposits of calcified material.

Spicules of calcium were found scattered through the tumor. No formation of bone was seen anywhere.

There were rather extensive areas of degeneration everywhere throughout the tumor, chiefly in the stroma. No glial tissue was found.

CASE 3.—*A year before admission to the hospital, in a boy, aged 9, convulsions, striking evidence of pressure, and endocrine disturbances developed, together with jocosity, visual hallucinations and tinnitus. He died after the bloodless removal of an encapsulated tumor from beneath the chiasm.*

Clinical History.—C. W., a boy, aged 9, was admitted to the neurosurgical service of the University Hospital on April 4, 1927. In the family there was no record of any endocrine disturbance. The patient had had a normal birth. He had scarlet fever, measles and otitis media between birth and February, 1927; otherwise, he had been well. In May, 1926, he was struck over the right eye with a ball of tar. Immediately after this, the father noticed a deviation of the eyes. He held the head inclined to the left and complained of pain in the neck. Then he began to have "nervous spells"; these were preceded by a cry and were followed by tremors and loss of muscular power. Sometimes the attacks were preceded by visual hallucinations. Since May, he had vomited frequently, his voice had become hoarse and his hearing affected, there was a tendency to sleepiness, and he had heard voices frequently which were not audible to others. Headache had been constant.

Neurologic Status.—There was no disturbance of the sensory or motor apparatus. There were no pathologic reflexes.

Endocrine Disturbances.—There were dwarfism, somnolence, adiposity, arrested development of the testes and prominent mammae (fig. 8).

Pressure Phenomena.—Headache and vomiting were present.

Ocular Disturbances.—There was secondary optic atrophy.

Associated Symptoms.—These symptoms consisted of jocosity, hoarseness of the voice, tinnitus, auditory and visual hallucinations and a diminished sense of smell and hearing.

Roentgen Observations.—The sella turcica measured 11 mm. in the anteroposterior plane and 9 mm. in depth. There were atrophy of the dorsum sellae, a calcified shadow over the sella turcica and convolutional atrophy.

Transfrontal Craniotomy.—On April 27, under ether anesthesia, Dr. F. C. Gram performed a transfrontal craniotomy, making the incision through the eyebrow, the middle of the forehead and above the hair line. The dura was tense. The anterior horn of the right ventricle was tapped, and from 40 to 50 cc. of clear fluid was evacuated. A dural incision was made above the sphenoid ridge. The frontal lobe was elevated and the tumor presented behind and below the chiasm between the optic tracts. As the right eye was amaurotic, the right optic nerve was cut to facilitate delivery of the tumor. The latter was readily mobilized and removed bloodlessly. Hemostasis was effected with one silver clip and a muscle graft. Pressure on the internal jugular veins by the anesthetist was not followed by hemorrhage. The dural incision was sutured, the flap replaced, and the scalp wounds closed with tier sutures. When the patient was removed from the table, his condition was excellent; the blood pressure was 90 systolic and 50 diastolic; the pulse rate was 115.

Postoperative Course.—The patient never regained consciousness. Within four hours after the operation, the pulse became extremely rapid, and the temperature

gradually rose. At 3 a. m. on the following day, the temperature was 106 F., and the pulse rate 156; he died at 3:05 a. m.

Postmortem Examination.—There was an inconsequential extradural hemorrhage, but beneath the dura there were no signs of hemorrhage or trauma to the frontal lobe. The pituitary body was grossly normal.

Histologic Report.—The tumor was a typical adamantinoma, with the epithelial columns invested with a layer of ameloblasts, the intermediate layer of cells lying at right angles to the ameloblasts, and the stellate cells in the center of the epithelial columns. The epithelial portion of the tumor was not very abundant. The stroma, on the other hand, was very profuse. It was a loose-meshed tissue in most areas, with very few cells within its meshes, and in other places it was dense and fibrillar. Often it had a myxomatous appearance. Degeneration was rather wide-

Fig. 8 (case 3).—Photograph of the patient at the age of 9 years. A year before admission, convulsions, striking evidence of pressure and endocrine disturbance plus jocosity, visual hallucinations and tinnitus developed. He died after the bloodless removal of an encapsulated tumor from beneath the chiasm. The pathologic diagnosis was adamantinoma of the craniopharyngeal duct.

spread. Calcium was seen in granules and in conglomerate areas of calcification. The latter was found within the epithelial columns, and also in the connective tissue stroma. Cysts were not very numerous, but epithelial nests were frequent.

CASE 4.—*A girl, aged 12, was under observation for a year with signs of increased intracranial pressure and atrophy of the dorsum sellae, headache, vomiting, choked disks, and arrest of growth and adiposity. Subtemporal decompression was performed with temporary relief. There were a recurrence of symptoms and sudden death two days after readmission. A large adamantinoma of the pituitary fossa was found at autopsy.*

Clinical History.—A. G., a girl, aged 12, was referred to the neurosurgical service of the University Hospital, by Dr. L. F. Appleman, on Sept. 15, 1926. The family history was without significance. The patient had had mumps, measles and chickenpox. For the ten months preceding admission the child complained of headaches, at first not severe and only once a month. On the day before admission it was discovered at the Wills Eye Hospital that she had choked disks, and she was referred to this service. Apart from projectile vomiting, of six months' duration, there had been no symptoms.

Neurologic Status.—With regard to the motor and sensory mechanism, examination gave entirely normal results. There were no signs suggesting a lesion either of the cerebral or of the cerebellar hemispheres.

Fig. 9 (case 4).—Photograph of the patient at the age of 12 years, with signs of intracranial pressure, atrophy of the dorsum sellae, headaches, vomiting, choked disk, arrest of growth and adiposity.

Endocrine Stigmas.—The child was short for her age. There was a tendency to adiposity, with a protuberant abdomen and prominent breasts (fig. 9). The basal metabolic rate was —4.

Roentgen Observations.—These showed convolutional atrophy without enlargement of the pituitary fossa (figs. 10 and 11).

Ocular Disturbances.—The fields were practically normal (fig. 12). Vision in the right eye was 6/21; in the left eye, 6/12. Papilledema in both eyes measured 5 diopters.

As there was no positive evidence of a pituitary lesion and there were highly choked disks, the indication for a subtemporal decompression seemed clear.

Subtemporal Decompression.—This operation, preceded by ventricular estimation (by Dr. F. C. Grant) was performed on September 24. Only 15 cc. of fluid was obtained from the left ventricle and 8 cc. from the right. Apparently there was

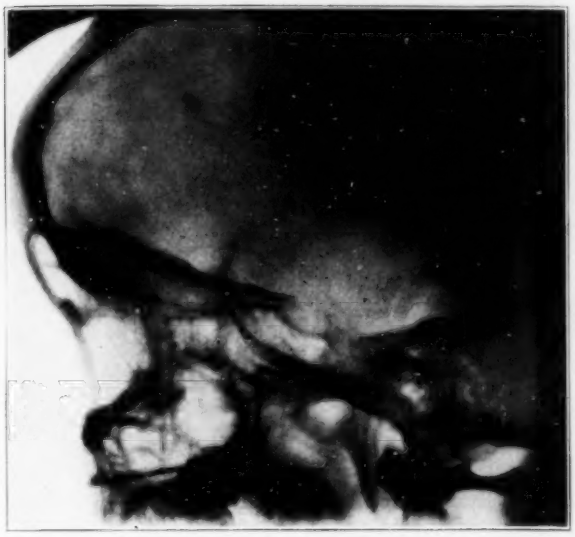

Fig. 10 (case 4).—Roentgenogram, showing moderate atrophy of the dorsum sellae, complete disappearance of the posterior clinoid processes with no enlargement of the pituitary fossa; convolutional atrophy.

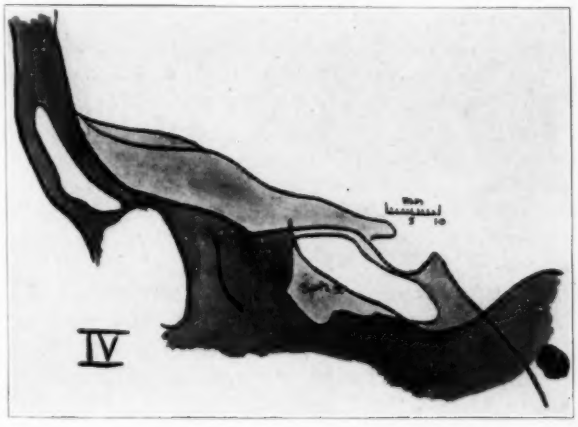

Fig. 11 (case 4).—A sketch of the roentgenogram (fig. 10), drawn to scale.

no hydrocephalus. Accordingly, the operator did a subtemporal decompression in the usual way, and as the ventricular tap had relieved entirely the intracranial pressure it was not difficult to approximate the temporal muscle and aponeurosis. Before this, a brain cannula was plunged into the right temporal lobe and forward into the right frontal lobe without encountering any resistance suggestive of a tumor.

Course.—Convalescence was uneventful, and the patient was discharged on October 4. At that time the papilledema measured 4 diopters in the right and 3.5 diopters in the left eye.

Second Admission.—Eight months had elapsed since the first admission (June 5, 1927). Up to ten days before the second admission, the child had had only mild headaches, but for the last ten days they had become more frequent and more severe.

The following changes since the first admission were noted: subsiding choked disk; secondary optic atrophy; bitemporal upper quadrantopia for colors; a drop

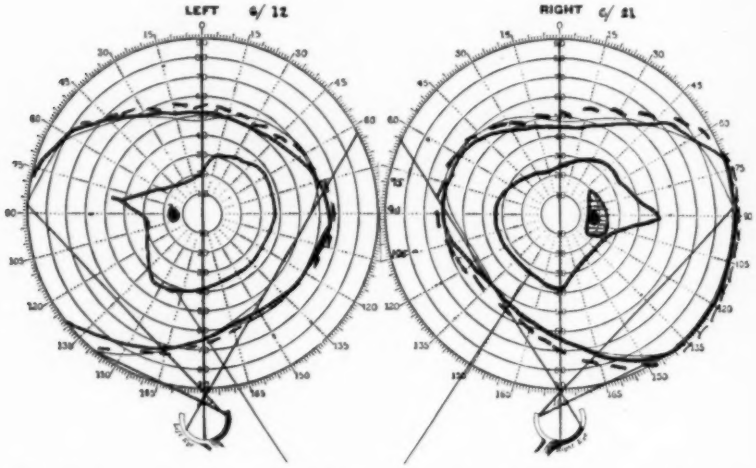

Fig. 12 (case 4).—Irregular fields nine months after subtemporal decompression, showing normal form fields, bitemporal cutting of the red fields in both eyes. Vision in the left eye was 6/12; in the right, 6/21. The solid line indicates 1 degree red, 1 degree white; the dotted line, 2 degrees white.

in the basal metabolic rate from —4 to —13; the presence of a hernia at the site of the decompression.

At a conference, a tumor of the pineal gland was eliminated from consideration, and the preponderance of evidence seemed to point to a suprasellar (extrapituitary) or pituitary lesion.

The patient was discharged on July 2, after arrangements had been made for readmission preliminary to operation.

Third Admission.—After a siege of more severe headache and frequent vomiting, the patient returned (September 9). During the preceding three months, vision had become blurred.

Magnesium sulphate dehydration and restricted fluids were ordered. At 8:40 p. m., on September 10, the patient was found dead in bed. Death was probably due to medullary compression.

Pathologic Report.—Gross Description: Necropsy revealed a tumor, measuring 3.5 by 5.5 cm., occupying a large area at the base of the brain, extending from the anterior perforated space to the anterior margin of the pons. It lay on the optic chiasm, and from beneath it emerged the optic nerves. It had compressed the undersurface of the frontal lobe, and apparently entirely obliterated the pituitary body. It had grown upward to fill the third ventricle. The tumor consisted of two portions, an upper cystic portion filled with a coagulated green substance of the consistency of a gel, and a lower solid portion composed of a loose, crumbly material. The upper portion lay in the third ventricle, compressing the pineal body. The lower portion occupied the interpeduncular space (fig. 13).

Fig. 13 (case 4).—Note the large tumor at the base of the brain. It extended into the third ventricle.

Microscopic Description: The tumor was composed of cells arranged in a sort of epithelial tree, with numerous offshoots and branches. The cells were arranged in papillary formation, interdigitating and connected with one another like the branches of a tree, or like a system of complexly interlocking canals. These ran in numerous directions, and were therefore cut at many angles. The thickness of each cord or papilla varied considerably from a thin projection, about three or four cell layers thick, to a stout projection with many cell layers. Often the papillae had been cut in cross-section, and appeared as round cellular masses, the nature of which will be described.

Among the interlacing groups of cells was a stroma composed of a loose tissue and containing blood vessels in moderate amounts. This stroma was composed of fibrous tissue chiefly and contained relatively few cells.

The epithelial columns possessed a well defined basement membrane. Lying close to this was a basal layer composed of columnar cells, which lined the papillae on all sides. These were arranged usually in a single layer, but sometimes were seen in multilayered formation. This was probably due to the angle of cutting the papillae, which probably lay in several planes during the length of their course. The basal layer of ameloblasts was composed of columnar cells with oval nuclei, though some tended to be thin, others carrot-shaped, and still others crescentic. The nuclei possessed well defined membranes, were vesicular, contained a few scattered chromatin granules, and in most instances showed no nucleolus. The cell membrane was not well defined in the basilar layer. Immediately above the latter lay cells that usually ran at right angles to the ameloblasts. Their shape varied from thin, spindle-like elements to more plump forms with characteristics similar to the cells of the basal layer. Above these cells lay what are termed the stellate cells. These constituted the pulp of the epithelial columns. They consisted of rather flat cells with large roundish nuclei, possessing a well defined membrane, extremely little chromatin and a fairly well defined cell membrane, which was so shaped as to give the cells a stellate or even a squamous appearance. The cytoplasm of these cells stained a light pink, but was often vacuolated and undergoing hydropic degeneration. These cells were arranged usually in a very loose fashion, so much so that the tissue had a myxomatous appearance in many places.

Within the inner parts of the epithelial cords were often seen nests of cells that were arranged in concentric fashion. In their midst there appeared to be a small blood vessel. Often there were many such cell nests within a column.

Cysts were numerous everywhere throughout the epithelial tree. They varied in size from small to relatively large.

Calcification was seen both in the epithelial portions of the tumor and in the stroma. It was found as small calcified granules, or collections of calcified granules, which sometimes attained a large size. Calcification could be seen starting in some of the cell nests. Numerous small homogeneous and granular areas were found in the stroma. Their nature was not clear, though they represented probably a hyaline change in groups of collagen fibrils, with probably eventual calcification. These were sometimes present in large groups. Large areas of degeneration were present in the stroma. Large cysts were also found here. They were filled with a colloid material.

Case 5.—*A boy, aged 12, complained of headache, vomiting and failing vision. There were practically no pituitary stigmas; sella changes were not marked; vision on the left was 1/60, on the right, 2/60. A large cystic tumor, occupying the sella turcica and removed almost in toto, proved to be an adamantinoma. The patient was discharged improved, but died at home ten months later. Autopsy was not permitted.*

Clinical History.—T. C., a boy, aged 12, was referred from the Wills Eye Hospital, by Dr. Smith, to the neurosurgical service of the University Hospital, on Dec. 1, 1923. His mother was dead; the father and four siblings were living and well. The patient had had measles and otitis media. Until eight months before admission, he had been perfectly well. Then he noticed that his vision was not good; he had to hold a page nearer to the eyes than formerly. Simultaneously he began to have severe frontal and bitemporal headache, which was often accompanied by projectile vomiting. These attacks occurred at first every three or

four days, then more frequently, though he had had none for three weeks. Meanwhile, vision had become progressively worse until he could see only large type held near the eye; vision was better with the right than with the left eye.

Neurologic Status.—The patient appeared to be a healthy normal boy without any physical stigmas. There was no evidence of any disturbance in the function of the cerebral or cereballar lobes. Sensation, motion, reflexes, gait, station, equilibrium, sense of position and stereognostic sense were undisturbed.

Ocular Disturbance.—Vision in the right eye was 2/60; in the left, 1/60. The fields showed on the left a nasal hemianopia; on the right, barrel vision. There were: postpapillitic atrophy and loss of convergence (fig. 14).

Pituitary Stigma.—None was found. The basal metabolic rate was —34.

Roentgen Observations.—There was some enlargement of the pituitary fossa with undermining of the posterior clinoid processes. The picture suggested an extrasellar growth (figs. 15 and 16).

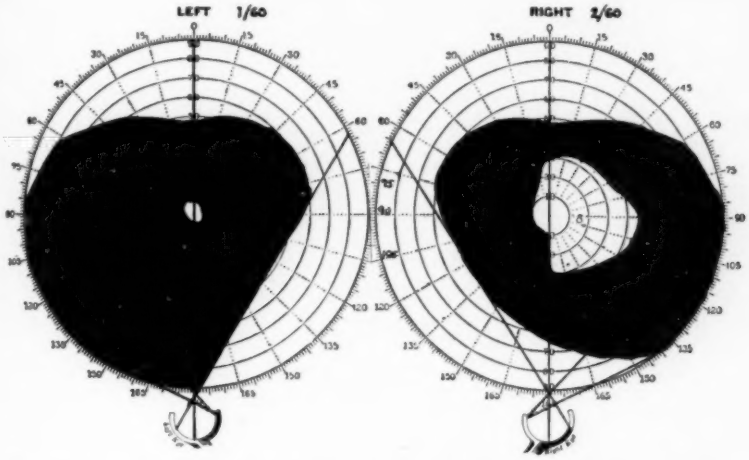

Fig. 14 (case 5).—The fields before operation, showing nasal hemianopia with concentric contraction in the remaining field of the right eye, and contraction to central vision in the left eye. Vision in the left eye was 1/60; in the right, 2/60.

Laboratory Tests.—A Wassermann test of the blood and spinal fluid showed negative results. The cerebrospinal pressure was 113 mm.

Diagnosis.—At a conference, various opinions were expressed as to the localization and character of the lesion. Because of this uncertainty and because the patient had improved during the past few days, operation was deferred.

Second Admission.—On December 20, the condition in every way was unchanged, excepting that he was constantly drowsy and slept almost all day. The vision, visual field and roentgen observations were as previously recorded. The overcoming somnolence and stationary vision seemed to call for exploration.

Transfrontal Craniotomy (left).—On Jan. 18, 1924, under ether anesthesia, this operation resulted in exposure and removal of a pituitary cyst. When the flap was reflected, the dura was found under considerable tension. Attempted

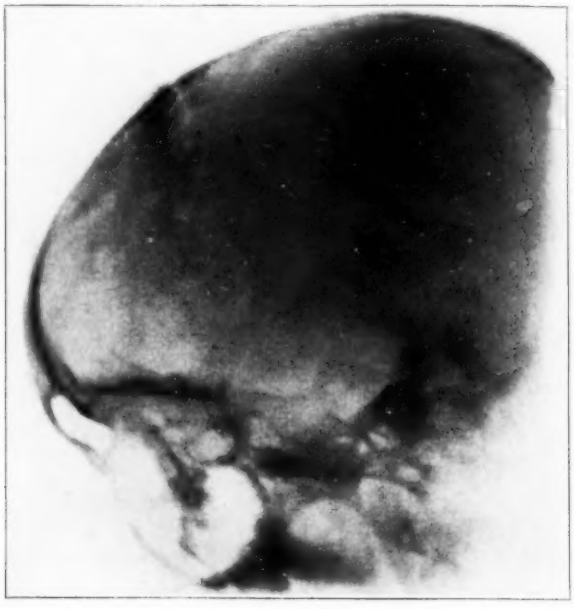

Fig. 15 (case 5).—Roentgenogram, showing marked atrophy of the dorsum sellae, complete disappearance of the posterior clinoid processes, and moderate enlargement of the pituitary fossa.

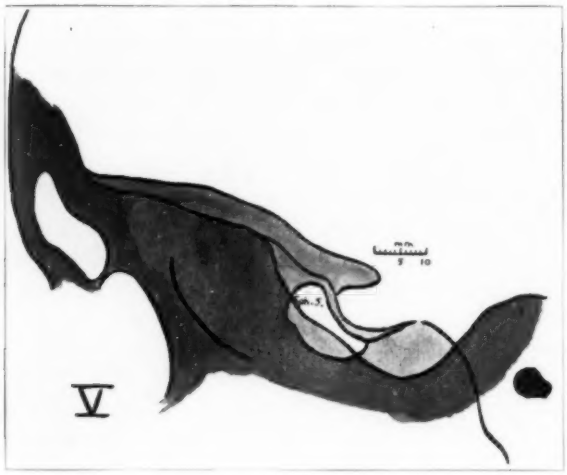

Fig. 16 (case 5).—A sketch of the roentgenogram (fig. 15), drawn to scale.

puncture of the anterior horn of the left ventricle failed. However, when the dura was incised so much fluid escaped that the operator was able to elevate the frontal lobe without undue pressure. Soon what seemed to be a cyst wall appeared just to the left of the optic foramen. In a moment the cyst wall ruptured and a yellowish puslike liquid escaped. Practically the entire wall of the cyst, which seemed to fill the entire sella, was excised until nothing remained except a small bit of tissue that seemed to terminate at the midline in a stalk. There was no bleeding. The manipulations were carried on without difficulty, yet there was a marked fall in blood pressure, and for possibly two hours it was not necessary to give any ether. Under moderate stimulation the patient reacted satisfactorily, and preparations for a blood transfusion were abandoned. The wound was closed with tubular drainage.

Postoperative Course.—There were no untoward symptoms in the immediate convalescence, and the patient was discharged on Feb. 13, 1924.

On June 2, 1924, the patient reported to the follow-up clinic for review. He was completely amaurotic; the reflexes were normal; the flap was bulging; he was excessively fond of candy, and he was drowsy most of the time. His appearance suggested an early Fröhlich syndrome.

On Sept. 27, 1924, the mother wrote that "Thomas could see again but his memory was poor and he always wanted to sleep."

On Oct. 14, 1924, the patient died at home. No autopsy was performed.

Histologic Report.—The tumor was a typical adamantinoma. The fragments submitted for study showed a tumor with the typical interlacing epithelial columns and the basal layer of ameloblasts or enameloblasts. These were on the whole very few, and constituted a relatively small part of the tumor.

Hemorrhage was abundant in the stroma. Cysts were not prominent. The stroma was abundant, and in many areas was quite cellular. Throughout the tumor were large areas that seemed to be undergoing hyalinization. In some of them calcium had already been deposited in a granular form. These areas were composed of prickle-like cells, which were seen only in outline, and took a homogeneous pink stain with eosin. The change was degenerative. Calcification was rather abundant all through the tumor and was seen particularly in the stroma. Epithelial pearls were found in the columns of cells.

CASE 6.—*A boy, aged 15, stunted in growth, blind in one eye with barrel vision in the other, and with signs of pituitary dysfunction, had a large cystic duct tumor. The tumor was removed; the patient survived the operation for twenty months.*

Clinical History.—L. F., a boy, aged 15, was admitted to the neurosurgical service of the University Hospital on Nov. 9, 1928. In the spring, 1928, his vision had begun to fail. At the time of admission, the vision of the left eye was practically lost, and in the right eye vision was beginning to be affected. He had had occasional frontal and occipital headaches, at times severe, but there were no other subjective complaints.

Neurologic Status.—There was a residual paralysis of the lower extremities (infantile paralysis).

Pituitary Stigmas.—Dwarfism was apparent. There was a delayed development of the external sexual characteristics. The basal metabolic rate was —15.

Ocular Manifestations.—The left eye was blind; vision in the right eye was reduced to light perception only. There was a grayish discoloration of both disks. The fields showed the left eye to be blind; the right eye had concentric contraction (barrel vision) (fig. 17).

Roentgen Observations.—There was a marked enlargement, vertically and anteroposteriorly, of the pituitary fossa. Pansinusitis was present, except in the sphenoid sinus (figs. 18 and 19).

Diagnosis.—Because of the manifest enlargement of the pituitary fossa, the arrest of growth and sexual development, and of the patient's age, a preoperative diagnosis of a Rathke pouch tumor was made.

Transfrontal Craniotomy.—On November 9, a flap was reflected on the right side because the patient was blind in the left eye, and there was hope only of restoring vision in the right eye. The dura was moderately tense, but an attempt to tap the anterior horn of the ventricle failed. A horizontal incision was made in the dura and the frontal lobe was elevated, following the line of the greater wing of the sphenoid bone. Soon a lesion of large dimensions was seen presenting in front of the chiasm.

The lesion proved to be chiefly cystic, and with an aspirating syringe 17 cc. of a yellowish-red, crystal-laden fluid was evacuated. The capsule, then collapsed,

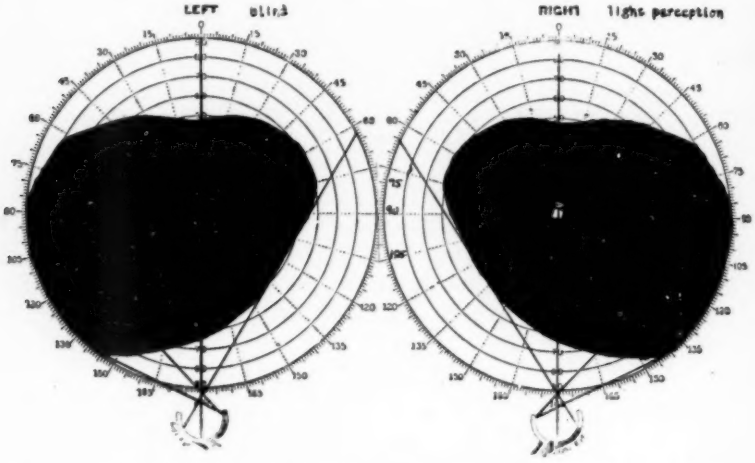

Fig. 17 (case 6).—Fields just before operation. The left eye was blind. The right eye had central vision, with only light perception.

was incised, and a large amount of solid tissue was removed with a curet. With a pair of long handled curved scissors, a considerable portion of the capsule on the right side was removed. The lesion was so extensive that the portion adjacent to the left optic nerve could not be readily exposed. When the operation was concluded, the right optic nerve was entirely free, and a cavity the size of an English walnut remained. Hemostasis was effected with tampons of epinephrine, the cavity swabbed with iodine, and the wound closed without drainage.

Postoperative Course.—Convalescence was uneventful. A week after the operation the patient could count fingers with the right eye, and on the ninth day vision in that eye was 6/9 (before operation there was only light perception). The fields had widened considerably (fig. 20). On November 28, nineteen days after the operation, the patient was discharged. During the course of the next two years the patient was seen from time to time. Signs of pressure recurred; the patient became somnolent, he gained 10 pounds (4.5 Kg.); he had attacks of

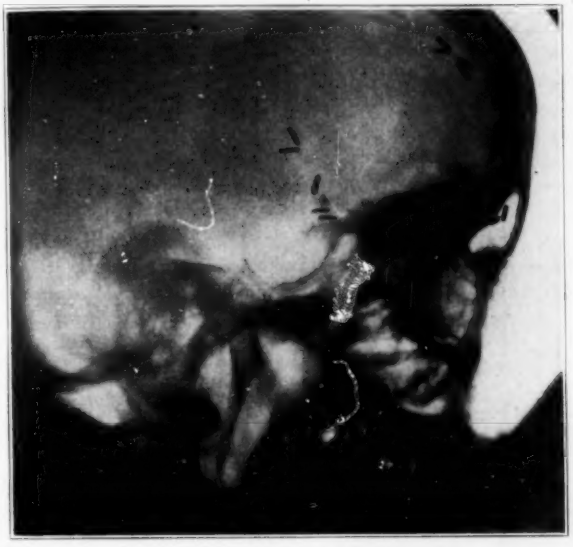

Fig. 18 (case 6).—Roentgenogram, showing moderate atrophy of the dorsum sellae and marked enlargement of the pituitary fossa.

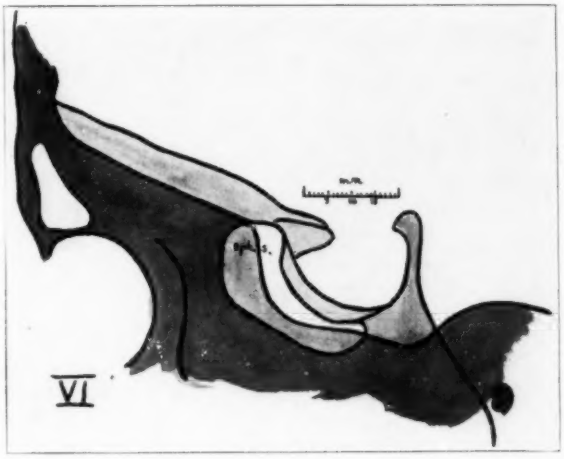

Fig. 19 (case 6).—A sketch of the roentgenogram (fig. 18), drawn to scale.

headache and vomiting, and the metabolic rate was —46. He died on July 8, 1930, twenty months after the transfrontal craniotomy.

Histologic Report.—There was a thick fibrous capsule which formed the wall of the tumor. This capsule was composed of dense bands of fibrous tissue which lay in parallel rows. Penetrating among them were tumor cells that could not be identified.

The tumor itself was composed of the typical epithelial columns of cells, interlacing and anastomosing. These columns possessed a basilar layer of columnar cells, said to be ameloblasts. They were sometimes stratified, but usually lay in a single cell layer. Their cell membrane was poorly defined, and their nucleus oval and rather darkly staining. In none of the cells did one see the granules that characterize the normal enamel-forming cells. Lying above the basilar layer one sometimes saw a rudimentary stratum intermedium, and above this the stellate layer, which filled the innermost part of the epithelial columns. The latter

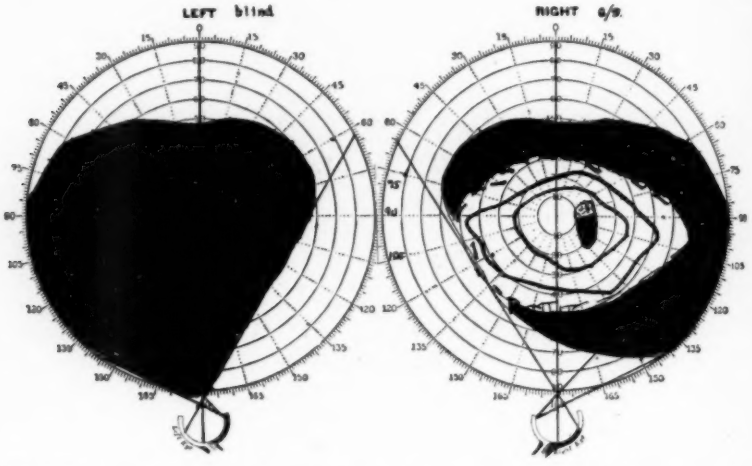

Fig. 20 (case 6).—Fields fourteen days after operation. The left eye was blind. The right eye showed a marked expansion of the field.

cells were arranged rather loosely, and were in a sort of syncytial arrangement; often the cells of the stellate layer were round, with a well defined cell membrane, but the cytoplasm had disappeared. Many of them were degenerated. Blood vessels were not seen in the epithelial columns. Tooth-budlike projections were commonly found budding from the columns. Epithelial nests were frequently found in the columns. Degenerative cysts were frequently seen both in the columns and in the stroma. Here and there were cells of the stellate layer. Calcification was frequent.

Hydropic degeneration of the cells was seen in some areas. This was so marked that the cells were markedly swollen and filled to the brim with droplets of varying size. Their nuclei were small and pyknotic, and most of them were probably dead.

The stroma was undergoing rather extensive degeneration in some areas. Here it had a myxomatous appearance. There was nothing left to it in some places except strands of fibers, among which were cysts and areas of hydropic degeneration.

Hemorrhage was common in some areas of the tumor.

CASE 7.—*After six years of arrested growth, a boy, aged 15, was admitted with signs of pituitary cachexia. He died sixteen months after the partial removal of a large calcified cystic tumor.*[5]

Clinical History.—J. B. T., a boy, aged 15, was referred to the neurosurgical clinic of the University Hospital by Dr. William G. Spiller and Dr. J. W. McConnell, on Dec. 17, 1926. The family history was unessential. Dentition and other features of early life appeared to have been normal. He had had many of the diseases of childhood.

Up to the age of 9, growth had been undisturbed. From the ninth to the thirteenth year, he was apparently well, though growth had been arrested. At this time he began to have occipital headaches, attacks of dizziness and later projectile vomiting, somnolence and polyuria. Latterly, he had found it difficult to keep up with his classes.

Physical Examination.—The patient was extremely restless, with the facies of an adult; he was emaciated, and his skin was dry and rough. The Wassermann reaction of the blood was 2+, and of the spinal fluid, 4+.

Fig. 21 (case 7).—Roentgenogram, showing only slight atrophy of the dorsum sellae, no enlargement of the pituitary fossa, and marked evidence of calcification behind the dorsum sellae.

Pituitary Stigmas.—The external genitalia were underdeveloped. There was no pubic or axillary hair. In 1925, he had weighed 96 pounds (43.5 Kg.); at the time of writing this article, he weighed 70 pounds (31.8 Kg.).

Roentgen Observations.—An abnormal shadow, circular, 1 inch (2.5 cm.) in diameter, was present immediately above the posterior clinoid processes, more than half of it to the left of the median line.

Ocular Manifestations.—There was bilateral secondary optic atrophy; the left pupil was larger than the right; the fields were somewhat contracted (figs. 21 and 22).

5. As this case was reported in detail at a meeting of the American Neurological Association, in May, 1928, only a brief abstract will be included in this series (Frazier, C. H.: Pituitary Cachexia, Arch. Neurol. & Psychiat. **21**:1 [Jan.] 1929).

Transfrontal Craniotomy (Right).—The first stage was performed on Dec. 19, 1925. The operation was completed at the second stage on December 24, under light ether anesthesia; the flap was reflected; the suprasellar region was readily exposed, and at once a cyst with its bluish coloration was seen behind the chiasm. When the fluid contents were evacuated, a partly calcified tumor remained. As much of this as presented between the optic tracts and chiasm was removed. A hard calcified mass at the base of the tumor, which was responsible for the shadow seen in the roentgenogram, could not be detached. Hemostasis and wound closure were made without drainage.

Postoperative Course.—Recovery occurred, and the patient was discharged from the hospital on Jan. 14, 1926. There were many interesting features in the

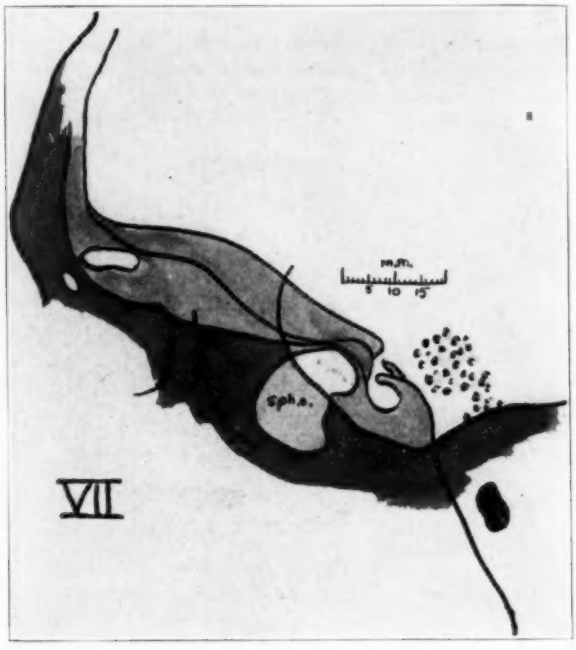

Fig. 22 (case 7).—A sketch of the roentgenogram (fig. 21), drawn to scale.

period following the operation. These will be found in the original report. Suffice it to say that he died in April, 1927, having survived the operation for sixteen months.

Histologic Report.—There was a very small portion of tumor tissue in the specimen taken for biopsy. It appeared to be an adamantinoma, with a typical basilar columnar layer and some evidence of a stellate layer. There were much hemorrhage and degeneration in the tissue. The stroma was very abundant.

CASE 8.—*Always underdeveloped, the patient was admitted in his sixteenth year. Somnolence, headache, ptosis (left) and convulsions were the outstanding symptoms. At operation a large cystic tumor was revealed.*

Clinical History.—C. M., a boy, aged 16, was admitted to the neurosurgical service of the University Hospital on June 18, 1930. His father was

subject to convulsions; his mother was living and well; there were no brothers or sisters. The patient had had diphtheria at 9, whooping cough at 6 and measles at 4. He had always been underdeveloped. Three years previously, he became backward in school, refused to study, complained of headache and was sleepy most of the time. One year before admission, vision began to fail. In April, 1930, he had 3 convulsions, in each of which he lost consciousness.

Neurologic Status.—Though 16 years of age, the child's stature was that of a boy of 10 years. There were no neurologic signs other than ptosis of the left eyelid. There were no pituitary stigmas other than arrested growth, and at times somnolence.

Ocular Disturbance.—Vision in the right eye was 6/60; in the left eye, 6/30. The fields showed bitemporal hemianopia (fig. 24). Primary optic atrophy was present.

Fig. 23 (case 8).—A photograph of the patient at the age of 16 years. He had always been underdeveloped and was three years behind in his studies. He complained of headache and sleepiness most of the time; one year previously his vision began to fail. There were convolutional atrophy, a shadow of a calcified tumor and complete atrophy of the dorsum sellae, and the floor of the sella was markedly depressed. There was bitemporal hemianopia. Vision in the right eye was 6/60; in the left, 6/30. The pathologic diagnosis was adamantinoma of the craniopharyngeal duct.

Roentgen Observations.—There were convolutional atrophy, with widening of the sutures; the shadow of a calcified tumor, and almost complete atrophy of the dorsum sellae and the posterior clinoid processes. The floor of the sella was markedly depressed (figs. 25 and 26).

Metabolism.—The basal metabolic rate was — 37.

Transfrontal Craniotomy (Right).—On June 19, 1930, the operator removed two thirds of an enormous sellar tumor. Tribromethanol ether anesthesia was used. The wound was closed without drainage.

As vision was worse on the right side, it was decided to approach from the right rather than from the left side. A flap of the scalp was reflected forward and a bone flap temporalward. An attempt to tap the anterior horn of the right ventricle failed. A considerable amount of fluid was evacuated from the subarachnoid space. The frontal lobe was elevated after an incision in the dura parallel with the margin of the anterior margin of the bone defect. Soon the lesion was exposed, and from 40 to 50 cc. of a yellowish fluid was evacuated. (The fluid was reported by the laboratory as containing a number of cells resembling mononuclear leukocytes or endothelial cells, some of which contained a large number of highly refractile granules.) The capsule of the tumor was dissected from the anterior wall of the sella turcica and from the right optic

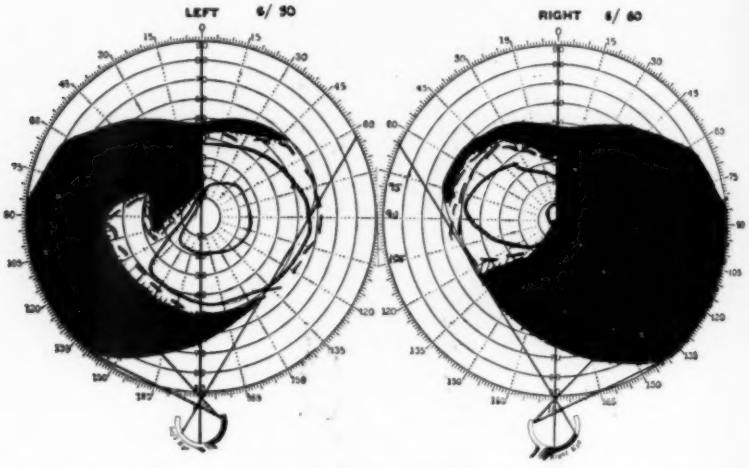

Fig. 24 (case 8).—Fields, showing bitemporal hemianopia with partial obliteration of the nasal field in the right eye and incomplete hemianopia in the left eye. Vision in the right eye was 6/60; in the left, 6/30.

nerve, which was displaced far to the right. When the capsule was opened, the major portion of its contents was removed with a curet. As much of the capsule as presented on the lateral and anterior aspects was excised. The tumor was of such large dimensions that it was not thought prudent to attempt at this sitting to mobilize or remove the left portion of the capsule. The operation was concluded by suturing the dura, replacing the flap and closing the scalp wound.

Postoperative Course.—The immediate result was recovery. For three days after the operation, the patient was somnolent and refused nourishment. He was fed through a nasal tube. He was given thyroid extract. On the sixth day he was out of bed, and from that time until discharge, on June 30, convalescence was uninterrupted. On discharge, the vision and visual fields were the same as before the operation.

Early in August, 1930, the patient returned to the hospital for a second stage operation, but at the last minute the mother refused to give consent, and he was discharged.

Fig. 25 (case 8).—Roentgenogram, showing marked atrophy of the dorsum sellae, complete disappearance of the posterior clinoid processes, with marked enlargement of the pituitary fossa, and evidence of calcification above the pituitary fossa; convolutional atrophy.

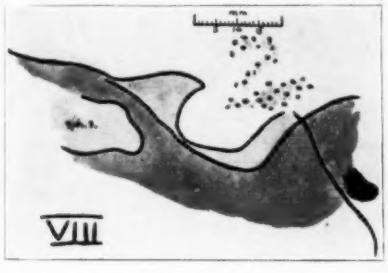

Fig. 26 (case 8).—A sketch of the roentgenogram (fig. 26), drawn to scale.

On August 26, the patient was readmitted in a state of stupor. Dr. Grant removed 20 cc. of a dark brown fluid from the cyst without any relief. Dehydrating agents seemed of no avail, and the patient lingered in a state of unconsciousness for eight weeks and died on October 6.

Pathologic Report.—Gross Description: Necropsy revealed a large tumor at the base of the brain, which had eroded a large part of the base of the skull. It seemed to be a part of the sella. The pituitary body was not seen. It had been destroyed apparently by the tumor. The tumor extended from the middle of the orbital surfaces of the frontal lobes to the anterior surface of the pons. It was probably primary within the sella, and had an enormous extrasellar extension. The tumor was markedly calcified and filled with a degenerated material (fig. 27).

Microscopic Description: The tumor was a typical adamantinoma. It was composed of a thick, firm fibrous capsule which was made up of dense bands of

Fig. 27 (case 8).—The tumor extends from the frontal lobes to the pons. It is almost completely calcified and cystic. The middle cerebrals have been compressed with resultant softening of the cerebrum on both sides.

fibers lying in parallel rows. Beneath this was a mass of degenerated substance. It was surprising to find how much of the tumor was degenerated tissue, and how little was actual tumor tissue. The latter was composed of typical interlacing columns of epithelial cells, forming a tree. There was a basilar layer of columnar cells, the so-called ameloblasts. Above these was sometimes seen the stratum intermedium, and above this the stellate layer of cells. The basilar layer was often stratified. This was so pronounced a feature of some columns in the tumor that it could hardly be attributed to technical effects. We believe that the

basilar layer is frequently stratified, in contrast to the state of affairs in the enamel organ in which it is a single cell layer. The stellate layer was of interest. It was a loose layer of anastomosing cells with a stellate appearance, but often the cells were compressed and tended to lose this characteristic shape. Sometimes they were round. Epithelial nests were common. Blood vessels were seen within the stellate layer of the epithelial columns. Small cysts were found in the columns, beginning apparently as degenerated areas in the cell nests, and extending to cause a complete degeneration and cyst formation within these nests. Other types of degeneration, which sometimes went on to calcification, were present within the cells of the stellate layer. Here one saw groups of cells more or less concentrically arranged which stained a homogeneous pink with eosin. Sometimes calcium granules were seen in these areas. Calcification was widespread everywhere, and large degenerated portions of the tumor were frequently seen.

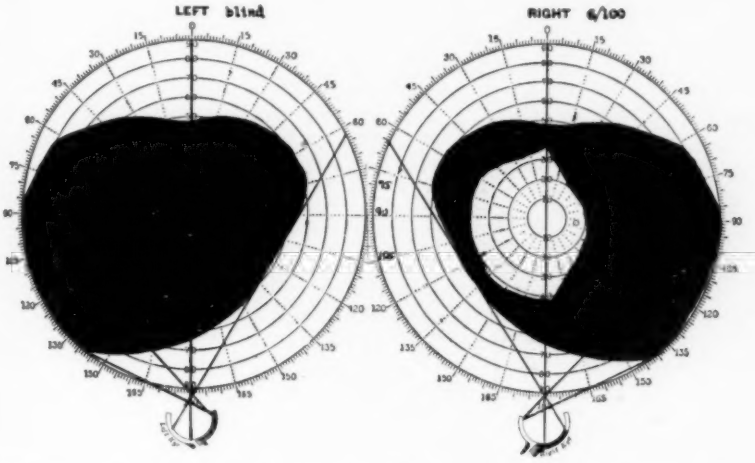

Fig. 28 (case 9).—The left eye was blind. The right eye showed temporal hemianopia; vision, 6/100.

CASE 9.—*After arrest of growth and vomiting for seven years, the patient came under observation in his seventeenth year, blind in one eye and with evidences of infantilism. He survived the removal of a large calcified cyst for eight years.*

Clinical History.—J. E., a boy, aged 17, was referred to the neurosurgical service of the University Hospital on Jan. 18, 1921, by Dr. William G. Spiller. He had had a cerebral injury at the age of 10, with a period of unconsciousness lasting two hours. Although 17 years of age, there had been no growth since the age of 10. The mother gave a positive Wassermann reaction and had had several miscarriages. When about 10 years of age, the patient had had attacks of vomiting every six weeks. These grew less frequent and finally stopped altogether. In their place he began to have headaches, lasting a day or so. His eyesight is said to have been imperfect since birth, and at the time of admission he was blind in the left eye, with loss of the temporal field in the right. His intelligence was only fair; lately he had become irritable.

Examination.—The patient had the stature of a boy aged 10.

Pituitary Stigmas.—There were dwarfism, undescended testes, infantilism of the external genitalia and no pubic hair.

Cerebrospinal Fluid.—The pressure was 260 mm.; globulin was present; the Wassermann reaction of the spinal fluid and of the blood was negative.

Ocular Disturbances.—The left eye was blind; vision in the right eye was 6/100. The fields of the right eye showed temporal hemianopia. There were an internal strabismus and a nystagmus on looking to the left; also advanced atrophy of both disks and paralysis of the right external rectus (fig. 28).

Roentgen Observations.—There was marked deformity of the sella turcica with a linear shadow suggesting the calcified wall of a cyst. Convolutional markings were evident (figs. 29 and 30).

Transfrontal Craniotomy (left).—On January 20, under ether anesthesia, a flap was reflected. When the dura was exposed, much less tension was found than

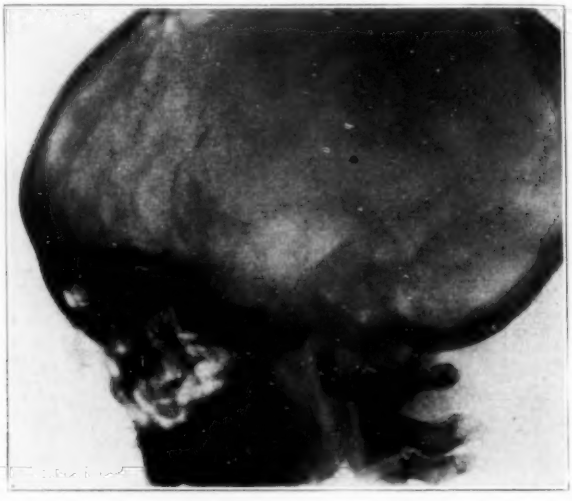

Fig. 29 (case 9).—Roentgenogram, showing marked atrophy of the dorsum sellae, complete disappearance of the posterior clinoid processes, with marked enlargement of the pituitary fossa, a calcified rim outlining the wall of the cyst, and evidence of calcification in the anterior portion of the tumor itself; convolutional atrophy.

was expected, judging from the convolutional markings in the roentgenogram. The anterior horn of the left lateral ventrical was tapped, but only 3 cc. of fluid was recovered. The left frontal lobe was elevated and the lesion exposed, mostly on the left but extending a little to the right, a little behind and on a level with the greater wing of the sphenoid bone. The lesion seemed to have the consistency of a solid tumor, but on the introduction of an exploratory needle, 80 cc. of a dark fluid was evacuated. Even after the aspiration of fluid the wall of the cyst did not collapse. The wall of the cyst was 1 cm. thick and calcified. Its removal could be effected only with rongeur forceps. The calcified wall accounted for the linear shadow seen with the x-rays. The cavity was illuminated, and one could see crustations on the wall and on the floor, and areas of erosion of the base of the skull. What remained of the wall was swabbed with a 3 per cent solution

of tincture of iodine and the wound closed. At the conclusion of the operation the patient was conscious; the pulse rate was 150 and of fair volume. The patient was given 500 cc. of citrated blood.

Postoperative Course.—The patient was placed on pituitary and thyroid extracts after the operation. He made an uneventful recovery and was discharged on Jan. 31, 1921. He was readmitted to the hospital on Feb. 22, 1921 because of recurring headaches. During this period of hospitalization he had only one attack of vomiting, and was more alert than at the previous admission, but his condition otherwise had not changed. The temporal hemianopia of the right eye and visual acuity had not improved.

For the first two years after the operation, the improvement was striking. His mother wrote that he had grown 3 inches (7.6 cm.) and weighed 90 pounds (40.8 Kg.). He could read and write; his memory was remarkably improved; he was alert and participated in boys' games, which he had never done before.

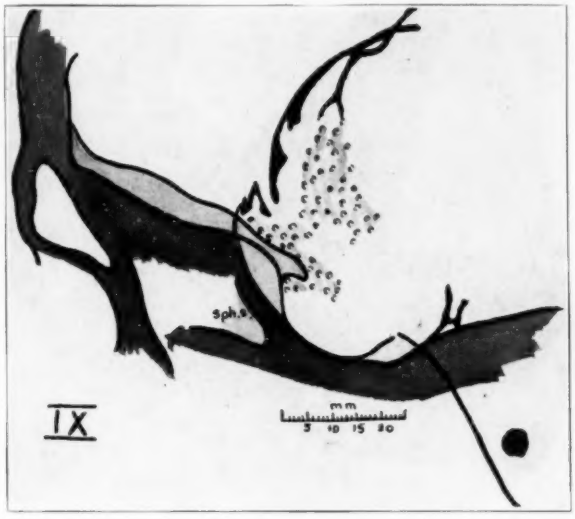

Fig. 30 (case 9).—A sketch of the roentgenogram (fig. 29), drawn to scale.

In a follow-up report, in 1927, it was stated that the condition had changed little except for the fact that vision was failing again. In January, 1929, eight years after the operation, he continued in a state of unconsciousness for two weeks and died.

Pathologic Diagnosis.—The specimens removed at operation were hardened in formaldehyde. Microscopic examination showed a dense fibrous tissue stroma in which there was a diffuse calcification. The classification of this case as one of adamantinoma was based solely on the age of the patient and the presence of a calcified cyst.

CASE 10.—*A man, in his twenty-fifth year, had had headache, dimness of vision and tinnitus for five months. There were no endocrine symptoms, save somnolence, and the ventriculographic evidence suggested a tumor of the third ventricle. He died after the first stage of an exploratory craniotomy.*

Clinical History.—J. C., a man, aged 25, was referred to the neurosurgical service of the University Hospital by Dr. Glendon R. Lewis, on Dec.

19, 1926. The family history was essentially unimportant. The patient had had scarlet fever and measles. In August, 1926, he began to complain of headaches and dimness of vision and later of ringing in the ears. Soon he had daily attacks of projectile vomiting. He slept a great part of the day, and within the week before admission he "began to act queerly" and his memory had become defective.

Neurologic Status.—Cooperation and attention were poor; the gait was ataxic; the Romberg test was positive; there were purposeless and almost continuous movements of the hands. The patellar reflexes were exaggerated; no pathologic reflexes were observed. The Bárány reactions excluded a lesion of the posterior fossa.

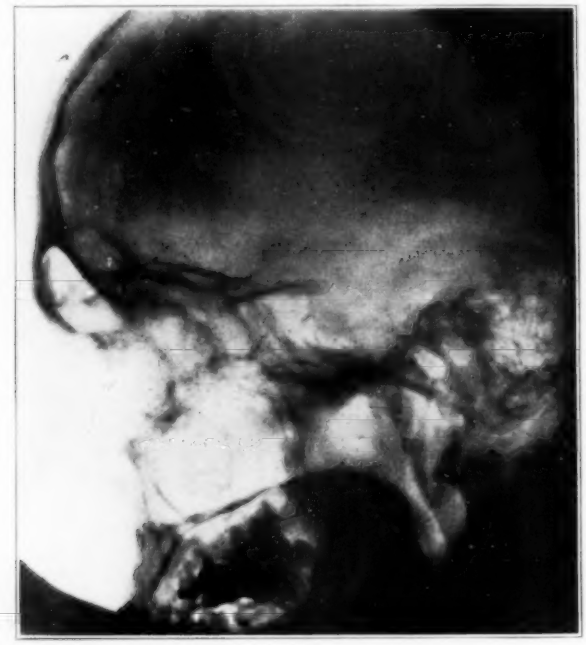

Fig. 31 (case 10).—Roentgenogram, showing moderate atrophy of the dorsum sellae, complete disappearance of the posterior clinoid processes and moderate enlargement of the pituitary fossa.

Laboratory Tests.—The pressure of the cerebrospinal fluid was normal; the globulin was considerably increased, and the sugar was increased. The Wassermann reaction of the blood was negative. The basal metabolic rate was + 5.

Pituitary Stigmas.—None was found.

Ocular Manifestations.—Vision in both eyes was 6/15. Papilledema was present in both eyes and measured 4 diopters. The fields were full.

Roentgen Observations.—There was atrophy of the dorsum sellae and the posterior clinoid processes, with some depression of the sellar floor. The picture suggested a suprasellar lesion (figs. 31 and 32).

Ventriculogram.—This revealed bilateral symmetrical hydrocephalus with complete obliteration of the third ventricle.

Exploratory Craniotomy.—The first stage was performed on December 31. In the absence of all evidence of a primary intrasellar lesion and with the ventricular evidence of complete obliteration of the third ventricle, a preoperative diagnosis of "third ventricle tumor" was made.

The condition of the patient was anything but satisfactory, so it was planned to divide the operation into two stages. Under ether anesthesia, a flap was reflected to uncover the space between the right rolandic fissure and the occipital pole. The dura was under great tension, which subsided when the ventricle was tapped. At this point the blood pressure dropped, the pulse became accelerated, and it was not thought wise to proceed further. He was given 400 cc. of citrated blood, and the wound was closed without drainage.

Postoperative Course.—The patient's condition did not improve; he became irrational and restless, and died on Jan. 11, 1927, twelve days after the operation. When the brain was removed, there were no signs of hemorrhage in the operative field.

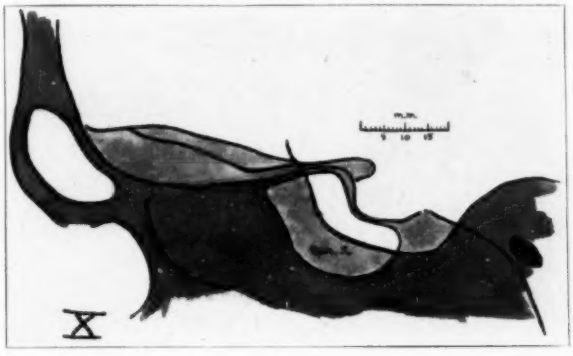

Fig. 32 (case 10).—A sketch of the roentgenogram (fig. 31), drawn to scale.

Pathologic Report.—Gross Description: Necropsy showed a large green tumor filling the entire interpeduncular space, and extending from the optic chiasm to the anterior border of the pons. The tumor was described as having the consistency of rubber. It was pea green and was definitely encapsulated. At the basilar portion, the tumor was infiltrated by a small gray cheeselike mass.

Microscopic Description: The tumor was an adamantinoma in which there was marked evidence of widespread calcification. Further details were not possible because of the lack of microscopic material.

CASE 11.—*After only six months of paroxysmal headache, a man, aged 28, presented a left homonymous hemianopia, exaggerated reflexes, and signs of increased intracranial pressure and endocrine disturbance. Marked improvement followed a subtemporal decompression. He survived an exploratory operation of the occipital lobe for six weeks. There was an error in localization.*

Clinical History.—W. G. R., a man, aged 28, was referred to the neurosurgical service of the University Hospital by Dr. W. T. Henderson of Mobile, Ala., on Dec. 4, 1921. He had been well until six months before when he began to complain of paroxysmal headaches, both frontal and occipital. Two months before admission, the headaches were accompanied by attacks of projectile

vomiting associated with vertigo. Almost simultaneously, vision became dim, and at the time of admission he could read only large type. On admission, he was stuporous and speech was sluggish.

Neurologic Status.—There were no disturbances of motor or sensory function. The left biceps and triceps reflexes and both patellar and both achilles reflexes were exaggerated; abortive ankle clonus was present. There were no cranial nerve palsies save that of the optic nerve.

Pituitary Stigmas.—There were stupor, accession of weight, feminine distribution of pubic hair and prominent mammae.

Ocular Manifestations.—There was homonymous hemianopia on the left. Vision in both eyes was 6/12. The disks showed swelling of from 4 to 5 diopters. Both pupils responded sluggishly to light (fig. 33).

Roentgen Observations.—The sella turcica measured 12 mm. in the antero-posterior and 11 mm. in the vertical plane. There was atrophy of the posterior clinoid processes (figs. 34 and 35).

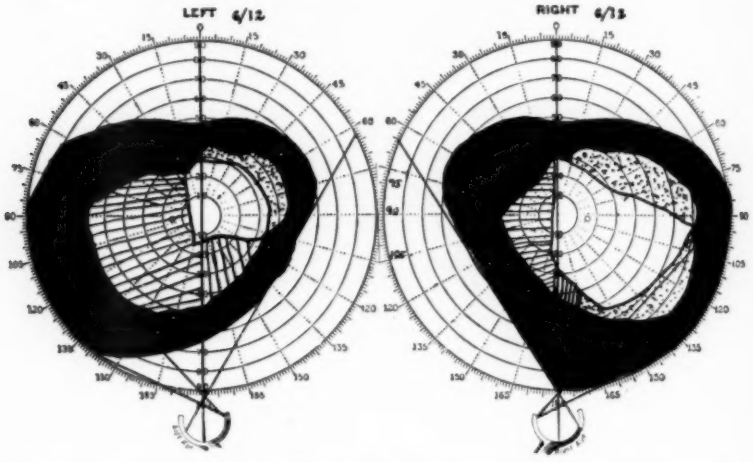

Fig. 33 (case 11).—Left homonymous hemianopia. Vision in both eyes was 6/12. The dotted area shows expansion of the field following decompression.

Cerebrospinal Fluid.—The pressure was 23 mm. The Wassermann reaction was negative. Sugar was positive, and there was a trace of globulin.

Subtemporal Decompression.—On December 9, as a temporary expedient, this operation was performed and resulted in considerable improvement. The stupor disappeared, and the patient became ambulant. The fields enlarged.

Ventriculogram.—This showed enormous dilatation of the lateral ventricles, no filling of the third ventricle and some encroachment on the posterior portion of the left lateral ventricle.

Exploratory Craniotomy.—The right temporo-occipital region was explored on Feb. 3, 1922. No tumor was found.

Course.—The patient survived the operation for seven weeks. In the interval the only unusual feature was a transitory period of visual hallucinations; the patient described the objects that he saw as trees, pictures on the wall, carpet, boxes and crates and scaffolding.

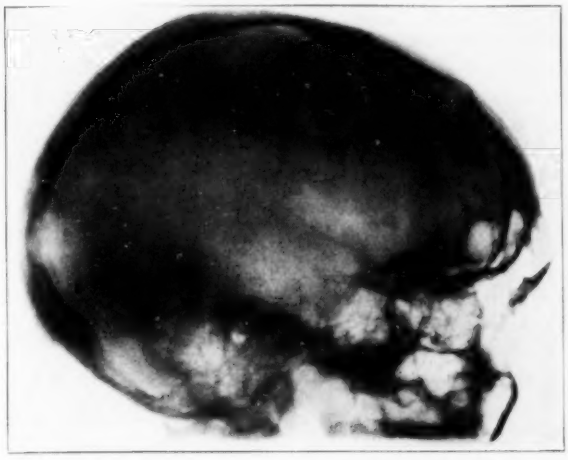

Fig. 34 (case 11).—Roentgenogram, showing marked atrophy of the dorsum sellae, and complete disappearance of the posterior clinoid processes. The pituitary fossa measured 12 mm. in the anteroposterior and 11 mm. in the vertical plane.

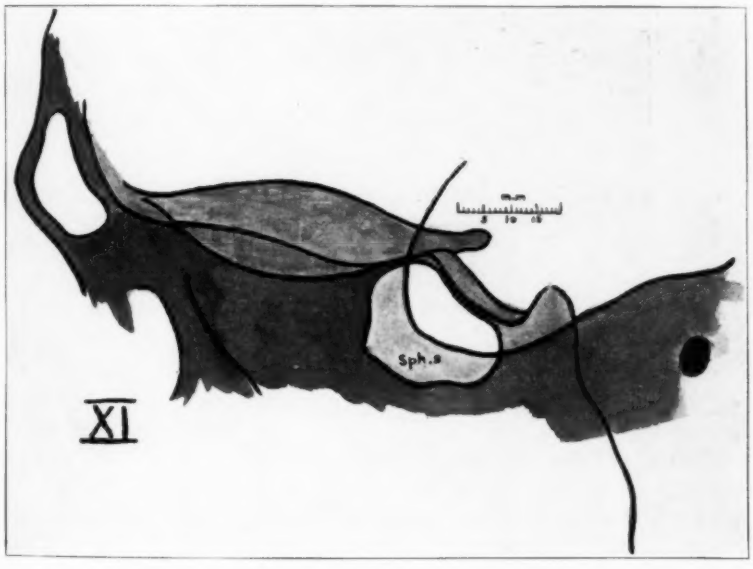

Fig. 35 (case 11).—A sketch of the roentgenogram (fig. 34), drawn to scale.

Necropsy.—This revealed a tumor, the size of a walnut, in the interpeduncular space, posterior to the chiasm. The tumor extended into the third ventricle.

Histologic Report.—The tumor was a typical adamantinoma. The epithelial columns were lined by ameloblasts. Within the columns lay stellate cells. The striking feature of this tumor was its markedly cystic character. Everywhere were large cysts, which were surrounded by the epithelial columns and filled with a homogeneous material that contained some cells. It appeared as if this material had developed from a degenerated stroma. The latter was fairly abundant. Calcification was frequently seen throughout the tumor.

Fig. 36 (case 12).—Roentgenogram, showing moderate atrophy of the dorsum sellae and complete disappearance of the posterior clinoid processes. The pituitary fossa measured 10 mm. in the anteroposterior and 5 mm. in the vertical plane.

CASE 12.—*A well developed woman, aged 33, had complained of headaches for over a year. There were a bitemporal hemianopia and amenorrhea, but the sella turcica was not enlarged. Four years after the removal of a cystic tumor beneath and behind the chiasm, the patient was well. Benefit followed the administration of thyroid.*

Clinical History.—K. A. K., a woman, aged 33, was referred to the neurosurgical service of the University Hospital by Dr. Raymond H. Bloss and Dr. William G. Spiller, on Dec. 16, 1926. The previous medical and family history was unessential. In October, 1925, the patient began to have headaches, at first dull but constant,

later becoming very severe and at intervals of several days. They were referred to the midfrontal region, with much pain over the right eye. In June, 1926, she suddenly became aware of failing vision and in August, she had the first vomiting spell. On one occasion she had diplopia. On December 4, vision became much worse and on December 5 for the first time she was unable to read. She had been receiving courses of roentgen treatment, but the fields continued to contract and the sight to fail.

Neurologic Status.—The patient was well developed and moderately obese. Her average weight for the past ten years had been from 150 to 155 pounds (68 to 70 Kg.). There were no sensory or motor disturbances. The reflexes were normal.

Cerebrospinal Fluid.—The pressure was 182 mm.; the fluid contained 4 lymphocytes; the Wassermann reaction was negative. Globulin was not increased.

Roentgen Observations.—The pituitary fossa measured 10 mm. in the anteroposterior and 5 mm. in the vertical plane.

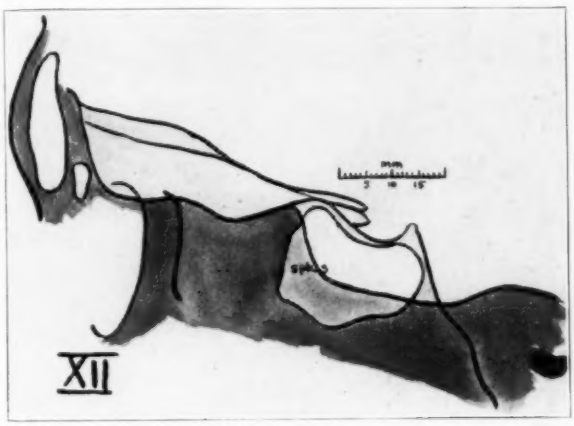

Fig. 37 (case 12).—A sketch of the roentgenogram (fig. 36), drawn to scale.

Pituitary Stigmas.—The basal metabolic rate was —15. The menses had been regular until three months before admission. (Figs. 36 and 37.)

Ocular Manifestations.—Vision in each eye was 2/60. The fields showed practically a bitemporal hemianopia, although vision was not wholly lost in the upper quadrant of each temporal field (fig. 38).

Transfrontal Craniotomy.—On December 20, under local anesthesia, a flap was reflected from the right frontal region. The anterior horn of the ventricle was tapped, but the fluid was not under pressure. The frontal lobe was elevated, the right olfactory nerve divided, and the lesion exposed as it presented in front of the chiasm. A straw-colored fluid was withdrawn with a syringe. A considerable portion of the cyst wall, lined with tissue, was removed. The cyst, the greater part of which seemed to be beneath and behind the chiasm, did not appear to be much larger than an English walnut. After the cyst wall was removed, there was a considerable space beneath the optic nerves and the chiasm. For hemostasis a small muscle graft was used. The wound was closed without drainage. At the conclusion of the operation, which had been well borne, there was a transitory

collapse of both respiration and circulation. The pulse became imperceptible, and the blood pressure fell to 60 mm. The condition responded promptly to the administration of caffeine, epinephrine and pituitary extract.

Postoperative Course.—Recovery ensued promptly. Before discharge on Jan. 23, 1927, vision had not improved, and the fields were still hemianopic.

The patient returned for examination at various intervals from the date of discharge, and the last report was received from her physician on Jan. 7, 1931, four years after the operation. During this time she had gained 20 pounds (9 Kg.); the hemianopia had persisted, but vision in each eye was 5/5 (fig. 39). Menstruation had not returned. To combat the sleepy spells and accession in weight, the physician had prescribed, in October, 1930, 3 grains (0.19 Gm.) of thyroid extract daily. Under this treatment the basal metabolic rate rose from —19 to +12, the weight dropped from 178 to 168 pounds (80 to 76 Kg.), and the sleepy spells disappeared.

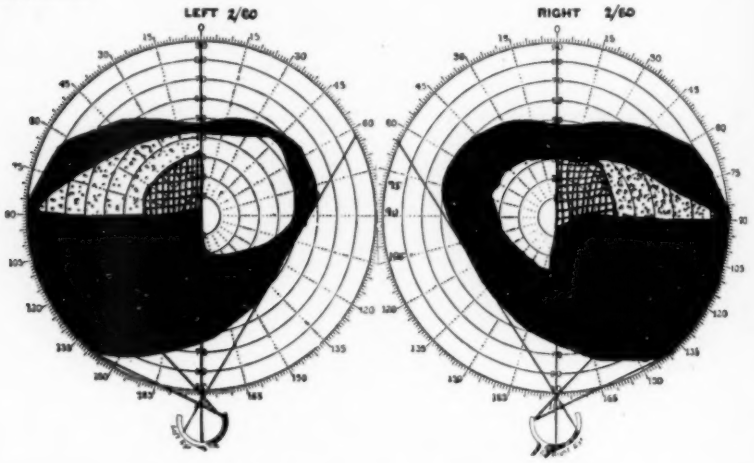

Fig. 38 (case 12).—Fields taken ten days before operation, showing the transition stage between a bitemporal quadrantanopia and hemianopia. Vision in both eyes was 2/60.

Histologic Report.—The tumor was an adamantinoma. While these tumors appear very similar in their general characteristics, they differ in certain respects. This tumor was composed of the typical epithelial tree, with its interlacing columns of epithelial tissue. Among these were large areas of stroma, around which were wrapped the epithelial columns.

The latter, while characteristic, differed somewhat from the typical adamantinomatous tumor. The basal layer of ameloblasts or enameloblasts, which was usually composed of columnar epithelium, was in this instance formed by columnar, cuboidal or even a flat type of cell, the shape in all probability depending on the angle of section of the cell. The most frequent type of cell seemed to be cuboidal or a transition from cuboidal to columnar. The basal epithelium invested the outer portion of the epithelial column. The inner portion of the columns was made up of stellate cells with a star-shaped cytoplasm, and often with a squamous appearance. The shape of these cells varied much, but in general they had an

irregular, stellate shape. Between the cells could be seen clearly numerous intercellular bridges which made a rich series of cell connections everywhere. It was of extreme interest that in the epithelial columns there were almost no nests or pearls, and no evidence of calcification or cyst formation. Nevertheless, the general structure of the columns was typical, except for the variation in the morphology of the basal layer.

The stroma, which was scattered abundantly among the epithelial columns, was seen in a sort of round island. It was very fibrillar and relatively poor in cells. There were much fibrous tissue and few fibroblasts. Leukocytes were scattered throughout the islands of tissue. The connective tissue was composed of collagen and fibrous bands which stood out in fibrillar splendor. Blood vessels were numerous both in the stroma and in the epithelial columns.

The capsule of the tumor was very thick. It was composed of fibrous tissue, within which were numerous phagocytes filled with hemosiderin pigment. These

Fig. 39 (case 12).—Photograph of the patient taken four years after operation for removal of adamantinoma. Vision in each eye was 5/5, although hemianopia persisted.

were present everywhere. Scattered throughout the capsule were islands of cells with a peculiar appearance arranged in irregular columns, with round vesicular nuclei and indistinct cytoplasm. Their nature was not clear. Calcium granules were found in the capsule; they were not very abundant. The tumor proper invaded the capsule, with which it was intimately connected.

CASE 13.—*Blind in one eye, with a temporal cut in the other and with no evidence of endocrine disturbance, the patient, a man, aged 38, was first operated on by the transsphenoidal route. Eighteen months later, through a transfrontal craniotomy, a portion of a large tumor was removed. Hyperthermia developed, and the patient died forty-eight hours later.*

Clinical History.—C. F. E., a man, aged 38, was referred to the neurosurgical service of the University Hospital by Dr. J. P. Baker, of Findley, Ohio, on Oct. 15, 1917. Two years before, he had noted impairment of vision and discovered some limitation of the field of the left eye. A year before, a physician

prescribed mercury and sweat baths. In the spring, 1916, a transsphenoidal hypophysectomy was performed, with transitory improvement of vision. He has had occasional headaches.

Neurologic Status.—Except for the visual field distortions, the neurologic examination in all respects gave negative results.

Roentgen Observations.—There was evidence of a large pituitary growth. The fossa was very large; the floor of the fossa seemed to be intact.

Bárány Tests.—These gave negative results as to involvement of the labyrinths, auditory nerves, cerebellar hemispheres and medulla oblongata.

Ocular Manifestations.—The left eye was blind; vision in the right eye was 6/22. The right field showed a temporal cut. The disks were atrophic.

Cerebrospinal Fluid.—The pressure was normal. The Wassermann reaction of the spinal fluid and of the blood was negative.

Transfrontal Craniotomy.—On November 1, under ether anesthesia, on reflection of a flap on the right side and a horizontal incision in the dura, the surface of the brain appeared edematous. The pia-arachnoid was punctured to permit the escape of cerebrospinal fluid. After ligation of three veins between the dura and arachnoid, the frontal lobe was mobilized. With scarcely any retraction and by gravity the lobe dropped back sufficiently to expose the right optic nerve. The tumor presented to the inner side of the nerve and was removed piecemeal, leaving a cavity, 3 cm. in diameter. Oozing, which was moderate, was readily controlled with a muscle graft. The wound was closed without drainage.

Postoperative Course.—Immediately after the operation the pulse became accelerated and the temperature began to rise, reaching 104 F. The condition did not respond to appropriate treatment, and the patient died forty-eight hours later.

Postmortem Examination.—The operative field showed that only a portion of the tumor had been removed at the operation. There remained a portion the size of a plum, postchiasmal in position, extending well beyond the confines of the sella turcica and into the posterior fossa.

Pathologic Report.—The tumor was fibrous and very vascular. The epithelial portion was composed of cells arranged around a cavity or in a papilla-like arrangement. There was a layer of columnar cells, but no typical stellate layer. Most of the cells outside these basilar cells were oval or elongated. They appeared like fibroblasts.

CASE 14.—*In a middle aged woman, signs of pituitary dysfunction developed, at first without change in the fields or the sella turcica. Later, homonymous hemianopia developed, and an exploratory (transfrontal) craniotomy was performed. No tumor was visible in the prechiasmal or pituitary space. Some improvement was followed by a relapse, with frontal lobe symptoms superimposed. Death occurred one year after the first observation. The pathologic diagnosis was adamantinoma (retrochiasmal) of the pharyngeal duct.*

Clinical History.—Mrs. C. W. K., aged 50, was referred to the neurosurgical service of the University Hospital by Dr. Burton Chance, on Dec. 4, 1924. The family history and the history of previous illness were inconsequential. The patient was married and had had one miscarriage. In April, 1924, there appeared dimness of vision; it seemed as though there was a cloud before the eyes. Since May, sight had failed considerably. She had noticed no narrowing of the fields; she had a ravenous appetite, had increased in weight from 173 to 243 pounds (78.5 to 110.2 Kg.) and was always tired and ready to sleep. She had to

void urine frequently, sometimes every half hour. Since July, she had been able to read only the headlines of a newspaper. In August, she had an hallucination; she thought that she was surrounded by big black dogs. She was restless and had occasional bitemporal headaches.

Neurologic Status.—On admission, the following were noted:

Endocrine Stigmas: There was an accession in weight (50 pounds [22.7 Kg.]); she fatigued easily; polyuria was present; the basal metabolic rate was —21.

Ocular Disturbances: Vision in the right eye was 6/22; in the left, 6/15. There were diplopia, lack of convergence, sluggish pupils and grayish-yellow fundi (fig. 40).

Roentgen Observations.—The measurements of the sella turcica were: depth, 7.5 mm.; anteroposterior plane, 10.5 mm. In all other respects the examination gave negative results (figs. 41 and 42).

Bárány Reactions.—These suggested a cerebral rather than a cerebellar lesion.

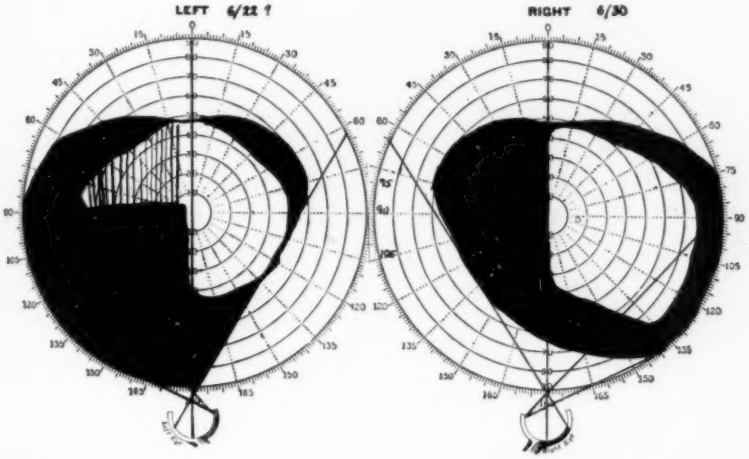

Fig. 40 (case 14).—Fields taken four days before operation, showing left homonymous hemianopia with some retained vision in the upper temporal quadrant. Vision in the right eye was 6/30; in the left, 6/22.

Course.—In the absence of any signs of sellar deformation or any pressure phenomena, the patient was discharged on December 11, to continue under Dr. Chance's observation.

Readmission.—The patient was readmitted to the hospital on Jan. 14, 1925. Since discharge, there had been a definite deterioration of vision, and there had developed for the first time marked field distortions. The nervousness, polyuria, sleeplessness, headache and diplopia had persisted.

Further examination revealed a basal metabolic rate of —25, an intracranial pressure of 234 mm. and a left homonymous hemianopia. Vision in the right eye was 6/30; in the left, 6/22. The measurements of the sella turcica had not changed (7.5 by 10.5 mm.).

With these manifest signs of pituitary dysfunction, the oncoming field distortion and the deteriorating vision, a cranial exploration seemed indicated. The provisional diagnosis was "extrasellar tumor."

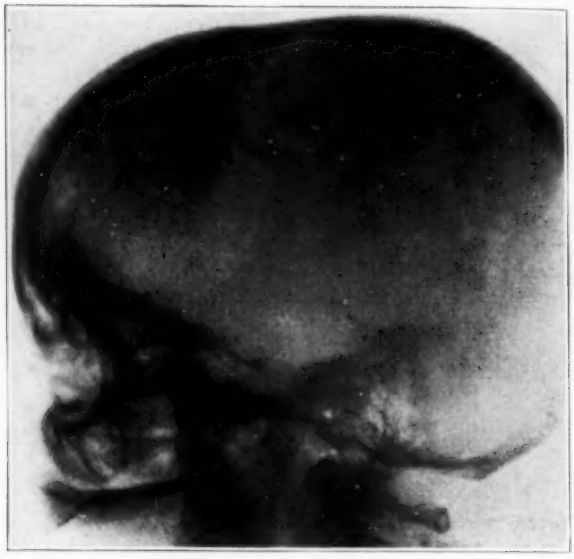

Fig. 41 (case 14).—Roentgenogram, showing moderate atrophy of both the dorsum sellae and the posterior clinoid processes. The pituitary fossa measured 10 mm. in the anteroposterior and 7.5 mm. in the vertical plane.

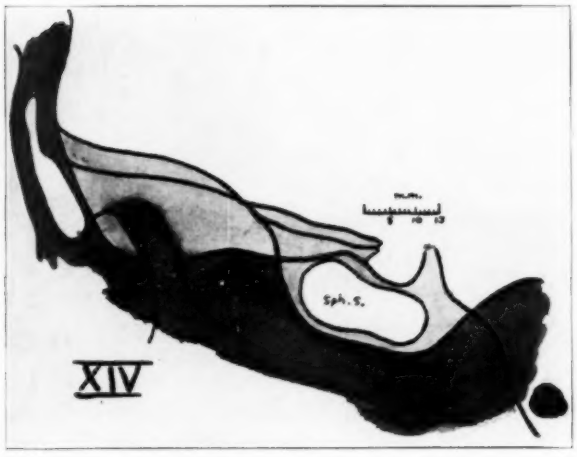

Fig. 42 (case 14).—A sketch of the roentgenogram (fig. 41), drawn to scale.

Right Transfrontal Craniotomy.—On January 19, under local anesthesia, a flap was reflected. The dura was especially adherent, particularly in the region above the orbit. There appeared to be no increase in intracranial pressure. There was an excessive amount of cerebrospinal fluid, which on evacuation facilitated elevation of the frontal lobe. A liberal exposure was obtained of the chiasm and optic nerves, but there was no sign of a tumor in the sella or outside of it. The wound was closed. In the middle of the operation the blood pressure rose suddenly from 125 to 175, soon to drop again to the original level. It seemed as though an additional amount of pituitary extract might have been liberated during the manipulations.

Except for one convulsion, the patient's convalescence was uneventful, but before discharge it was thought wise, because of the negative observations in the pituitary region, to do a subtemporal decompression. This was performed on February 11, by Dr. F. C. Grant, and the patient was discharged on February 25.

Course.—Between Feb. 25, 1925, and the date of death, Jan. 15, 1926, the following notes were made:

March 19, 1925: The patient was very much depressed, seemed to have hallucinations, and spoke of imaginary sounds: "the kids," "turtles."

June 8, 1925: The left homonymous hemianopia had disappeared and vision was about the same: right eye, 2/60; left eye, 6/60. The disks were of fairly good color though somewhat blurred at the edges; the retinal veins were engorged.

June 19, 1925: The patient was depressed, childish and dirty in personal habits, had delusions and an enormous appetite, and drank 4 quarts of milk daily. She had much headache.

Jan. 10, 1926: The patient was readmitted to hospital in a semistuporous state and died five days later. For the first time the sella had increased in size; the measurements were: 10.5 in the anteroposterior and 10 mm. in the vertical plane. At this time the fields could not be taken; the patient was practically blind, but there was no elevation of the disks.

Pathologic Report.—Gross Description: Necropsy revealed a tumor extending from the optic chiasm to the pons with which it seemed to be continuous. The infundibulum was included in the mass, but nothing was said about the pituitary body. The surface of the tumor was irregular, with cysts projecting above it.

Microscopic Description: The tumor was composed of interlacing columns of epithelial cells. These varied considerably in diameter, some being thin and others many cells in thickness. The effect was that of an epithelial tree with numerous branches and offshoots.

The epithelial columns were lined by a basement membrane on which lay a basal layer of epithelial cells, which were columnar. This layer was from 1 or 2 to 3 cells in thickness, but was on the whole a single cell layer. It completely invested the epithelial papillae. The nuclei were oval or thin, with a well defined membrane and an extremely vesicular structure. The inner portions of some of the columns were composed of cells similar in structure to the columnar cells. In these they formed a rather dense cellular structure. In other columns the cell arrangement was more orderly; above the columnar layer of ameloblasts or enameloblasts lay cells that were placed at right angles, and above these, within the center of the epithelial columns, were large, plump, squamous-like cells. Among these were occasionally seen mitoses. On the whole, the epithelial columns in this tumor did not have the regular structure previously described, but were composed of cells irregularly arranged above the ameloblastic layer. Stroma was not abundant in this tumor.

Large cysts were everywhere present in the tumor. They were filled with a homogeneous, hyalin-like material, within which were scattered cells. Epithelial pearls were found in the columns of which the tumor was composed. Many of these had undergone a homogeneous degeneration. They stained pink, and showed no structure except the outline of definite prickle cells. What have been described as tooth-budlike projections were seen sprouting from the epithelial volumns. Calcification was present, but was not abundant. Small hemorrhages were seen rather frequently in some parts of the stroma. In some places the tumor was vascular. Areas of degeneration were present throughout the tumor.

PART II. CLINICAL MANIFESTATIONS

Life History.—It is of interest to note the variation in the duration of the lesion, as far as one can judge from the onset of the first symptom. In 6 cases, or a little less than half of the cases, it was a matter of months (four, six, six, six, eight and ten) from the time the first symptom appeared until the patient was admitted to the hospital; in the remaining 8 cases it was a matter of years (one, one, two, three, four, six, seven and several). In 2 cases, for example, there had been arrest of growth for six and seven years, respectively. In one instance (case 2), that of a child, aged 8, the parents said that the child had complained of attacks of headache ever since she could talk. In one instance (case 8), the patient had headache and somnolence for three years, and the child was said always to have been underdeveloped. In the youngest patient of our series (case 1), the child had had headache and, later, vomiting attacks for four years. The first symptom to appear in 6 cases was headache, in 2, headache and dimness of vision, in 1, headache and somnolence, in 1, dimness of vision, in 3 arrest of growth, and in 1, convulsions.

Sex and Age.—It is said that the sexes are about equally affected. Series from other clinics have not been analyzed, but in our series of 14 cases, 10 patients were males and 4 females.

It is generally conceded, however, and this is a matter of no little importance in differential diagnosis, that pharyngeal duct tumors predominate in children and young adolescents. This is true in our series in which 9 of the 14 patients were between the ages of 7 and 17. Three of the patients were in the first decade (7, 8 and 9 years), 6 in the second decade (12, 12, 15, 15, 16 and 17 years), 2 in the third decade (25 and 28 years), 2 in the fourth decade (33 and 38 years), and 1 in the fiftieth year. In this series of adamantinomas, therefore, 70 per cent of the patients were under 20 years of age, whereas in a series of 20 cases of adenomas taken at random, 85 per cent of the patients were over 20 years of age.

The youngest patient is said to be that of Olivecrona [6] and Lipholm, (5 years), and the next youngest a patient of 6 years, referred to by Bailey.[7] Our youngest patient was 7 years of age, but in this case symptoms were first observed when the child was only 4. In one patient, aged 8, the parents said that the child had had headaches ever since it could talk. Therefore, in considering the diagnosis it should be remembered that adenomas are unusual before 20 and suprasellar endotheliomas rare before 30, and that the majority of adamantinomas appear before the twentieth year.

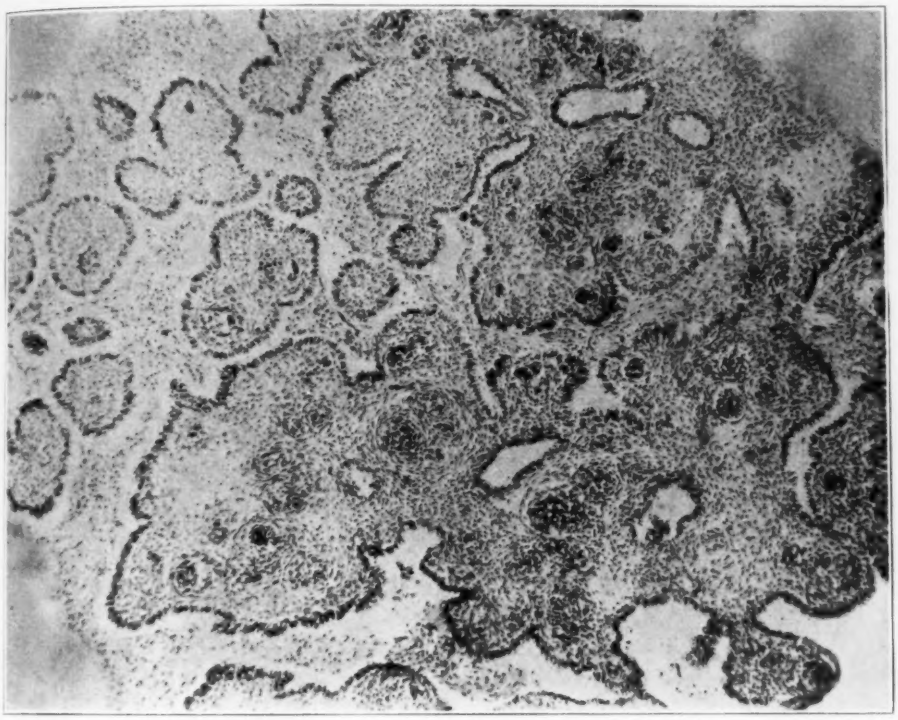

Fig. 43.—The anastomosing arrangement of the epithelial columns is striking. There are numerous cell nests everywhere in the columns of epithelial cells. Hematoxylin-eosin stain.

Endocrine Disturbances.—Generally speaking, the endocrine picture is that of the Fröhlich type. According to Critchley and Ironside,[2] in the suprasellar adamantinomas one never sees gigantism or acro-

6. Olivecrona, Herbert: Die chirurgische Behandlung der Gehirntumoren, Berlin, Julius Springer, 1927.

7. Bailey, Percival: Concerning the Cerebellar Symptoms Produced by Suprasellar Tumors, Arch. Neurol. & Psychiat. **11**:137 (Feb.) 1924.

megaly. In the intrasellar adamantinomas they observed 6 cases of acromegaly. This is not in accordance with our observations. Neither acromegaly nor gigantism was manifest in any of the 14 cases. The signs of pituitary dysfunction, in the order of frequency, were: dwarfism, 7; somnolence, 6; adiposity, 5; regressive sex characteristics, 4; femininity, 4; polyuria, 3; amenorrhea, 1; emaciation, 1.

According to age, these signs are expressed in table 1. It is apparent from this table that endocrine changes are more frequent in younger patients than in those over 20 years of age. In 1 patient, aged 38, there were no endocrine symptoms; in 1, aged 33, amenorrhea was the only manifestation of pituitary dysfunction; in 1, aged 25, somnolence alone was the only sign of glandular disturbance.

Cachexia is one of the infrequent manifestations of pituitary dysfunction. In another communication,[8] I reported a striking illustration

TABLE 1.—*The Incidence of Endocrine Disturbances with Relation to Age*

Case	Age	Dwarfism	Somnolence	Adiposity	Sexual Defect	Femininity	Polyuria	Amenorrhea	Emaciation	
1	7	+	..	..	..	..	+	..	..	Under 20 years of age
2	8	..	..	+	..	..	..	..	..	
3	9	..	+	+	+	+	..	..	..	
4	12	+	+	..	..	+	..	..	..	
5	12	+	..	+	..	..	..	..	..	
6	15	+	+	..	+	..	+	..	+	
7	15	+	..	..	+	..	..	..	..	
8	16	..	+	..	+	..	..	..	..	
9	17	+	..	..	..	+	..	..	..	
10	25	..	+	..	..	..	..	..	..	Over 20 years of age
11	28	..	+	+	..	+	..	..	..	
12	33	..	..	..	..	..	..	+	..	
13	38	..	..	..	..	..	..	..	..	
14	50	..	..	+	..	..	+	..	..	

of this (case 7). Beckmann and Kubie,[4] in 12 cases of adamantinomas, observed 2 cases of cachexia.

In the young, arrest of growth is the commonest endocrine disturbance. It was a striking symptom in 7 of 9 of our patients under 20 years of age. In the series of Beckmann and Kubie, in the first 10 cases (8 to 18 years) there was a life-long defect in growth. The next most common endocrine symptom was somnolence; in our series in 6 of 14 cases, in that of Critchley and Ironside in 10 of 15 cases. According to Peet,[3] somnolence may be due indirectly to subnormal metabolism. Scanty hair, with the feminine arrangement of the pubic hair, loss of sex vigor and amenorrhea are common among the adult patients, and in the cases of Beckmann and Kubie none of the adolescents had passed through a normal pubescence; of the females,

8. Frazier, C. H.: Pituitary Cachexia, Arch. Neurol. & Psychiat. **21**:1 (Jan.) 1929.

only one had menstruated. Not one woman had married, suggesting an early disturbance of the psychosexual constitution, whereas 6 of the 7 male patients were married.

Basal Metabolism.—The metabolic rate is not a matter of great significance viewed from any angle. As a matter of fact, one sees but an occasional record of the metabolic rate in the reported cases. Of the 14 cases in this series, the metabolic rate was estimated in 7, and in 6 of the 7 the rate was minus. The readings were —6, —13, —15, —15,

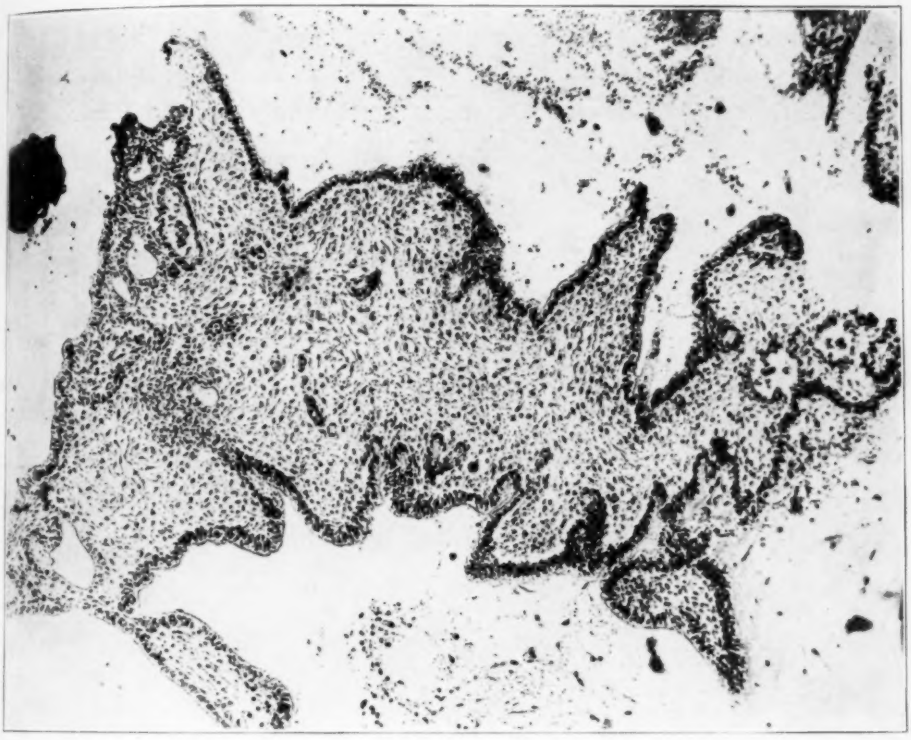

Fig. 44.—An epithelial projection, showing under low magnification the typical structure, particularly the stellate layer. Hematoxylin-eosin stain.

—21 and —34. As I have observed in previous communications on the results of pituitary dysfunction, no matter what the lesion may be, when the basal metabolism is disturbed, in the majority the rate is subnormal. Glancing over a series of 20 consecutive cases of adenomas, all but two of the figures were in the minus column. Hence, a minus metabolic rate has no significance in differentiating between tumors of the pharyngeal duct, as adamantinomas, and tumors of the pituitary body, as adenomas.

Intracranial Pressure and Headache.—When contemplating the effects of pressure, one must divorce the effects of direct pressure from those of indirect pressure, or to put it in another way, the effects of direct pressure without increase of intracranial pressure from those that may be the result of increased intracranial pressure. Whether there are present one or the other of these physical conditions or perhaps both combined will depend on whether the tumor takes origin from the upper epithelial anlage or from the lower. If from the upper site, the third ventricle will soon be encroached on and a ventricular block established with all that that implies.

As expressions of pressure, headache and vomiting, papilledema and optic atrophy may be considered. Headache is mentioned first because it is the most constant of all symptoms and usually the first symptom to be observed. Headache was a conspicuous feature in all of our

TABLE 2.—*The Incidence of the Signs of Intracranial Pressure with Relation to Age*

Case	Age of Patient	Headache and Vomiting	Papilledema, Diopters	Optic Atrophy	
				Primary	Secondary
1	7	+	—	+	..
2	8	+	—	..	+
3	9	+	—	..	+
4	12	+	—	..	+
5	12	+	+ 5	—	—
6	15	+	—	+	..
7	15	+	—	..	+
8	16	+	—	+	..
9	17	+	—	+	..
10	25	+	+ 4	—	—
11	28	+	+ 4	—	—
12	33	+	—	+	..
13	38	+	—	+	..
14	50	+	—	+	..

14 cases. In another series it was present in 19 of 21 cases. In our 14 cases, headache was the first symptom in 10, and in 3 of these it is recorded that headache appeared simultaneously with dimness of vision. In only 2 cases is it said that the headaches were only occasional, and in only 2 that headaches appeared simultaneously with loss of visual acuity. As to location, the headaches are described as occipital, frontal and occipital, frontal and bitemporal and midfrontal. In one patient in whom the tumor was altogether extrasellar and retrochiasmal, thus differing essentially in location from the intrasellar adenoma, the headache was bitemporal, and yet one is wont to regard bitemporal headache as rather characteristic of and occurring exclusively in primary intrasellar adenomas and suprasellar fibroblastomas. Whatever the cause of headache, in only 3 of 14 cases were the ventricles found dilated: in a patient aged 8 (case 2), in 1 aged 9 (case 3) and in 1 aged 25 (case 10).

Associated with headache, vomiting is mentioned as a conspicuous symptom in only half of the 14 cases, and this in patients aged 7, 8, 9, 12, 17, 25 and 28 years (cases 1, 2, 3, 4, 9, 10 and 11). This confirms the statement made by others that the signs of intracranial pressure are observed chiefly in the stalk tumors of childhood and adolescence. There are, however, a certain number of cases which, from the standpoint of age, overlap the period of incidence of the adenomas. So one cannot differentiate these two classes, the stalk tumor and the

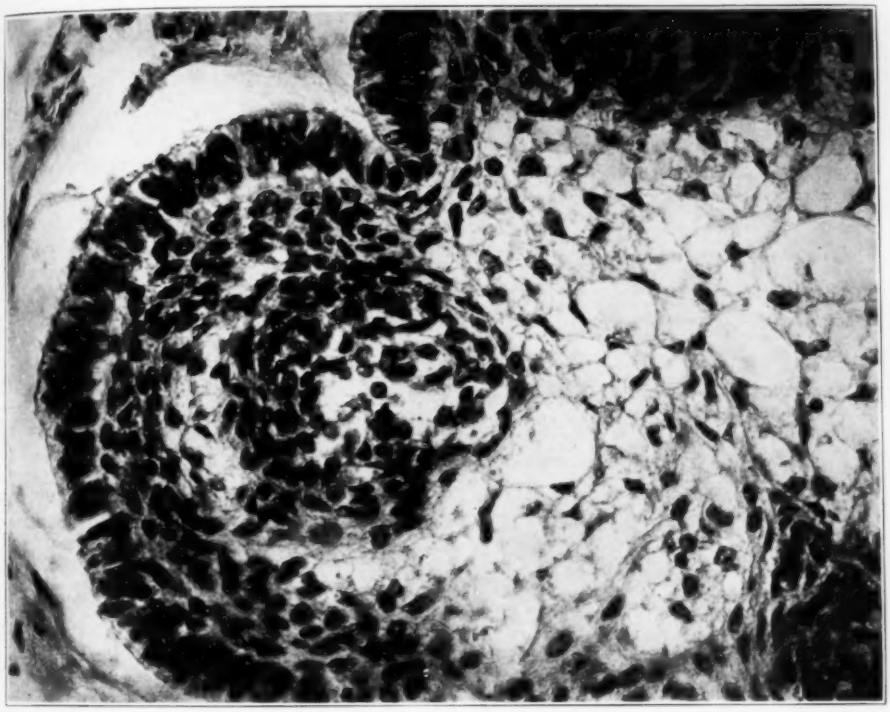

Fig. 45.—The basilar layer of columnar ameloblasts, the stratum intermedium and the stellate layer are clearly seen. There is a cell nest in the papillary projection. Hematoxylin-eosin stain.

adenomas, wholly on the presence or absence of signs of increased intracranial pressure.

Optic Disks.—The physics of papilledema are well understood. Presumably one would expect papilledema or secondary optic atrophy in all adamantinomas arising from the upper epithelial anglage, and a primary optic atrophy when the tumor arises from the lower epithelial anlage. Of the 14 cases, there were 7 with primary optic atrophy and 7 with papilledema or secondary postpapillitic atrophy. From the

exposure at operation it is not always possible to determine whether the tumor took origin from the upper or the lower anlage, but from the operative notes the locations given in table 3 are the ones at which the tumor is described as presenting in the 14 cases.

In all cases of primary optic atrophy but 1, the tumor presented prechiasmally at the operation and presumably arose from the lower of the two possible sites; whereas in cases of secondary optic atrophy, 5 of the 7 cases are described as retrochiasmal and 2 as prechiasmal. In all instances in which at the time of examination there was a papilledema, the tumor was retrochiasmal and presumably from the superior anlage. Of the remaining 4 cases of secondary or postpapillitic atrophy, in 2 the tumor presented as prechiasmal and in 2 as retrochiasmal. It is difficult to generalize further as to the relation of

TABLE 3.—*Location of Tumors in Fourteen Cases*

Case		Age in Years
	Primary Optic Atrophy	
1	Prechiasmal	7
6	Prechiasmal	15
8	Prechiasmal	16
9	Suprachiasmal	17
12	Prechiasmal	33
13	Prechiasmal	38
14	Retrochiasmal	50
	Papilledema or Secondary Optic Atrophy	
2	Prechiasmal	8
3	Retrochiasmal	9
4	Retrochiasmal (+ 5 diopters)	12
5	Prechiasmal	12
7	Presumably retrochiasmal (not exposed) (plus 4 diopters)	15
10	Retrochiasmal	25
11	Retrochiasmal (plus 4 diopters)	28

origin of the tumor to the condition of the disks. It has been said that papilledema is commoner in the younger patients. In our series the average age of the primary optic atrophies is 14 years and of the papilledemas or secondary optic atrophies 28 years. In the 12 cases of Beckmann and Kubie there was only 1 adult with papilledema; in our series of 14 cases there was 1 adult with papilledema and 1 with postpapillitic atrophy.

Visual Fields.—In summarizing the various types of visual fields in our series (table 4) there were 6 cases of temporal or bitemporal hemianopia, 1 of bitemporal quadrantanopia, 2 of homonymous hemianopia, 1 of binasal hemianopia; in 1 the fields were full; in 2 there was a concentric contraction of the fields; in 1 the patient was blind. It has been of interest to note that in every case of temporal or bitemporal hemianopia the tumor at the operation presented prechiasmally. In the binasal, the homonymous and in 1 of the concentric contractions the tumor was retrochiasmal.

Theoretically, in tumors taking origin from the upper group of cells, if the tumor grows upward, obstructing the third ventricle with a secondary hydrocephalus, there will follow choking of the disks and a concentric contraction of the visual fields. If, from the same origin, the tumor grows downward there will follow a primary optic atrophy, and the chiasm will be pushed downward and forward with first a lower quadrantanopia, then a bitemporal or homonymous hemianopia (Peet and Critchley and Ironside). If the tumor arises from the lower anlage, pressure on the chiasm is directed from below and behind, and there develops first a bilateral upper quadrantic defect (Critchley and Ironside). To this statement, however, Beckmann and Kubie took exception. Because of the relative vulnerability of the macular bundles,

TABLE 4.—*The Character of the Visual Fields with Reference to the Location of the Tumor and the Visual Acuity*

Case	Age of Patient	Vision: Right Eye	Vision: Left Eye	Fields	Tumor Presenting
1	7	5/ 6	Blind	Temporal hemianopia of right eye..	Prechiasmal
2	8	Blind	Large objects	Temporal hemianopia of left eye....	Prechiasmal
3	9	Blind	Blind	.....	Retrochiasmal
4	12	2/60	1/60	Binasal hemianopia	Retrochiasmal
5	12	6/21	6/12	Bitemporal quadrantanopia	Prechiasmal
6	15	Normal	Normal	Concentric contraction	Prechiasmal
7	15	Light	Blind	Barrel vision	Retrochiasmal
8	16	6/60	6/30	Bitemporal hemianopia	Prechiasmal
9	17	6/60	Blind	Temporal hemianopia of right eye..	Suprachiasmal
10	25	6/15	6/15	Fields full	Retrochiasmal
11	28	6/12	6/12	Homonymous hemianopia	Retrochiasmal
12	33	6/60	6/12	Bitemporal hemianopia	Prechiasmal
13	38	6/22	Blind	Temporal cut in right eye.....	Prechiasmal
14	50	6/22	6/15	Homonymous hemianopia	Retrochiasmal

pressure frequently gives rise, according to Critchley and Ironside, to an early involvement of central vision with paracentral scotomas.

There were only 3 cases in our series in which there was a quadrantic cut, and in all 3 it was in the lower rather than in the upper field. In 1 of these (case 1), the sella was enlarged and the tumor presented prechiasmally. According to the rules cited, there should have been an upper quadrantic cut. In the second (case 14), the tumor was retrochiasmal and the fields were in a transition from a lower bitemporal quadrantanopia to a bitemporal hemianopia. In this case the tumor was retrochiasmal, pressing forward and downward, and as one would expect, the lower quadrants were obscured. In the third (case 12), as in the first, the tumor presented prechiasmally, but the quadrant cut was below and not above. Beckmann and Kubie believe that bitemporal hemianopia is as common in the older groups of stalk tumors as in the adenomas.

Roentgen Observations.—The roentgenograms in our series vary from each other in many particulars. The variations from the normal may be expressed as follows:

Pituitary fossa not enlarged	5
Pituitary fossa moderately enlarged	4
Pituitary fossa markedly enlarged	4
Atrophy of the dorsum sellae	11
Moderate	6
Marked	5
Shadows of calcification	6
Convolutional atrophy	4

In all 4 cases in which the pituitary fossa was markedly enlarged, the tumor presented prechiasmally and occupied the sella turcica. On the other hand, in 4 of the 5 cases in which the pituitary was not enlarged, the tumor was retrochiasmal.

The most characteristic feature of the x-ray picture in the adamantinomas, however, is the shadow of calcified deposits. In this series, shadows of calcification were observed in 6 of the 14 cases, and at least in 1 other specimen calcification was found though no shadow was reported by the x-rays. The shadows of calcification may appear as irregular areas scattered through the tumor or as outlining the cyst wall. In 1 of our cases (case 9), the cyst wall was at least 1 cm. thick and the calcification so pronounced that it was necessary to use rongeur forceps for removal of the cyst wall. According to Duffy,[9] 50 per cent of all squamous epithelial tumors will show shadows of calcified deposits; of the 9 proved cases in the series of Critchley and Ironside, there was evidence of calcification in 6, and in 2 of the remaining 3 cases calcification was found post mortem.

Calcification is of great significance when considering differential diagnosis. Glancing over the roentgen reports in 50 consecutive cases of adenomas in my files, there was not a single instance of calcification. Therefore, when the roentgenogram shows unmistakable evidence of calcification in a patient with evidence of endocrine disturbance, with field distortions and characteristic changes in the disks, it can be said with more than reasonable certainty that the lesion is an adamantinoma or a Rathke's pouch tumor.

Associated or Neighborhood Symptoms.—There were here and there isolated instances of symptoms of extraneous origin, that is, not related to either the pituitary body, the disks or the fields. In 3 instances there were visual hallucinations (cases 3, 11 and 14); in 2 instances they followed the operation and were comparatively late phenomena. In 1 instance they lasted but a week. One of these 3 patients also

9. Duffy, W. C.: Ann. Surg. **72**:537 (Nov.) 1920.

heard imaginary voices. Two patients complained of deafness (cases 3 and 11); 2 of tinnitus (cases 3 and 10); 1 of dizziness (case 11). In 1 case there was nystagmus, in 1 diplopia, in 1 loss of associated movements and convergence in ptosis, and in 1 inequality of pupils. In several there were evidences of involvement of the frontal lobes, either directly or indirectly, defective memory, psychosis, delusions, jocularity, irritable and vicious temperament, mental apathy and depression.

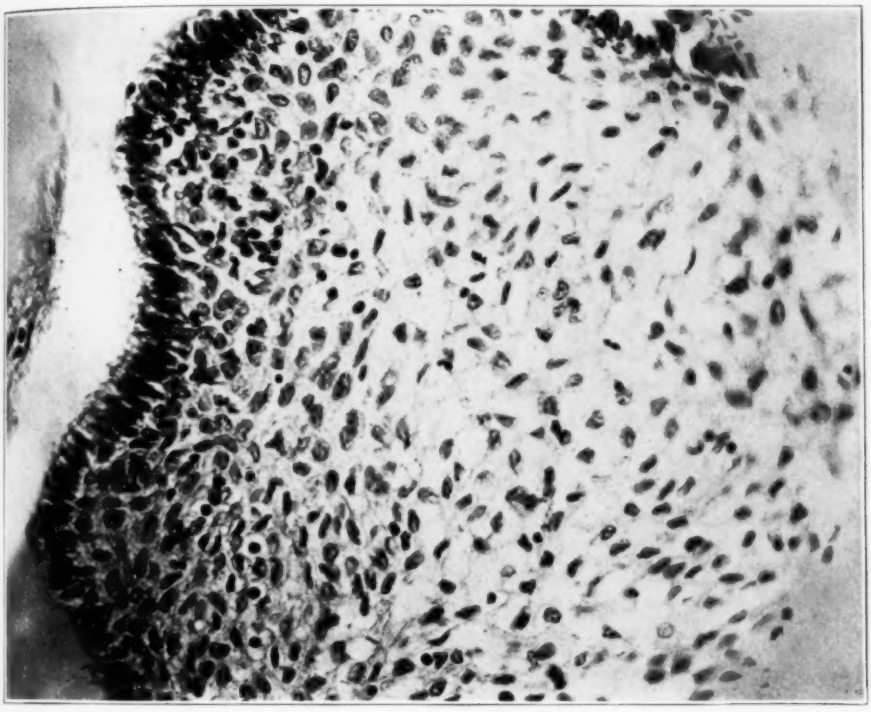

Fig. 46.—The minute arrangement of the epithelial column is clear, just as in figure 45. In this figure the stratum intermedium is not so evident. Hematoxylin-eosin stain.

Critchley and Ironside [2] referred to the development of toxic symptoms before and after operation. Among these were hypopyrexia, restlessness and delirium appearing in 3 cases, from eight hours to three weeks after opening the capsule. Restlessness was a conspicuous feature in 1 of the cases reported (case 7), and in 1 (case 14) the patient was restless and delirious for a short period after the operation. Urticaria, itching, prickling, hyperidrosis and hot flushes we have

never observed. It has been said that the appearance of toxic symptoms after an operation is due to the liberation of some metabolic substance, possibly cholesterol. Hyperpyrexia we have seen, as have others, occasionally in fatal cases, but as this is so often a phenomenon in lesions at the base of the brain we doubt its relationship to a pharyngeal duct tumor.

Prognosis and Treatment.—Of the entire series, 3 patients died from the immediate effects of an operation, and in each of these the operation was ill planned: In 1 a transsphenoidal exposure was executed on the assumption that we were dealing with an intrasellar adenoma. This patient had a large tumor, extending into the posterior fossa. In another we presumed a tumor of the third ventricle because there was no air shadow in the ventriculogram. A two-stage operation was planned, and the patient died after the first stage. In the third, an error in localization was made, and the parieto-occipital region was explored.

In 2 instances no operation was performed. In the remaining cases a transfrontal craniotomy was done, and all of the patients recovered from the immediate effects of the operation.

The outlook as to the expectation of life in the majority of such cases is gloomy, although of the 9 survivors in our series, 1 patient is alive thirteen years after the operation and 1 five years; 1 survived the operation for nine years. Of the remaining 6, survival was a matter of months (one, three, five, twelve, twenty and twenty). These results conform with those of others. In the experience of Critchley and Ironside, 11 of 18 patients who were operated on died within six months.

PART III. THE PATHOLOGY OF CRANIOPHARYNGEAL DUCT TUMORS

Gross Characteristics.—The craniopharyngeal duct tumors are usually large growths lying at the base of the brain. In all our cases that came to necropsy, the tumors were extremely large, extending roughly from the optic chiasm to the anterior border of the pons. In 1 case the tumor had grown forward to about half way along the orbital surface of the frontal lobes, and backward to the pons. In none of the cases that came to necropsy did the tumor fail to extend from the chiasm to the pons. Smaller growths have been reported, but in our series at any rate the tumor covered a large portion of the base of the brain.

By virtue of their position these tumors naturally compress the optic nerves, chiasm and tracts. Usually they lie in intimate relationship to the chiasm, and in 1 instance the optic tracts were so tightly stretched around the tumor that they were flattened out to thin bands which retracted perceptibly when they were cut on removal of the brain. In 1 of our cases, the tumor had reached such a large size that it had

compressed the middle cerebral vessels as they left the internal carotids and caused a cerebral softening in the distribution of these vessels.

The tumors vary a good deal in shape and consistency. Some have a more or less rounded contour, while others are elongated. Occasionally they may have a lobulated appearance. They are usually firm tumors, which may be fluctuant in some areas due to the formation of cysts within them. There is a thick, well defined capsule, which gives the tumors a false appearance of being benign, but though they are

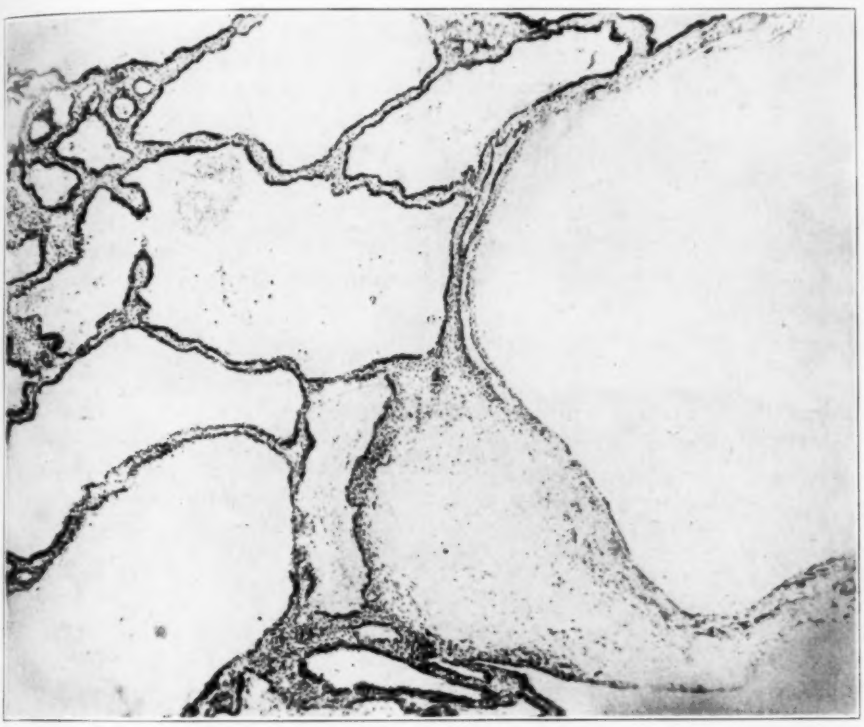

Fig. 47.—Cyst formation is widespread in this region. Hematoxylin-eosin stain.

encapsulated these tumors are so intimately related to the structures at the base of the brain that they cannot be removed without grave injury. At some point or another they seem to become a part of the brain, and they are therefore probably malignant tumors in this sense.

Most of the tumors are cystic, some more than others. The cystic material varies in appearance. In 2 of our cases the cysts contained a thick green fluid which coagulated on fixation. Another tumor was largely cystic and was filled with a viscid yellow fluid. Section of the

tumor may reveal the presence of one or more cysts of varying size. The amount of solid tumor material is variable. In some specimens, solid tumor growth is easily found. In 1 of our cases it occupied half of the tumor, while in another the cystic formation was so widespread that it was almost impossible to find a solid portion of the neoplasm for identification. It is said that these tumors show small papillary growths from the tumor wall projecting into the cyst cavities. We were unable to find such proliferations in our tumors.

Calcification is present in many of the tumors. The amount and degree vary with the individual specimen. In some one sees only scattered islands of calcification, while in others the calcification is widespread. One of our specimens was almost two-thirds calcified. Small calcified concretions are found lying on and in the tumor wall. In other portions the entire tumor wall may be completely calcified.

A feature of some interest is the relation of the pituitary body to the tumor. In none of our necropsy specimens could the pituitary be found. It had probably been so compressed by the advancing tumor that nothing remained of it, or else so little remained of an identifiable nature that it could not be seen on gross examination.

Critchley and Ironside spoke of tumors of high and lower origin, depending on whether they arise from the upper or the lower group of cells described by Erdheim. We have been unable to make a clearcut distinction between these two types of tumor. By the time these cases come to necropsy, the tumor has reached such a large size that it has often spread upward into the third ventricle, regardless of its point of origin.

Microscopic Characteristics.—The description of the adamantinomas by Critchley and Ironside as a "solid epithelial tree with branching and anastomosing offshoots" is particularly apt and to the point. They are composed of epithelial columns which intertwine and anastomose, forming a complicated and often confusing network of columns, among which is a more or less abundant stroma. The amount of the epithelial structure varies a good deal with different tumors. In some it is abundant, in others scarce. The caliber of the columns varies from a very thin cordlike structure to very plump epithelial growths.

The tumors are said to resemble the embryonic enamel organ, and typical sections from the epithelial tree show a basilar layer of columnar cells, a stratum intermedium and a stellate layer. Often, however, these three layers are not seen in the epithelial columns. Either the stratum intermedium is missing, or the stellate layer lacks the absolutely characteristic appearance that it possesses in the enamel organ. The latter is a common observation. The layer of columnar cells is necessary for the diagnosis of an adamantinoma. This basilar layer is spoken of

as the layer of ameloblasts. It has a well defined basement membrane, above which lie columnar cells with oval, elongated nuclei of a vesicular nature, and with poorly defined cytoplasm. Unlike the ameloblasts in the enamel organ, these cells are often not in a single layer but tend to assume a more or less stratified formation. The distinction between one cell and another in this layer is not sharp because the cytoplasm of one cell seems to blend imperceptibly with that of another. Above this ameloblastic layer there sometimes lies a layer of cells, two or three

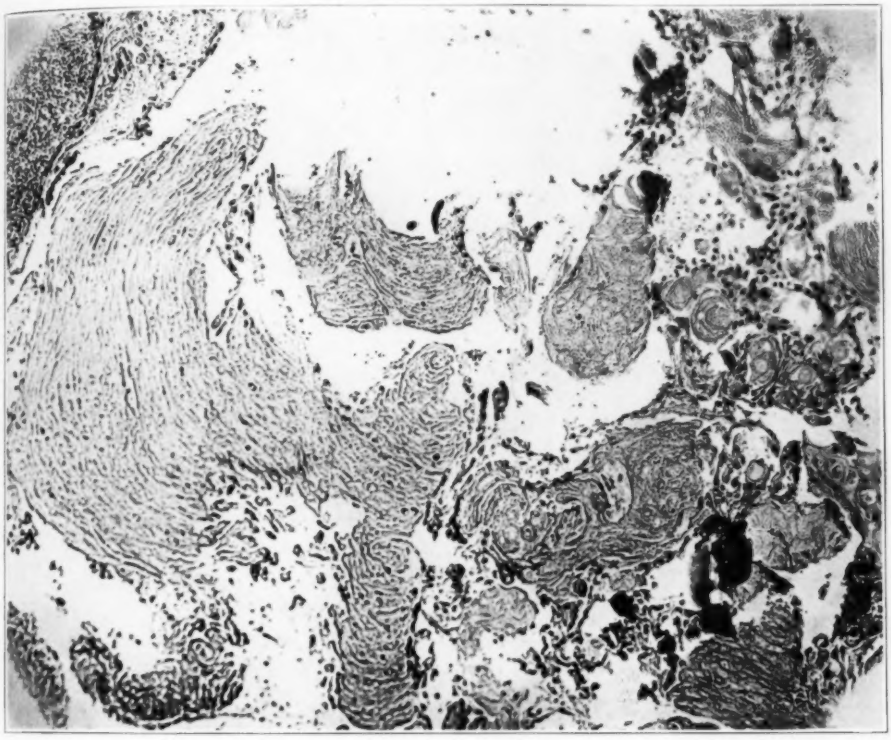

Fig. 48.—In this area the degeneration is widespread and has involved a large part of the tumor. Note the striated appearance of the degenerated areas. Hematoxylin-eosin stain.

cells thick, which lie at right angles to the ameloblasts. These cells have properties similar to the ameloblasts, but they are often lacking in many of the epithelial columns. Above them lies the stellate layer, which forms the pulp, so to speak, of the epithelial columns. These cells, when typical, appear as stellate cells, which form an anastomosing, almost syncytial mass, looking much like primitive mesenchyme. They are often not found in this true stellate arrangement, the center of the epithelial column being made up of cells looking much more like the

cells of the stratum intermedium. The nuclei in the cells of the stellate layer are vesicular and oval. Cytoplasmic bridges are sometimes seen.

The stroma of these tumors varies in abundance. In some it is plentiful, and in others scanty. It is by no means uniform in appearance. In some portions it has a distinctly fibrillar nature; in others it has a myxomatous appearance, and in still others it is almost completely degenerated. The number of cells within the stroma varies widely, but on the whole, cells are not very numerous within it. Many of the cells are of a fibroblastic nature. Often polynuclear cells are found within its meshes, and large, vacuolated cells are often seen.

Evidences of degeneration constitute one of the most constant and interesting features of the adamantinomas. Cysts are present in most of the tumors, sometimes in great abundance, and in others in small numbers. Some tumors are so cystic that they appear to be a conglomeration of cysts lying among epithelial columns. The cysts may be very small or may be so large as to fill almost an entire low power field. They are usually filled with a homogeneous, pink-staining, colloid-like material. Within the stellate layer are often large, swollen, round cells with very small nuclei and with vacuolated cytoplasm. These cells probably represent cells of the stellate layer that have undergone hydropic degeneration. Such cells are sometimes seen in the stroma. Some tumors contain them in large numbers while others have very few of these elements.

In most of the tumors groups of stellate cells are seen that have undergone a sort of hyaline degeneration. These cells are usually compressed, take a homogeneous pink stain, and appear to be definitely degenerated. In some of them small granules of calcium are present, and it is possible that they may undergo calcification eventually. One of our tumors had a tremendous number of these areas. In a few tumors it was possible to see the beginning of this degenerative process in the epithelial nests that are often seen in the epithelial columns, and the possibility exists that these nests may eventually undergo degeneration of the sort described.

Calcification is seen in almost all the tumors. In some it is so abundant that it is seen in every field. In others it is less abundant, but present in such quantities that it can be found without any difficulty. The calcified areas are found in equal degree in the stroma and in the epithelial columns. It is probably more abundant in the former. It is seen as small calcified granules, as a conglomeration of granules, as small flat sheets of calcified material or as large irregular calcified masses. Bone formation is said to occur in some parts of the tumor, but we have not observed it in a tumor of our series.

An important feature of the epithelial columns is the epithelial nests, composed of concentrically arranged cells in the columns. These are extremely abundant in some tumors and in others are a rather unimportant feature. Similar cell collections are sometimes found near the developing tooth in man. Their significance is not clearly understood. Keratinization has been found in some of these cells, but Erdheim denied the presence of keratin granules.

Giant cells have been described in the tumors, but we have not seen them even in areas in which degeneration has been very active. Simi-

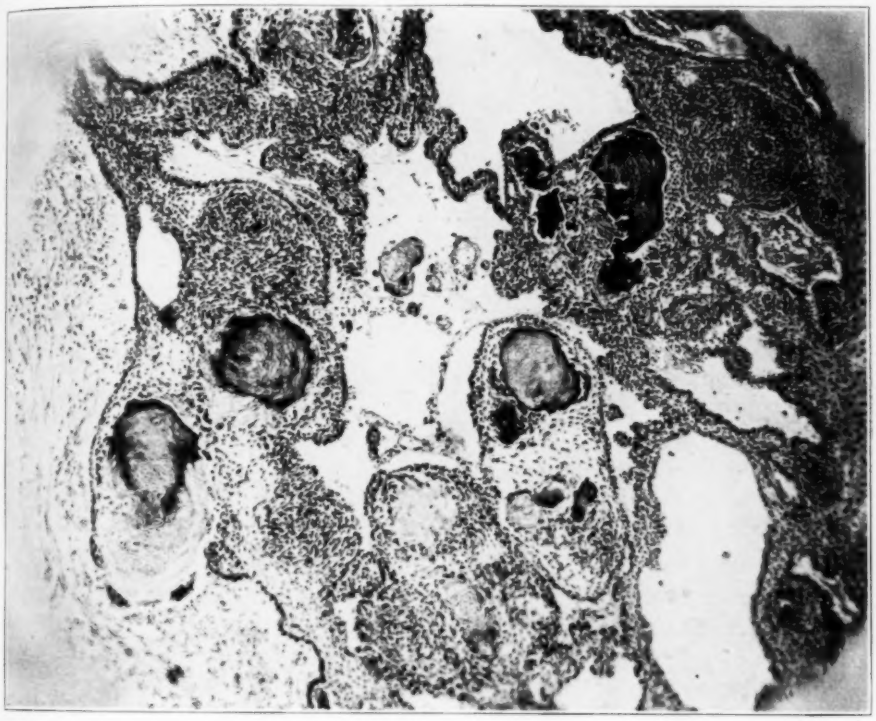

Fig. 49.—The degeneration within the cell nests of the stellate layer is seen, with calcium deposition in some of them. Hematoxylin-eosin stain.

larly, glia cells are said to be present in the stroma, but a careful study of our tumors has failed to reveal the presence of neuroglia cells.

One interesting feature deserves further attention. The similarity of the adamantinomas to the embryonic enamel organ has often been mentioned. In some instances the similarity is striking and in others much less so. In a rough sort of way they resemble the enamel organ, but it is strange that in none of the tumors described has there been found enamel. The ameloblasts of the tumors contain no granules

within their cytoplasm, and the tumor itself possesses no structure that can be said to resemble enamel even remotely.

Origin of the Tumor.—Little need be said of the ontogenesis of these tumors. This has been well described by Duffy, and more recently by Critchley and Ironside. Erdheim has pointed out that in the normal person there are often collections of epithelial cells at the junction of the infundibulum and the base of the brain, and the junction of the infundibulum and the hypophysis. These he considered to be remnants of the embryonic craniopharyngeal duct, and Erdheim was the first to suggest that the adamantinomas are in reality craniopharyngeal duct tumors. In 13 normal adult brains that he examined, Erdheim found epithelial nests in 10 in the situations mentioned. It would be difficult to understand why the cell groups should be found in the locations mentioned did one not know that the pituitary gland rotates during the course of its development, carrying with it the remains of the craniopharyngeal duct 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 or from beneath the capsule of the anterior lobe." Critchley and Ironside have divided the adamantinomas into 2 groups, depending on whether they take origin from the upper or the lower groups of cells. If the tumor arises from the upper group of cells, it lies above the sella, extending upward, pushing before it the floor of the third ventricle, and in some instances filling this entire space and insinuating itself between the thalami. The adamantinomas growing from the lower group of cells lie within the sella, deepening it in all directions and compressing the pituitary. Most of our tumors arose from the lower cell group, but grew to such large size that they occupied positions similar to those coming from the upper cluster of cells also.

Still another possible source of origin of the adamantinomas must be mentioned. It has not been sufficiently emphasized, though theoretically it should be one of the most prolific sources. This is the hypophysis accessoria canalis craniopharyngei found in the body of the sphenoid bone. Here are probably remnants of the craniopharyngeal duct which are capable of giving rise to tumors. That these cells, while potentially neoplastic, are not practically so, is shown by the fact that adamantinomatous tumors involving the sphenoid bone are rare. Indeed we know of no reported instances of this sort.

Ewing stated that "it is impossible to determine where many recorded cases really belong, and quite likely that too many have been referred to misplaced remnants of the hypophyseal duct." He hinted at a com-

mon origin of the adamantinomas, cholesteatomas, dermoids and teratomas.

Classification and Nomenclature.—It is no easy task to classify the type of tumor under consideration. The types of tumors taking origin from the embryonic craniopharyngeal duct include: (1) the adamantinomas; (2) Rathke's pouch tumors, and (3) possibly some teratomas.

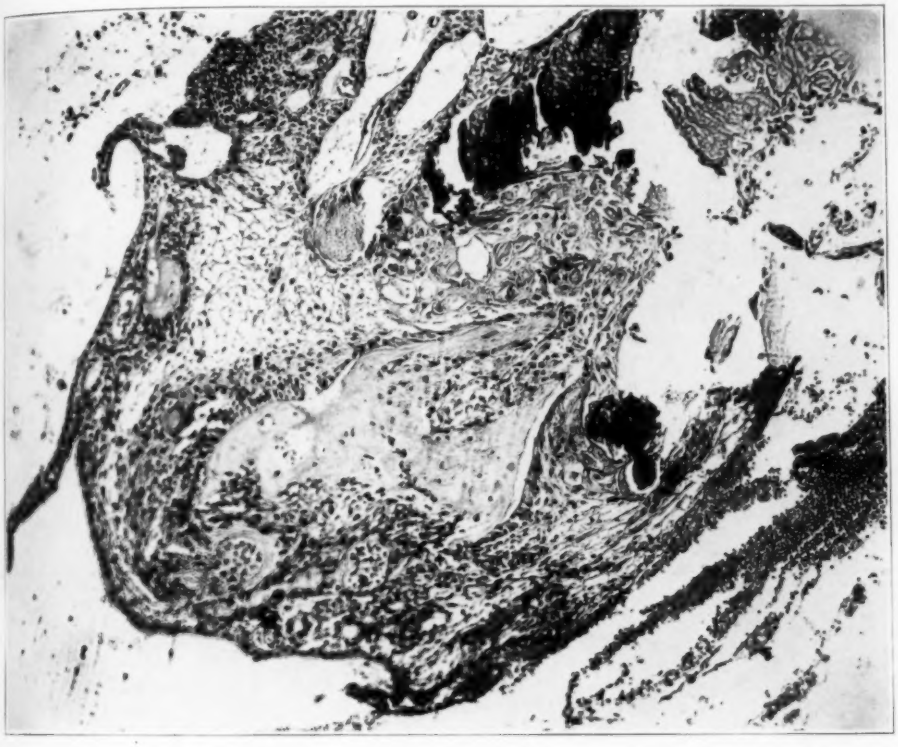

Fig. 50.—The degeneration within the stellate layer is clearly seen. Hematoxlin-eosin stain.

It is not difficult to imagine the course of events in the formation of an adamantinoma from the craniopharyngeal duct. The latter is derived originally from the oral epithelium of the embryo, from which also arises the dental lamina and the embryonic enamel organ. The same group of cells, therefore, gives rise to the enamel organ and the type of tumor that closely resembles this organ in structure. The similarity in some instances is striking and in others less so. On the whole, however, one is probably justified in speaking of these tumors as resembling the enamel organ, at least in its more gross characteristics.

One point of interest that has been demonstrated by our study is that there were fewer true Rathke's pouch tumors in our series than we had supposed. The tumors in question have received many names: craniopharyngeal duct tumors, tumors of the hypophyseal duct, craniopharyngiomas and tumors of Rathke's pouch. The latter, at least in our series, are much less common than we are led to believe. Indeed, there are many fewer tumors of this sort in our verified series than there are adamantinomas. The tumors of Rathke's pouch should show char-

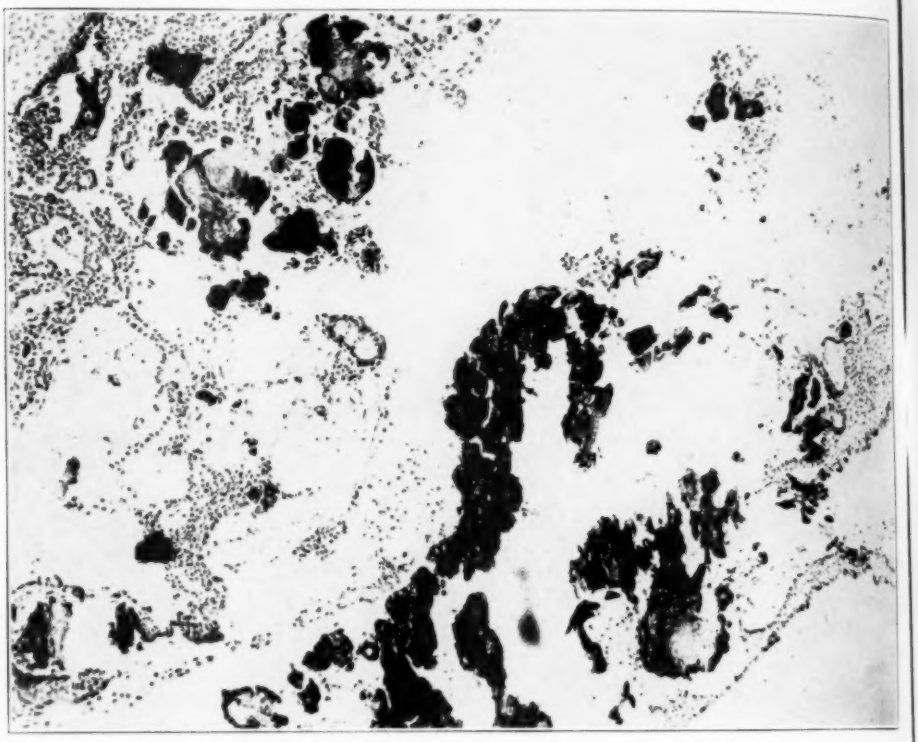

Fig. 51.—Calcification is quite widespread. Hematoxylin-eosin stain.

acteristics different from those of the adamantinomas. As Duffy pointed out, the hypophyseal vesicle or sac is composed of stratified cylindric epithelium, which is said to be ciliated. Tumors composed of this sort of cell have been relatively rare in our experience. In any event, we should separate Rathke's pouch tumors from the adamantinomas because of their different characteristics, even though they take origin from the same region of the brain.

Duffy has suggested that the hypophyseal duct tumors be divided into: (1) benign squamous epithelial cysts; (2) benign or locally

malignant adamantinomatous cystic or solid tumors of the hypophysis or infundibulum (the largest number of craniopharyngeal duct tumors fall into this group); (3) malignant spindle cell carcinomas, which are rare.

More recently, Cornil has advocated the following classification: (1) Rathke's pouch tumors; (2) pharyngo-hypophyseal epitheliomas; (3) teratomas.

It seems to us that the following classification would probably cover the various tumor derivations of the craniopharyngeal duct: (1) adamantinomas or ameloblastomas; (2) Rathke's pouch tumors; (3) carcinomas; (4) teratomas.

The question arises as to the best term by which to designate these various tumor types, particularly the first two. The term craniopharyngiomas has the merit of being noncommittal, particularly in the present state of knowledge and doubt concerning the exact origin of some of these tumors. It is a term that comprises the entire group of tumors which, as we have tried to show, is composed of several types. So far as it fails to designate the various subgroups, it falls short of the mark. As a general term to designate the tumor derivations of the craniopharyngeal duct, it is probably the best term that has yet been proposed.

It seems to us that a better term should be available than that of the adamantinomas which comprises a large part of the tumors under consideration. The term is descriptive, but not wholly satisfactory. Ameloblastoma is probably a better name for the tumors. It has the merit of designating the type of cell that is characteristic of the tumor and of implying the similarity that the tumor bears to the enamel organ. It conforms, moreover, to the present tendency to designate tumors by the type of cell which comprises the tumor, and which by histochemical differentiation gives rise to the tumor proper. It is somewhat misleading in that while ameloblasts are present, no enamel has yet been discovered in these neoplasms.[10]

Until more is known about the histologic characteristics of Rathke's pouch tumors, we cannot give them a better name. The present term, however, is decidedly unsatisfactory.

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10. The use of the term ameloblastoma was first suggested by Soy and Churchill in an article entitled "The Need of a Standardized Surgical and Pathological Classification of the Tumors and Anomalies of Dental Origin," published in the Transactions of the American Association of Dental Teachers, 1929.

SQUAMOUS EPITHELIAL RESTS IN THE HYPOPHYSIS CEREBRI *

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The presence of groups of cells resembling squamous epithelium in the hypophysis cerebri, and the occurrence of tumors in the hypophysis and infundibulum, the histologic appearance of which resembles that of these rests, are of interest because of the support they afford to Cohnheim's well known embryonal theory of the origin of new growths. It is my purpose in this paper to report the results of examination of the normal hypophysis removed at necropsy in a group of fifty-five cases. The infundibular region was studied in serial sections for squamous epithelial rests.

As knowledge of the development of the hypophysis is essential for an understanding of these rests, a short description of the steps in the development of the gland, in particular of the pars buccalis, will first be given. Throughout this paper, Tilney's nomenclature [1] for the different parts of the hypophysis will be followed.

The hypophysis is developed from two sources: (1) an upward evagination of the roof of the primitive oral cavity and (2) a downward evagination from the floor of the diencephalon. From the former is derived the pars buccalis, and from the latter the pars neuralis. The development of the pars buccalis from the primitive oral cavity was first suggested by Rathke [2] in 1838. For this reason, the upward evagination from the roof of this cavity has since been known as Rathke's pouch. It was not until 1875 that von Mihalkovics [3] demon-

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* Abstract of thesis presented to the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Neurology, 1930. Work done in the Section on Pathologic Anatomy, the Mayo Clinic, Rochester, Minnesota.

1. Tilney, Frederick: An Analysis of the Juxta-Neural Epithelial Portion of the Hypophysis Cerebri, with an Embryological and Histological Account of a Hitherto Undescribed Part of the Organ, Internat. Monatschr. f. Anat. u. Physiol. **30**:258, 1914.

2. Rathke, H.: Ueber die Entstehung der Glandula pituitaria, Arch. f. Anat., Physiol. u. Wissensch. Med. **5**:482, 1838.

3. von Mihalkovics, Victor: Wirbelsaite und Hirnanhang, Arch. f. mikr. Anat. **11**:389, 1875.

strated the various steps in development of the pars buccalis from Rathke's pouch in dogs. He showed that Rathke's pouch is connected at first by a hollow stalk, the hypophyseal duct, to the primitive oral cavity. He demonstrated that the pars distalis arises from the anterior layer of Rathke's pouch, and that the pars infundibularis is derived from the posterior layer of this pouch. He pointed out that the hypophyseal duct is lined with low cuboidal epithelium, whereas Rathke's pouch is lined with stratified cylindric epithelium. The hypophyseal duct disappears as the development of the pars buccalis proceeds, and the place where it was attached to Rathke's pouch in the early stage corresponds, in the adult gland, to a small area above the pars distalis and anterior to the lower part of the infundibulum, where the two merge into one another. Tilney, in 1913, called attention to the layer of glandular tissue that lies along the anterior surface of the infundibulum and surrounds the eminentia saccularis. For this he suggested the name "pars tuberalis." Atwell,[4] in 1926, investigated the hypophyseal region in a series of human embryos and fetuses, paying special attention to the pars tuberalis. Waterston,[5] in 1927, reported the results of his studies of the development of the hypophysis cerebri in the human being. Atwell showed that the pars tuberalis arises from two lateral outgrowths near the attachment of the primitive hypophyseal duct to Rathke's pouch, which fuse across the median line anteriorly, and which grow forward, backward and upward over the infundibulum and eminentia saccularis.

From the floor of the third ventricle downward to the region of the thyroid gland, rests of the various structures present in the human embryo have been described, and tumors arising from these rests have been reported in the literature.

Erdheim,[6] in 1904, at the time when he published his monograph on hypophyseal duct tumors, reported finding squamous epithelium in the region of the hypophysis and infundibulum in ten of a group of six newly born infants, one fetus and thirteen adults on whom studies were made by means of serial sections through the hypophysis. He

4. Atwell, W. J.: The Development of the Hypophysis Cerebri in Man, with Special Reference to the Pars Tuberalis, Am. J. Anat. **37**:159 (March) 1926.

5. Waterston, D.: The Development of the Hypophysis Cerebri in Man, with a Note upon Its Structure in the Human Adult, Tr. Roy. Soc. Edinburgh **55**:125 (May 20) 1927.

6. Erdheim, J.: Ueber Hypophysenganggeschwülste und Hirncholesteatome, Sitzungsb. d. k. Akad. d. Wissensch. in Wien **113**:537, 1904; I. Ueber Schilddrüsenaplasie. II. Geschwülste des Ductus thyreoglossus. III. Ueber einige menschliche Kiemenderivate, Beitr. z. path. Anat. u. z. allg. Path. **35**:366, 1904; Ueber einen Hypophysentumor von ungewöhnlichen Sitz, Beitr. z. path. Anat. u. z. allg. Path. **46**:233, 1909.

believed this epithelilum to be rests of the former hypophyseal duct. He found no rests in the six newly born infants and in the one fetus. Kiyono,[7] in 1924, investigated a group of fifty subjects by making serial sections through the infundibulo-hypophyseal region, and found squamous epithelium in seventeen of them. He found no rests in subjects who were less than 20 years of age at the time of death, and accepted Erdheim's explanation as to the origin of the rests.

METHODS AND MATERIALS

The hypophysis cerebri and the infundibulum were removed from the brain, attached together if possible. The specimen was fixed in commercial formaldehyde, 10 per cent, for at least twenty-four hours. As the majority of the rests described by Erdheim and by Kiyono were situated in the median line, near the infundibulum and the upper surface of the pars distalis, the lateral thirds of the gland were removed before the specimen was embedded in paraffin. The specimen was cut in serial sections 15 microns thick. Every fifth section was stained with hematoxylin and eosin and was mounted on a slide. The remaining sections were saved. The stained sections were examined under the microscope. If masses of squamous epithelium were found in any of the sections, the unstained sections immediately preceding and following the particular section were also stained and examined. In some of the latter sections, van Gieson and thionine stains, and Orlandi's modification of Bielschowsky's silver impregnation method, were used. In one case Bailey's natural ethyl violet orange-G stain was employed.

The specimens were not selected, except so far as to exclude the obviously abnormal hypophysis. In the great majority of the specimens, the infundibulum and gland were attached together. The age of the subjects at death varied from 1 hour to 99 years. The group included thirty-nine males and sixteen females. The causes of death were many and varied.

RESULTS

In eighteen of the fifty-five cases (32.7 per cent), masses of cells resembling squamous epithelium were found. Masses were not found in the nine subjects who were less than 20 years of age at the time of death. Thus, among the forty-six adults, squamous epithelial masses occurred in 39.1 per cent. These eighteen cases have been divided into three groups: (1) those in which the masses of cells appeared to be almost exactly like squamous epithelium; (2) those in which the masses resembled squamous epithelium, and (3) those in which there is some doubt as to the masses being squamous epithelium.

In the first group, the masses were rounded, oval or elliptic, and there was a peripheral layer of flattened cells, with small, darkly staining nuclei and little cytoplasm, which surrounded a central mass of larger, more lightly staining cells, with more cytoplasm and oval or

7. Kiyono, H.: Ueber das Vorkommen von Plattenepithelherden in der Hypophyse (zugleich ein Beitrag zur Kenntnis der Hypophysenganggewächse), Virchows Arch. f. path. Anat. **252**:118, 1924.

elliptic nuclei. Most rests of this type were found on the anterior aspect of the infundibulum, beneath the capsule. Whorl-like clusters of cells sometimes were seen. In one case there was a suggestion of intercellular bridges, but such bridges could not be positively identified in any case (Erdheim, in the course of his study, had been able to find intercellular bridges). In the second group, the masses were elongated in the form of cordlike strands or were irregular in shape, and occurred within or without the capsule of the hypophysis. There was a peripheral layer of cells, which was less distinct than that seen

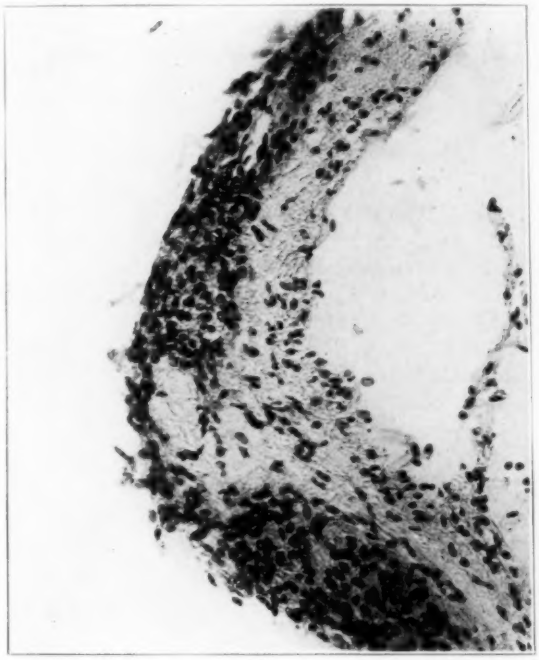

Fig. 1.—Thickening of the arachnoid; a mass of cells that might be confused with squamous epithelial rests may be seen. Hematoxlin and eosin; × 225.

in the first group. The central mass of cells was more irregularly arranged; the nuclei stained either deeply or lightly, and varied somewhat in size. Whorl-like clusters of cells were seen. The cytoplasm was less in amount than in the first group. In the third group, the masses were of various shapes, and might lie within or without the capsule of the hypophysis. The arrangement of the cells resembled that seen in the first and second groups, but was much more irregular. The nuclei stained deeply; the cytoplasm was much less in amount. Whorls

were not seen. The structure of the masses, which apparently were squamous epithelial in type, corresponded closely to the descriptions given by Erdheim and by Kiyono. In one instance, in the center of a mass of cells, there was the beginning of a cyst. It was difficult, in some instances, to decide whether or not the clusters encountered were squamous, epithelial-like masses. The difficulty has been, for the most part, in distinguishing the clusters of cells or thickenings that are present in the arachnoid, here as well as in other situations throughout the cerebrospinal system, from the groups of squamous epithelial

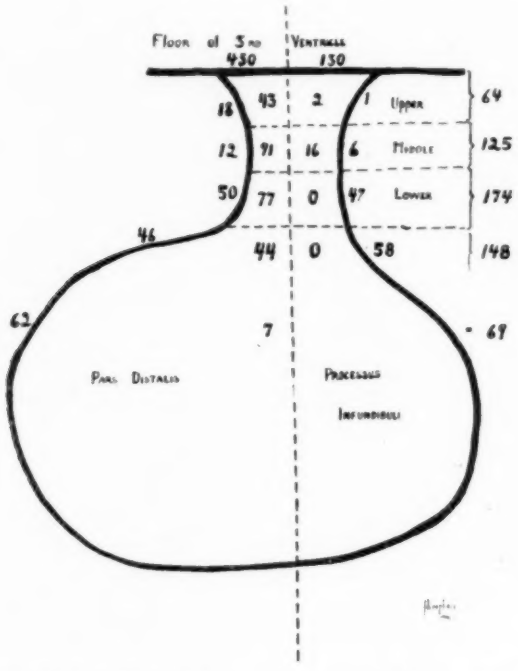

Fig. 2.—Midsagittal section of the hypophysis cerebri to show the situation of the rests of the hypophyseal duct, which apparently were squamous epithelial in type.

cells. The histologic appearance of these thickenings of the arachnoid (fig. 1) resembled that of the groups of squamous epithelial cells. Since there is no means of positively identifying squamous epithelium by staining reactions or otherwise, it may be almost impossible to decide which tissue is in hand. The thickening occurred, for the most part, along the course of a layer of arachnoid or along one of the arachnoid trabeculae, which usually were somewhat farther away from the hypophysis than the rests were likely to be. They consisted of irregularly arranged groups of small, darkly stained cells, varying in size and

shape, with very little cytoplasm as compared with the cells of the squamous epithelial masses, and with indistinct cellular outlines, which occurred at intervals along the course of a layer of arachnoid (fig. 1).

The total number of masses seen has been estimated, and the masses have been grouped as to their situation, according to the divisions of the infundibulum made by Kiyono. This division consists of upper, middle and lower thirds of the infundibulum in a transverse direction and of anterior and posterior parts in a longitudinal direction. Figure 2 is a diagrammatic representation of these different divisions, and in

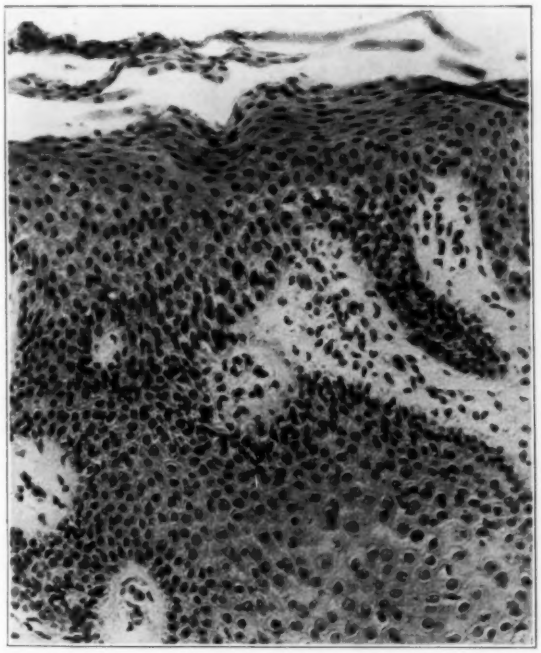

Fig. 3.—Epidermis. Hematoxylin and eosin; × 185.

numerals is given the incidence of masses found in each of the six divisions, as well as the incidence in or near the upper surface of the pars distalis and processus infundibuli (posterior lobe).

The masses predominated in or near the median line, anterior to the infundibulum or in the anterior part of it, and toward the lower third of the infundibulum and the upper part of the pars distalis.

Figure 3 represents squamous epithelium of the epidermis, figure 4 a tumor of the hypophyseal duct and figure 1 an arachnoidal thickening. There is a resemblance between these three structures and the epithelial rest (fig. 5).

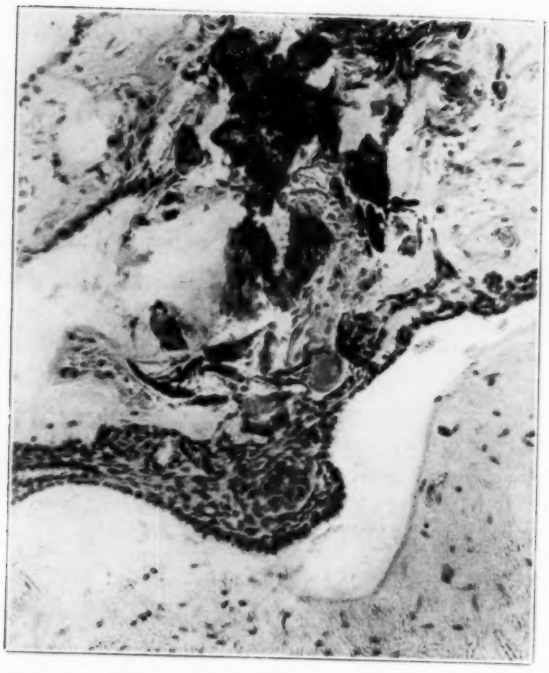

Fig. 4.—Tumor of the hypophyseal duct. Hematoxylin and eosin; × 160.

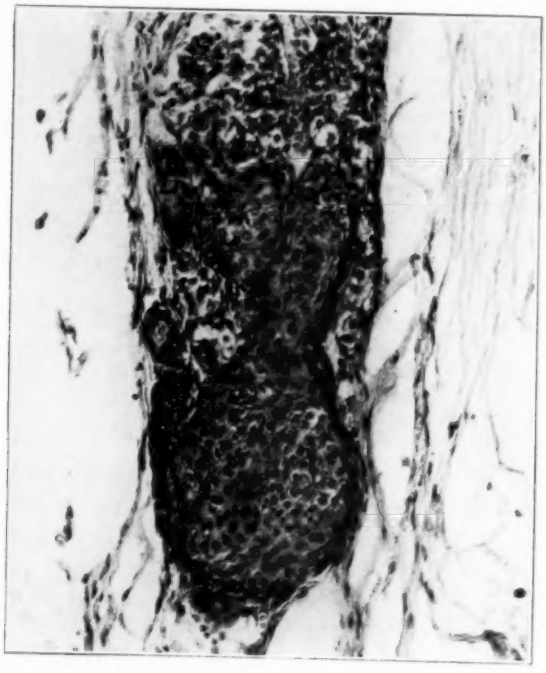

Fig. 5.—Squamous epithelial-like rest along the anterior aspect of the infundibulum, type 1. Hematoxylin and eosin; × 185.

COMMENT

As far as I am aware, there is no method by which squamous epithelium can be definitely identified. Various stains were tried, but were not helpful. Because of this fact, the results of this study are not final. The same applies to the results obtained by Erdheim and by Kiyono.

Whether or not these masses of cells, resembling in their appearances the lower layers of the epidermis that are seen in the region of the hypophysis cerebri, may be considered as arising from remnants of the lining epithelium of the embryonic hypophyseal duct, it is hard to say. The fact that the duct is lined with a low cuboidal epithelium, whereas the masses of cells here described are apparently squamous epithelium, must be taken into account. Erdheim has suggested that since the epithelium that lines the hypophyseal duct and the epithelium of the primitive buccal cavity merge without apparent differences, and since the epithelium of the primitive oral cavity in adult life is of the squamous epithelial type, it is possible that the lining epithelium of the primitive duct might, if any remnants were left behind when the duct disappeared, also become of the squamous epithelial type. If a simple type of epithelium may in some way or other become of a more complex type, then it is possible that these masses of apparent squamous epithelium seen in the region of the hypophysis may be derived from the lining epithelium of the primitive hypophyseal duct. There is a difference of opinion as to whether such a transformation, from a simple to a more complex type of tissue, does occur.

The manner in which rests of the former hypophyseal duct gain the sites in which they are found in the adult might be questioned. In the development of the hypophysis, the site of insertion of the hypophyseal duct into the primitive Rathke's pouch appears to have been carried upward and forward with the developing pars tuberalis, and to have come to lie in the region of the lower third of the infundibulum and the upper surface of the pars distalis, anterior to the infundibulum, in or near the median line. It is in this situation that most of the masses of cells resembling squamous epithelium are found, and it is here that some of the so-called tumors of the hypophyseal duct apparently arise. It may be that remnants of the former duct are carried along to this new site in this development of the pars tuberalis. This is the explanation given by Erdheim of the occurrence of the squamous epithelial-like masses in this situation.

It is interesting to note that more masses of cells apparently of squamous type were found in this study, nearer to the upper surface of the pars distalis and to the lower third of the infundibulum, than were found toward the upper third of the infundibulum.

It was suggested by Atwell, in his article on the development of the hypophysis of man, that possibly some of the tumors of the hypophyseal duct might have arisen from the pars tuberalis. In the sections examined in this study, there was a distinct difference between the histologic appearance of the rests and that of the pars tuberalis. It would therefore be expected that tumors arising from the pars tuberalis would not have an appearance under the microscope similar to that seen in tumors of the hypophyseal duct.

Erdheim, Kiyono and I failed to find any rests in specimens from subjects of less than 20 years of age. Erdheim explained the apparent absence of squamous epithelium in his group of one fetus and six newly born babies by suggesting that there was incomplete differentiation of the cells at that time of life. Kiyono accepted this explanation as being applicable to the specimens for nine subjects of less than 20 years of age in which he did not find squamous epithelial rests. It may be that this explanation is correct. It is conceivable that the squamous epithelial cells in infancy and adolescence may be present in very small groups of two or three cells only, and may be undifferentiated from the other epithelial cells in the neighborhood. In adult life differentiation of the cells and increase in the number of cells in a group may take place, thus enabling them to be recognized as squamous epithelium. It might be noted that the so-called tumors of the hypophyseal duct characteristically occur in children and adolescents, whereas they are relatively less common in adults (Cushing, 1927).[8] To correlate this fact with the apparent absence of the squamous epithelial rests in subjects who are less than 20 years of age, and the frequent presence of the rests in adults, seems difficult unless the explanation just given is used.

The small number of subjects who were less than 20 years of age in each of the three series (Erdheim's, Kiyono's and mine) might be offered as a possible reason for the failure to find rests in these cases. In all three series taken together, twenty subjects were in the age group 0 to 10 years, and five in the age group 10 to 20 years. From this it might be argued that if more subjects who were between the ages of 10 and 20 years had been examined, the probability of finding squamous epithelial rests would have been greater.

It is well known that many changes in the histologic structure of the various ductless glands occur at puberty. It might be postulated that similar changes may occur at this time in the rests of the former hypophyseal duct, so that they become recognizable in adult life, although previously seemingly absent on microscopic examination.

8. Cushing, Harvey: The Intracranial Tumors of Preadolescence, Am. J. Dis. Child. **33**:551 (April) 1927.

Judging from the apparent absence of rests of an apparently squamous epithelial type, in the hypophysis, in subjects less than 20 years of age, it is within the realm of possibility that the rests may not be derived from embryonic structures.

SUMMARY

1. The normal hypophysis removed at necropsy in a group of fifty-five cases was studied by means of serial sections. Masses of cells resembling squamous epithelium in histologic appearance were found in eighteen cases (32.7 per cent).

2. In the nine subjects who were less than 20 years of age, groups of cells resembling squamous epithelium were not found.

3. The incidence of these masses of cells, which apparently were squamous epithelial in type, among the forty-six adult subjects was 39.1 per cent.

4. It seems reasonable to attribute the origin of these groups of cells, which apparently were squamous epithelial in type, to rests of the former hypophyseal duct, and to accept their relation to the so-called tumors of the hypophyseal duct; that is, if it is accepted that the rests cannot be identified in subjects who have not reached the age of 20 years, because at that time the cells of the rests are not sufficiently differentiated from the other epithelial cells in the neighborhood.

THE HISTOPATHOLOGY OF TRIORTHOCRESYL PHOSPHATE POISONING

THE ETIOLOGY OF SO-CALLED GINGER PARALYSIS (THIRD REPORT) *

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AND
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In the first paper of this series [1] there was described a peculiar and new type of multiple neuritis which afflicted thousands of victims during the winter and early spring months of 1930. It appeared that the disease had resulted following the consumption of an adulterated fluidextract of ginger used for beverage or other purposes. In that paper consideration was given to the possible causes of the partial paralysis, and experiments were presented which indicated that a phenolic compound, demonstrated to be present only in samples of the adulterated ginger extract that caused cases of paralysis, was probably the immediate cause of the disease.

Subsequent work [2] fully confirmed these early tentative conclusions. Pharmacologic examination of the available phosphoric esters of the better known phenols, viz., orthocresol and paracresol, and of phenol itself showed conclusively that the phosphate of orthocresol alone had this specific action on the neuromuscular apparatus. Since this was published, the phosphoric ester of metacresol and several other esters of orthocresol have been examined, as shown in figure 1, with the result that the phosphoric acid ester of orthocresol appears to be the only compound so far found capable of reproducing in lower animals the symptom-complex as it occurred in man. The evidence for this, together with a more detailed analysis of the relation of chemical structure to pharmacologic action in so far as it concerns this particular group of phenol compounds, will be described elsewhere.

The clinical manifestations of the paralysis due to the consumption of an adulterated fluidextract of ginger, which were previously described in considerable detail,[1] point to a lower motor neuron involve-

* Submitted for publication, March 31, 1931.

1. Smith, M. I., and Elvove, E.: Pub. Health Rep. **45**:1703, 1930.

2. Smith, M. I.; Elvove, E., and Frazier, W. H.: Pub. Health Rep. **45**: 2509, 1930.

ment. It does not seem possible, however, to ascertain clinically the exact anatomic seat of the lesion of the neuromuscular apparatus. A systematic study was therefore undertaken on this phase of the problem, and the present report is the outcome of this investigation.

There have appeared recently several papers on the histopathology of paralysis due to adulterated fluidextract of ginger in man, the cases having come to autopsy apparently through causes other than the effects of the specific poison on the neuromuscular apparatus.

Jeter,[3] describing an autopsy on a patient who seemed to have died of cerebral edema and nephritis, gave thickening and edema of the meninges, perineural exudate in the cauda equina, thickening and fibrosis of the perineurium of the preipheral nerves and endarteritis of the vessels of the central nervous system as the essential changes.

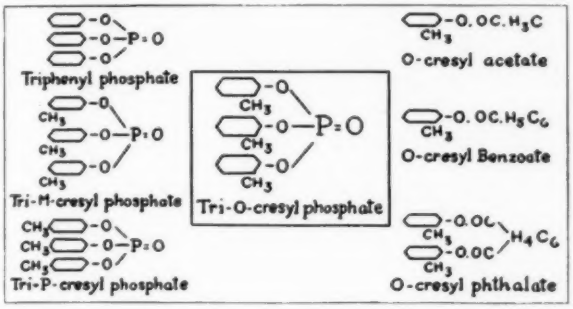

Fig. 1.—Structural formulas of various compounds mentioned in this article.

Bowden, Turley and Shoemaker,[4] reporting apparently on the same case as Jeter and on one other, in which the patient died of uremia, obtained by special methods of staining evidence pointing to degenerative changes in some of the anterior horn cells of the lumbar, upper thoracic and lower cervical regions of the cord. Similar changes were also found by these investigators in the medulla and the nuclei of the floor of the fourth ventricle. Marchi stains of the sciatic nerve revealed blackening in many fibers in both cross-sections and longitudinal sections.

More recently, Goodale and Humphreys [5] reported their observations in three cases of paralysis due to adulterated fluidextract of ginger at the Worcester City Hospital. In one case they found acute perineuritis

3. Jeter, H.: Autopsy Report of a Case of So-Called Jake Paralysis, J. A. M. A. **95**:112 (July 12) 1930.

4. Bowden, D. T.; Turley, L. A., and Shoemaker, H. A.: Am. J. Pub. Health **20**:1179, 1930.

5. Goodale, R. H., and Humphreys, M. B.: Jamaica Ginger Paralysis, J. A. M. A. **96**:14 (Jan. 3) 1931.

of the cauda equina somewhat similar to that in Jeter's case. The lesions considered characteristic by Goodale and Humphreys, however, were those of the peripheral nerves and of the anterior horn cells of the spinal cord. The nerve lesions were marked by degeneration of the myelin sheaths with occasional fusiform enlargement of the axis cylinders. The changes of the anterior horn cells were characterized by occasional absence of the nucleolus, migration of the nucleus to the periphery and formation of fine fatty granules in the cytoplasm.

The present work is a systematic study of the histopathology of triorthocresyl phosphate poisoning in a variety of experimental animals, and a comparison thereof with the pathologic changes in several cases of human paralysis due to adulterated fluidextract of ginger. The material from the human cases was made available to us through the cooperation of Prof. R. S. Austin of the Medical School of the University of Cincinnati. There were in all six cases, all the patients having died at the Cincinnati General Hospital of intercurrent diseases after several weeks of sojourn at the hospital to which they had been admitted for observation and treatment of paralysis of the extremities acquired as a result of drinking adulterated Jamaica ginger extract.

Our experimental material comprised a variety of laboratory animals used throughout the investigation on the etiology of paralysis due to adulterated fluidextract of ginger. Much of this material was obtained before the immediate cause of the paralysis was definitely ascertained. Our material therefore represents a variety of experimental procedures, in addition to the actual production of partial motor paralysis of the extremities by means of the adulterated ginger extract that had given rise to cases of paralysis in man or by the administration of triorthocresyl phosphate, either chemically pure or as isolated from the adulterated ginger extract. Only such material, however, as is likely to have a direct bearing on the present problem, together with what appears to be a sufficient number of controls, is included in this report. Because of the characteristic clinical manifestations of the disease process, the examination of the tissues was usually limited to certain parts of the central nervous system. In many cases some of the viscera and striated muscle were also examined. Attention will be called to these whenever the observations present points of interest.

TECHNIC

The routine procedure was to remove the tissues as shortly after death as possible, or immediately after the animal was killed. The tissues were then placed in a 10 per cent solution of commercial formaldehyde and submitted for examination under a key number to the pathologic laboratory, where nothing was known about the treatment or the clinical history of the animals from which the tissues had been removed. Primary fixation of all material in formaldehyde lasted several days.

Blocks were cut routinely, in duplicate, from three levels of the cord, lumbar, thoracic and cervical, and from the medulla, pons, cerebellum and midbrain through the oculomotor nerve roots and anterior colliculi. In the earlier phases of the work, blocks were also taken from the posterior portion of the thalamus, from the corpus striatum and from frontal, parietal, occipital and temporal regions of the cerebral cortex, as well as from the cornu ammonis; this was discontinued in later work as no significant changes were discerned. One set of blocks was hardened further for forty-eight hours in a 2.5 per cent solution of potassium bichromate, followed by 50 and 80 per cent alcohol, completion of dehydration in acetone, clearing in benzene, and embedding in paraffin in vacuo for twenty minutes. These blocks were sectioned at from 5 to 8 microns and stained routinely with toluidine blue for Nissl bodies and with Weigert's acid iron-hematoxylin and van Gieson's picrofuchsin for nerve tissues. The second set of blocks was impregnated in several changes of a 2.5 per cent solution of potassium bichromate for seven or eight days, then for a further seven days in two parts of a 2.5 per cent solution of potassium bichromate and one part of a 1 per cent solution of osmic acid, washed overnight, and dehydrated, cleared, embedded and sectioned as already

TABLE 1.—*Histopathology of the Paralysis Due to Adulterated Fluidextract of Ginger in Man*

		Nerve Lesions: Tigrolysis or Fatty Degeneration			
		Spinal Cord		Peripheral Nerves	
Case	Cause of Death	Nerve Cells*	White Substance	Roots	Nerves
N30189	Chronic nephritis; pulmonary tuberculosis; cerebral edema	+	+	+	..
N30197	Acute nephritis; pyelitis; pulmonary tuberculosis	−	Slight	+	..
N30257	Pneumonia; acute fibrinous pleuritis	−	++	+	..
N30258	Coronary sclerosis	−	Slight	Slight	..
N30278	Acute nephritis; cystitis; chronic meningitis	−	+	+	+
N30279	Pulmonary infaret; cardiac dilatation	−−	+	+	+

* Tigrolysis and fatty degeneration.

described. These sections were either lightly counterstained by various methods or, more often, were studied unstained.

Material from peripheral nerves was also blocked in duplicate, one set being treated by the Marchi procedure outlined, the second being embedded in a routine manner in paraffin and stained with hematoxylin and eosin, iron-hematoxylin and van Gieson's method and with other stains as they appeared indicated.

Various gold methods and supravital methylene blue (methylthionine chloride U. S. P.) were tried for the study of terminal ramifications and motor end-plates, but the results proved so uncertain that for the present it was deemed futile to attempt to estimate quantitative or qualitative changes in these structures.

The histologic observations were then reported back to the pharmacologic laboratory and there correlated with the clinical manifestations that resulted from the particular experimental procedure.

RESULTS

The results of the investigations are summarized in the accompanying tables. The lesions observed in the human cases, outlined in table 1, were characterized by some involvement of the anterior horn cells

and in most cases by considerable fatty degeneration of the white substance in the cord, as revealed in Marchi preparations. Changes of the nerve cells, which were most pronounced in case N30279, were marked by some tigrolysis, displacement of the nucleus to the periphery, deposition of clumps of Marchi-positive droplets in the cytoplasm, and distinct evidence of cytoplasmic disintegration in some cells, especially at their periphery (figs. 2 and 3). The changes in the peripheral nerves were, on the whole, perhaps more constant and more pronounced,

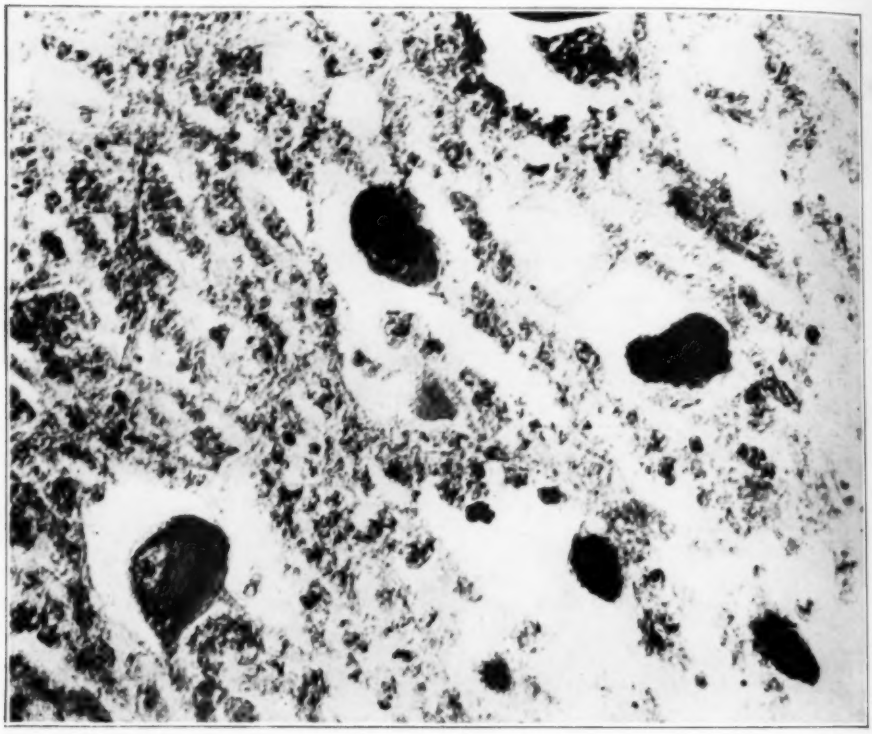

Fig. 2 (case N30279).—Photomicrograph of a section of the spinal cord, lumbar region; Marchi method. Note the fatty degeneration of some of the anterior horn cells and the nuclear displacement; × 400.

judging from an examination of the spinal nerve roots. The changes were well marked fragmentation and fatty degeneration of the myelin sheath, which involved groups of fibers throughout the nerve trunks (fig. 4). Unfortunately, the smaller peripheral nerves were available only in two cases. The nerve roots, however, were studied in all cases and were found to present the same picture as the small peripheral nerves.

In table 2 are presented the results of a similar study in the dog. It will be seen from the data in this table that the partial flaccid paralysis of the extremities produced by the subcutaneous injection of 0.5 Gm. or more per kilogram of technical or chemically pure triorthocresyl phosphate resulted in lesions of the nervous system comparable with those seen in the human paralysis due to the consumption of adulterated fluidextract of ginger. Figure 5 shows the fatty degeneration and nuclear displacement seen in some of the anterior horn cells

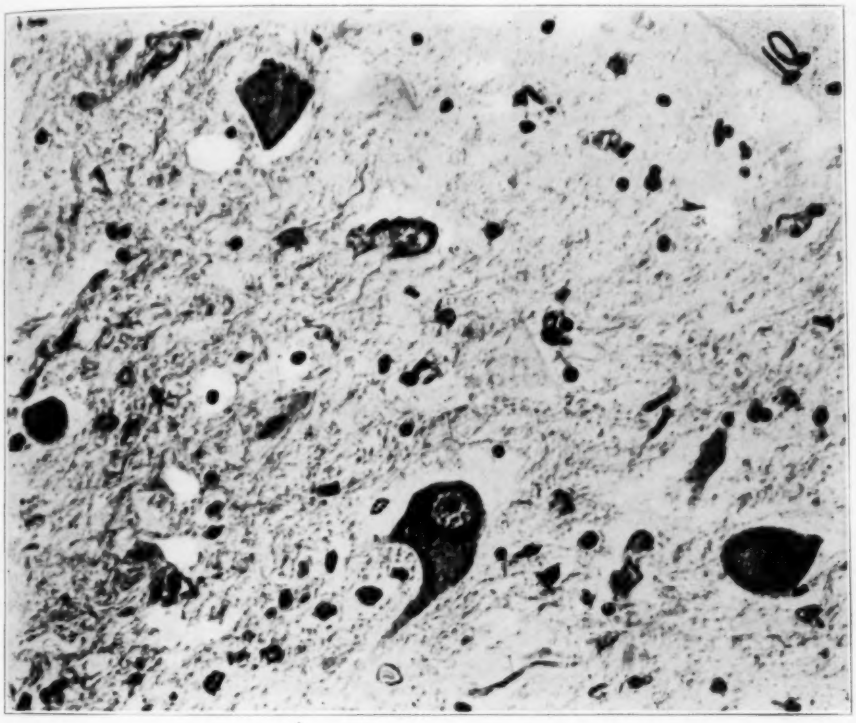

Fig. 3.—Same section as in figure *2*; iron hematoxylin and van Gieson's stain. It shows nuclear displacement, some chromatolysis and peripheral clumping of the tigroid bodies in some cells; × 400.

of dog 13 of the series, which compare well with the lesions shown in figure 2. It is to be noted, however, that the lesions of the spinal cord in the dog were rather variable, and in one instance could not be demonstrated at all. The lesions of the peripheral nerves, however, were constant and of a degree entirely comparable with those seen in the human cases.

Attention may also be called to the fact that chronic alcohol or phenol poisoning in the dog produces neither the clinical picture nor,

as a rule, the pathologic lesions produced by the phosphoric acid ester of orthocresol.

Table 3 summarizes the results of our studies in monkeys (Macacus rhesus). The interval between the administration of the drug and the appearance of the clinical symptoms of paralysis is not definite in every instance, since in some of the experiments the specific ester was injected in two or more doses and it is not possible to state whether paralysis resulted from the first or the last injection. In all eleven monkeys

Fig. 4 (case N30279).—Photomicrograph of a section of a peripheral nerve (tibial); Marchi method. The diffuse fragmentation and degeneration of the myelin sheath are conspicuous; × 400.

that received subcutaneous injections of the chemically pure or technical triorthocresyl phosphate or the ester isolated from the incriminated adulterated fluidextract of ginger, typical motor paralysis of the extremities developed. Lesions of the peripheral nerves were demonstrable in all but one case; well marked tigrolysis or fatty degeneration, or both, of the anterior horn cells in at least seven of the eleven animals, and some fatty degeneration of the white substance in the cord in six

TABLE 2.—*Histopathology of Triorthocresyl Phosphate Poisoning in the Dog*

No.	Weight, Kg.	Treatment; Gm. per Kg. Body Weight	Effect: Interval, Days	Effect: Paralysis, Days	Nerve Lesions; Tigrolysis or Fatty Degeneration: Spinal Cord: Nerve Cells	Spinal Cord: White Substance	Peripheral Nerves: Roots	Peripheral Nerves: Nerves
13	9.1	1.6 technical triorthocresyl phosphate subcutaneously	10	2	++ TF*	—	+	+
12	7.3	1.0 technical triorthocresyl phosphate subcutaneously	5	8	++ T	+	+	++
6	10.5	1.5 technical triorthocresyl phosphate subcutaneously	18	30	+ F	+	+	Slight
14	10.9	1.0 technical triorthocresyl phosphate subcutaneously	30	33	+ F	—	Slight	Slight
8	12.7	0.4 chemically pure triorthocresyl phosphate subcutaneously	7	1	+ F	+	+	++
9	7.3	0.6 chemically pure triorthocresyl phosphate subcutaneously	20	2	—	—	+	+
17	11.0	1.0 chemically pure triorthocresyl phosphate subcutaneously	7	1	+ T	+	+	+
18	4.6	70 95% alcohol per os, in 10 doses during an interval of 23 days	—	—	—	—	—	—
19†	5.7	70 95% alcohol per os, in 10 doses during an interval of 23 days	—	—	—	Slight	Slight	+
20	7.7	1.9 phenol per os, in aqueous 1% solution, divided in 8 doses over a period of 16 days	—	—	—	—	—	—
21	10.0	1.9 phenol per os, in aqueous 1% solution, divided in 8 doses over a period of 16 days	—	—	—	—	Slight	Slight

* T, tigrolysis; F, fatty degeneration.
† Animal showing meningomyelo-encephalitis and visceral focal lesions suggestive of distemper.

TABLE 3.—*Histopathology of Triorthocresyl Phosphate Poisoning in the Monkey*

No.	Weight, Kg.	Treatment; Gm. per Kg. Body Weight	Effect: Interval, Days	Effect: Paralysis, Days	Nerve Lesions; Tigrolysis or Fatty Degeneration: Spinal Cord: Nerve Cells	Spinal Cord: White Substance	Peripheral Nerves: Roots	Peripheral Nerves: Nerves
17A	3.7	2.0 technical triorthocresyl phosphate subcutaneously	2-13	2	+ TF*	—	+	+
11C	3.3	1.0 technical triorthocresyl phosphate subcutaneously	6	2	Slight F	—	Slight	+
3B	2.9	1.2 technical triorthocresyl phosphate subcutaneously	6-8	25	+ T	Slight	++	+
22A	4.0	1.5 technical triorthocresyl phosphate subcutaneously	7-12	6	+ TF	—	+	+
4D	3.5	1.0 technical triorthocresyl phosphate subcutaneously	6	11	+ TF	+	+	++
28	2.3	1.6 technical triorthocresyl phosphate subcutaneously	14	1	—	—	+	+
30	2.4	2.5 technical triorthocresyl phosphate subcutaneously	2-20	3	Slight F	Slight	—	—
1C	4.6	1.0 chemically pure triorthocresyl phosphate subcutaneously	7	40	+ F	+	Slight	+
29	3.4	1.0 chemically pure triorthocresyl phosphate subcutaneously	10	2	++ TF	++	++	++
23A	2.7	0.5 chemically pure triorthocresyl phosphate subcutaneously	5	2	—	+	+	+
25	3.3	2.0 specific ester isolated from adulterated fluidextract of ginger, subcutaneously	11	30	++ TF	—	+	+
26	2.1	77.0 95% alcohol, in 11 doses, over a period of 40 days, per os	—	—	—	—	Slight	—
27	3.0	112.0 95% alcohol, in 16 doses, over a period of 45 days, per os	—	—	—	—	—	—
6A	4.7	30.0 U.S.P. fluidextract of ginger in 3 doses, per os	—	—	—	—	—	—
24	2.4	0.75 phenol, 5% in 95% alcohol per os in 3 daily doses; acutely fatal	—	—	+ TF	—	—	Slight

* T, tigrolysis; F, fatty degeneration.

of the animals were also observed. It is of interest that two animals that received large doses of alcohol and one U. S. P. fluidextract of ginger showed no such changes in the central nervous system, while one animal with acute and fatal phenol poisoning showed a slight involvement of the peripheral nerves and distinct changes in the anterior horn cells. Figures 6 and 7 show the lesions in the anterior roots produced by triorthocresyl phosphate in this animal species.

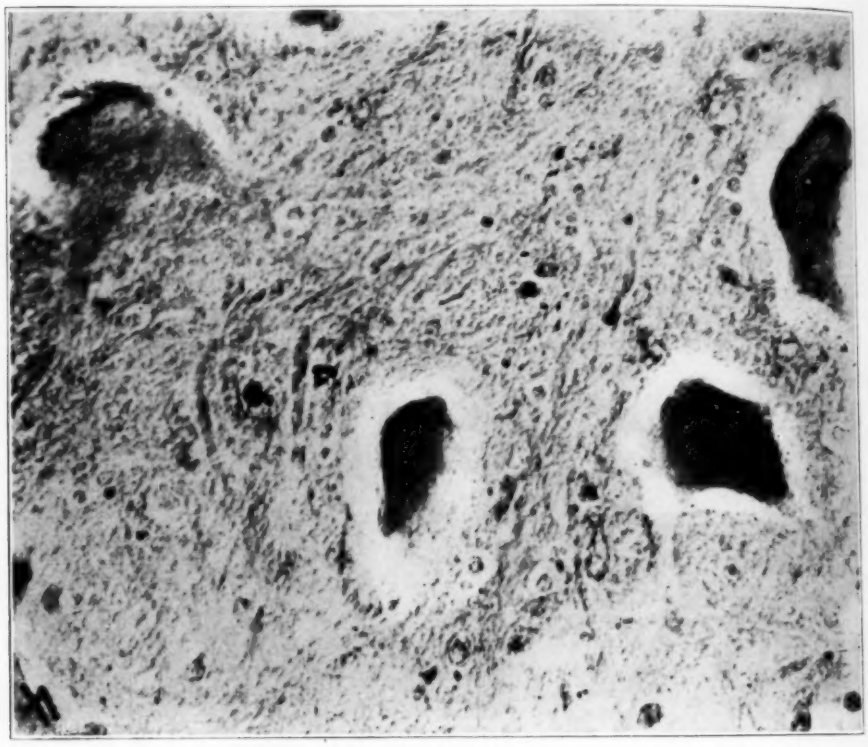

Fig. 5.—Photomicrograph of a section of the spinal cord in the lumbar region of dog 13 (table 2); Marchi method. Note the fatty degeneration of some anterior horn cells and the nuclear displacement (compare with fig. 2); × 400.

The histologic manifestations of triorthocresyl phosphate poisoning in the chicken are reported in table 4. In this series of experiments the animals were killed at regular intervals following the appearance of symptoms of paralysis in order to ascertain whether the relative degree of involvement of the peripheral nerves and of the spinal cord bears any relation to the duration of the paralysis. The results indicate, however, that while the peripheral nerves showed almost constantly the typical lesions of degeneration of the myelin sheaths, even

as early as the first day of the paralysis, the cellular degeneration in the spinal cord was seldom demonstrable in this species. Figure 8 shows the typical degeneration of the myelin sheaths in one of the small nerves of the leg of chicken 502 that had been paralyzed fifteen days after the oral administration of 0.4 Gm. per kilogram of technical triorthocresyl phosphate. Similar symptoms and lesions resulted from the oral administration of the specific ester isolated from the incriminated adulterated fluidextract of ginger. The oral administration

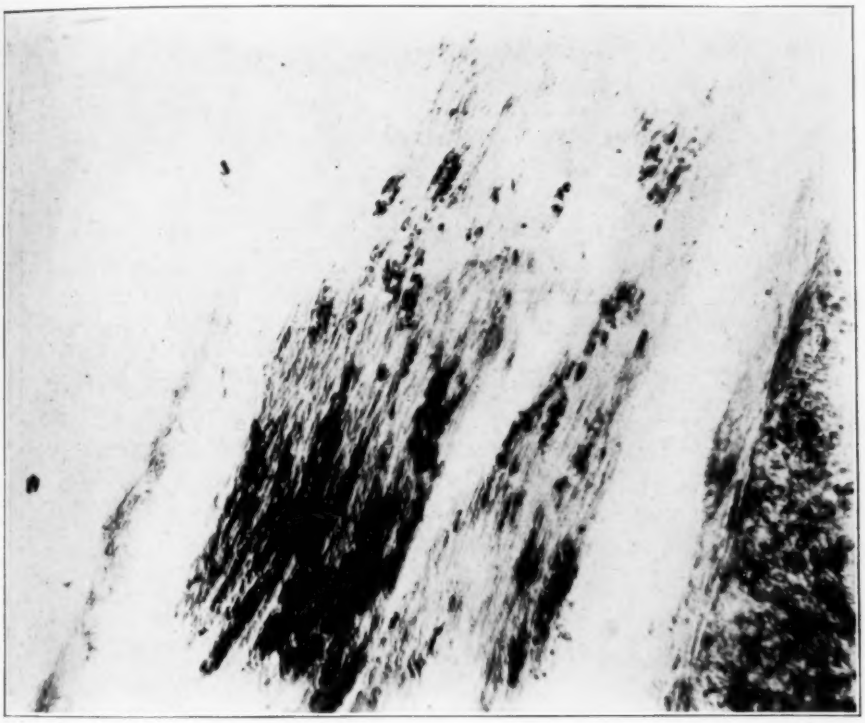

Fig. 6.—Marchi preparation of an anterior nerve root in the cervical region of monkey 3B (table 3) (compare with fig. 4); × 200.

of phenol or the several cresols, in sublethal doses, failed to produce any symptoms referable to the neuromuscular apparatus and gave negative results on histologic examination, as illustrated by fowl 650 in table 4. The negative observations in fowl 594 would have constituted a rather serious exception in this series of experiments were it not for the fact that this fowl had shown definite, though slight, improvement for about fifteen days before it was killed. It is, of course, also possible that the methods used may not be adequate to demonstrate changes in the nerves in the chicken at this later stage.

Our histologic studies of three calves yielded results entirely consistent with those just described. In the first two publications of this series [6] there were described experiments on three calves, all of which developed typical motor paralysis of the posterior extremities, one as a result of the oral administration of an adulterated fluidextract of ginger which had produced paralysis in man, another as a result of the oral administration of U. S. P. fluidextract of ginger diluted with alcohol and adulterated with 2.5 per cent commercial tricresyl phosphate, and the third following the oral administration of 0.2 Gm. per

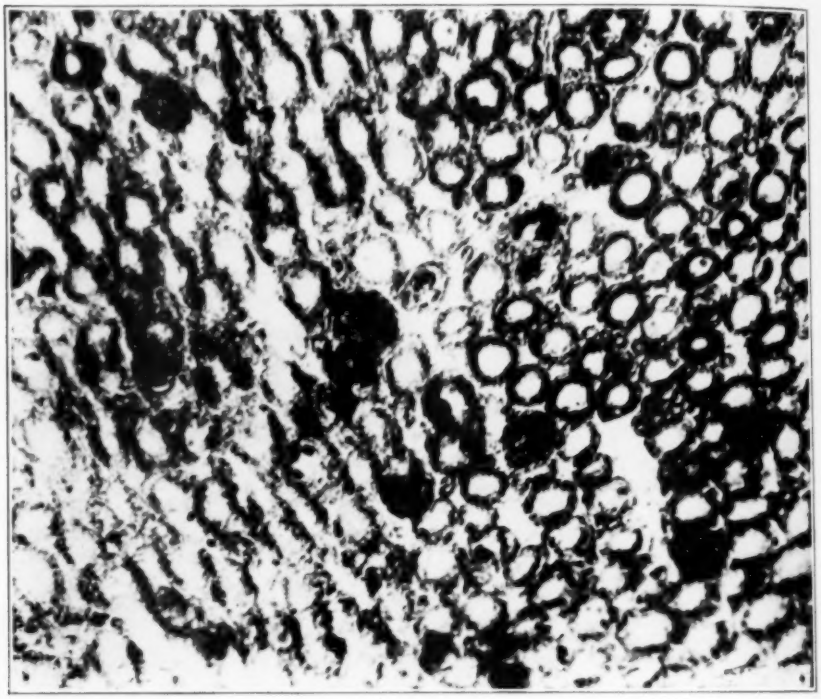

Fig. 7.—A cross-section of a preparation similar to figure 6; × 400.

kilogram of chemically pure triorthocresyl phosphate in alcohol. The histologic observations in these three calves, which were killed from three weeks to four months after the onset of the clinical manifestations of the disease, were: calf 1, peripheral parenchymatous neuritis; calf 2, parenchymatous central and peripheral neuritis; calf 3, peripheral parenchymatous neuritis.

Our observations on a small series of cats indicate the same general conclusions, except that in this species the central changes appear to

6. Smith and Elvove (footnote 1). Smith, Elvove and Frazier (footnote 2).

be relatively more pronounced than in the preceding species of animals. Our first two reports on this subject did not include any data on the action of triorthocresyl phosphate in the cat. Some experiments performed recently indicate: that the cat reacts typically to this poison; that 0.2 Gm. per kilogram is the minimal surely paralytic dose when administered subcutaneously or intravenously, though as little as 0.1 Gm. per kilogram may produce a moderate degree of motor paralysis of the posterior extremities; that the minimal lethal dose by subcutaneous or intravenous injection is about 0.5 Gm. per kilogram, and that the oral administration of this substance in alcohol is usually ineffective, even in doses up to 3 or 4 Gm. per kilogram. We have

TABLE 4.—*Histopathology of Triorthocresyl Phosphate Poisoning in the Fowl (Plymouth Rocks)*

No.	Weight, Kg.	Treatment: Gm. per Kg. Body Weight	Effect		Nerve Lesions; Tigrolysis or Fatty Degeneration			
					Spinal Cord		Peripheral Nerves	
			Interval, Days	Paralysis, Days	Nerve Cells	White Substance	Roots	Nerves
500	1.5	1.0 technical triorthocresyl phosphate per os	8	4	—	—	—	+
498	1.2	0.4 technical triorthocresyl phosphate per os	6	12	+ T*	Slight	..	++
502	2.1	0.4 technical triorthocresyl phosphate per os	8	15	Slight T	+	..	+
512	1.7	0.4 technical triorthocresyl phosphate per os	9	13	—	Slight	..	+
503	1.5	0.2 technical triorthocresyl phosphate per os	10	1	—	+	+	+
504	1.3	0.2 technical triorthocresyl phosphate per os	10	43	—	—	..	—
675	1.9	0.1 technical triorthocresyl phosphate intravenously	10	26	—	—	..	+
583	1.4	0.5 specific ester isolated from adulterated fluidextract of ginger per os	8	1	—	+	+	+
582	1.1	0.5 specific ester isolated from adulterated fluidextract of ginger per os	8	14	—	—	..	+
650	1.5	0.2 phenol in alcohol per os	—	—	—	—	—	—

* T, tigrolysis.

long suspected that the relative ineffectiveness of triorthocresyl phosphate by oral administration in certain animal species (monkey, dog, cat) was due to difficult and irregular absorption. We have recently secured some results that indicate that, in the cat at least, this substance appears to be absorbed from the gastro-intestinal tract with considerable regularity, though probably not completely, if administered as a fine emulsion with the aid of a 10 per cent aqueous solution of gum acacia. The question of the absorption of this ester is being investigated further, as is the problem of the fate of this substance in the animal body; for the present we offer the evidence summarized in table 5 to illustrate the points enumerated.

The histologic observations in the cat are given in table 6, from which it is evident that the lesions of the peripheral nerves were

uniformly present and the central lesions, though not as uniform, were on the whole perhaps more pronounced than in the other species examined.

Other lesions observed and not included in the tables may be briefly summarized as follows:

1. *Man.*—Fatty degeneration of the epithelial cells of the ependyma of the central canal of the spinal cord was seen in a greater or lesser degree in every case examined.

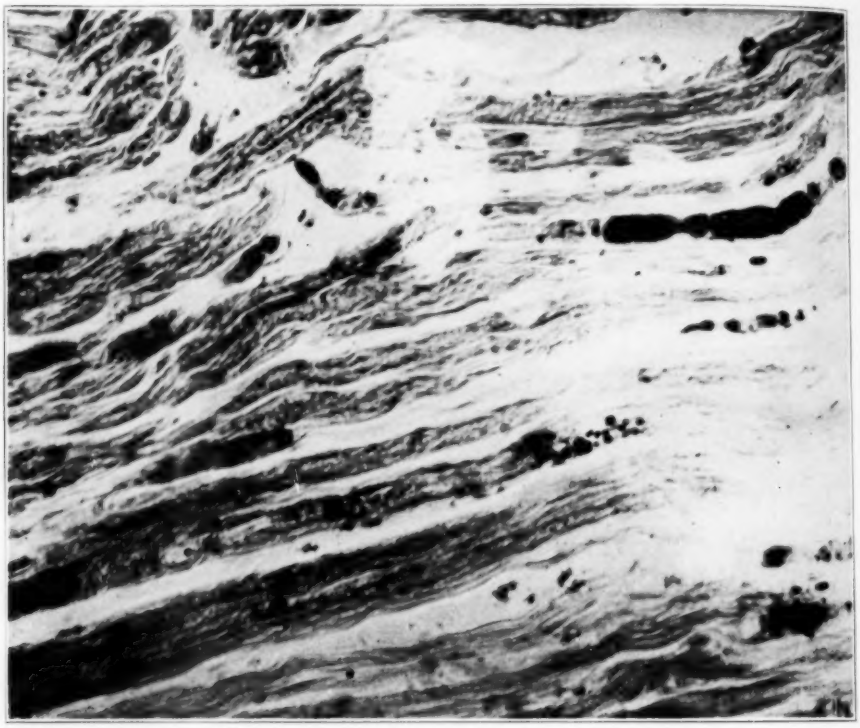

Fig. 8.—Marchi preparation of a small nerve of the leg of chicken 502 (table 4) that had been paralyzed for fifteen days (compare with fig. 4); × 400.

2. *Monkey.*—(*a*) Striated muscle, taken from the paralyzed extremities in four of the animals, showed some fragmentation, loss of striations and, in one case, hyaline degeneration. No abnormalities were found in three of the seven animals examined.

(*b*) Tigrolysis, with or without fatty degeneration involving some of the nuclei of the pons and medulla, was seen in several instances. Fatty degeneration of the choroid plexus was also observed once.

TABLE 5.—*Action of Triorthocresyl Phosphate in Cats as Determined by the Mode of Administration*

		Dose		Result		
No.	Weight, Kg.	No.	Total Gm. per Kg.	Interval, Days	Paralysis, Days	Comment
			Subcutaneous Injection			
2	2.4	1	1.0	5	..	Died
9	1.5	1	1.0	4	4	Died
8	2.6	1	0.5	7	11	Paralysis severe; killed
6	2.8	1	0.4	12	6	Paralysis severe; killed
7	2.3	1	0.3	11	2	Paralysis severe; died
4	2.0	1	0.2	18	40	Slight to moderate paralysis; apparently recovered
5	2.6	1	0.1	26	30	Slight paralysis; apparently recovered
			Intravenous Injection, 5 to 10% Suspension in 10% Gum Acacia			
12	2.5	1	0.5	..	..	Died in several hours
25	2.0	1	0.2	6	52	Moderately severe paralysis; condition unchanged
26	2.6	1	0.2	19	37	Slight to moderate paralysis, progressing
10	2.9	1	0.1	4	57	Slight paralysis, unchanged
11	2.0	1	0.1	40	40	Doubtfully slight paralysis
			Oral, 10 to 50% in Alcohol			
1	2.9	2	3.0	..	..	No effects
3	2.8	1	4.0	..	..	No effects
22	2.3	3	3.0	13 to 25	37	Slight paralysis, apparently improving
23	2.5	2	2.0	3 to 10	3	Died
24	3.1	3	3.0	30 to 50	20	Doubtfully slight paralysis
			Oral, 10% Suspension in 2% aqueous Solution of Saponin			
17	1.8	1	1.0	..	..	No effects
18	2.6	1	1.0	..	..	No effects
			Oral, 10% Emulsion in 10% Gum Acacia			
13	3.8	4	3.0	5 to 38	47	Moderately severe paralysis; condition unchanged
14	2.0	1	1.0	4	7	Severe paralysis; died
15	2.5	1	1.0	5	..	Died
16	1.9	3	3.0	7 to 35	20	Paralysis severe; died
19	3.2	3	1.5	5 to 23	47	Moderately severe paralysis; unchanged
20	2.5	2	1.0	3 to 13	3	Severe paralysis; died
21	3.0	3	1.5	1 to 19	6	Severe paralysis; died

TABLE 6.—*Histopathology of Triorthocresyl Phosphate Poisoning in the Cat*

			Effect		Nerve Lesions; Tigrolysis or Fatty Degeneration			
					Spinal Cord		Peripheral Nerves	
No.	Weight, Kg.	Treatment; Gm. per Kg. Body Weight	Interval, Days	Paralysis, Days	Nerve Cells	White Substance	Roots	Nerves
7	2.3	0.3 chemically pure triorthocresyl phosphate subcutaneously	11	2	—	—	—	+
6	2.8	0.4 chemically pure triorthocresyl phosphate subcutaneously	12	6	++ T*	—	—	Slight
8	2.6	0.5 chemically pure triorthocresyl phosphate subcutaneously	7	11	+ T	+	Slight	+
21	3.0	1.5 ester, 5% emulsion in 10% gum acacia, in 3 doses per os.....	1-19	6	++ T	++	++	++

* T, tigrolysis.

(*c*) The kidneys showed a variable degree of parenchymatous degeneration in four animals examined.

(*d*) Parenchymatous degeneration of the heart muscle was seen in two of the four animals examined.

(*e*) The liver, adrenals and spleen failed to show any abnormalities in five animals examined.

3. *Cat.*—Of the four animals reported on in this paper, three presented lesions in the striated muscle of the same character as those already described, and notable multiplication of muscle nuclei. Edema of the cortex of the brain was seen twice; there was also observed tigrolysis with or without cellular fatty degeneration in the red, oculomotor, caudate and pontile nuclei in two animals.

4. *Dog.*—In two animals of this series in which striated muscle was examined, nuclear multiplication was noted once. Likewise, the brains of two animals of this series showed tigrolysis and some cellular fatty degeneration in the nuclei of the stem.

5. *Chicken.*—(*a*) Striated muscle was examined twice; once it appeared normal and once it presented patchy multiplication of muscle nuclei.

(*b*) The ependyma of the cord presented well marked fatty degeneration twice.

(*c*) The heart muscle showed edema once, and a normal appearance four times.

(*d*) The kidney failed to show anything abnormal in the five birds examined.

(*e*) The liver presented fatty infiltration or degeneration without necrosis twice, and a normal appearance four times.

(*f*) The lungs and adrenals, examined in three animals, presented a normal appearance. In one bird a sympathetic ganglion appeared normal.

It may be concluded from this brief survey, therefore, that triorthocresyl phosphate is essentially a poison of the central nervous system, affecting primarily the lower motor neuron. The lesions observed in the striated muscle from the affected limbs probably indicate beginning atrophy.

COMMENT

It was hoped that three main points would be elucidated, at least in part, when the present experiments were undertaken: (1) A comparison of the pathologic lesions of paralysis due to the consumption of adulterated fluidextract of ginger in man with those of the experimental disease in animals. This was df particular importance when

this work was begun, at a time when all that was known about the etiology of this paralysis was that it had some relationship to adulterated Jamaica ginger extract. Now that the true nature of the immediate cause of this disease has been definitely established, this particular point has assumed a secondary importance. Nevertheless, it may be said that the questions arising in connection with this part of the problem appear to have been answered satisfactorily, as shown in the foregoing pages. (2) The manner of action of the specific ester. (3) What may be expected as the final outcome of the disease process.

The third point is obviously of immediate and practical importance as it concerns prognosis. Is this peculiar type of multiple neuritis primarily a process of central or peripheral degeneration? In other words, is the phosphoric ester of orthocresol, the acknowledged direct and immediate cause of this paralysis, a poison affecting specifically the nerve cell, the myelin sheath, the axis cylinder, the motor end-plates, or possibly all of these structures. On account of the technical difficulties involved in the histologic work with axis cylinders and motor end-plates and on account of the uncertainties attending the interpretation of such observations, it seemed best to defer such work until better and more certain methods become available. Considering the constancy with which degeneration of the myelin sheaths of the peripheral nerves was observed in practically our entire series of experiments, it seems that it can safely be asserted that the substance in question is probably essentially a myelin poison. The somewhat less certain, though definite, if not uniform, damage found in the motor nerve cells of the spinal cord might indicate one of two possibilities: Either the process is secondary to the axonal degeneration or, what seems perhaps a more likely interpretation, the action of the poison may also extend to the lipoids of the nerve cells, the relative involvement of the myelin sheath and nerve cell being merely a function of the distribution of the poison or its degradation products manifesting a special affinity for the lipins of the nervous system. In support of the first alternative we have the evidence of Ranson[7] and others of retrograde degeneration of groups of anterior horn cells subsequent to section of peripheral nerve trunks. The second alternative, however, seems to be well sustained by the fact revealed in the present work, that the central damage appears to bear little, if any, relation to the peripheral lesions, to the clinical severity of the disease or to the duration of the paralysis, but rather seems to be a characteristic of the species. Thus, in the fowl, in which the disability appears most pronounced, damage of the nerve cells in the spinal cord was seldom

7. Ranson, S. W.: J. Comp. Neurol. **16**:265, 1906.

observed, while in the cat, on the other hand, with seeming less disability, the central lesions were well defined in most cases.

It may be recalled here also that the effects of the specific ester in the rabbit appear to be restricted chiefly to the spinal cord, the action being characterized by primary and lasting stimulation followed by depression, with final medullary paralysis.[2] Dr. Smith had previously suggested a possible mode of action of this substance, postulating its accumulation and storage in the lipins of the central nervous system with perhaps subsequent hydrolytic cleavage of the ester in situ, possibly through the influence of certain enzymes.[2] We have as yet no evidence for this, but such a mechanism which is not outside the limits of possibility would fit in with, and also account in some measure for, our present observations.

SUMMARY AND CONCLUSIONS

The histology of the nervous system in paralysis due to adulterated fluidextract of ginger in man has been studied and compared with the effects produced by triorthocresyl phosphate in suitable experimental animals.

The results indicate that the multiple neuritis of this paralysis is essentially a degeneration of the myelin sheaths of the peripheral nerves, with a variable amount of relatively moderate central degenerative changes affecting the anterior horn cells throughout the spinal cord, but more often in the lumbar and cervical regions.

Essentially similar lesions were observed in experimental animals in which partial paralysis was produced by means of triorthocresyl phosphate.

A PRODUCTIVE-DEGENERATIVE FORM OF ENDARTERITIS OF THE SMALL PIAL VESSELS

REPORT OF A CASE SHOWING UNUSUAL CLINICAL AND HISTOLOGIC FEATURES *

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Within recent years considerable attention has been devoted to the study of vascular disorders of the central nervous system. Owing to thorough histopathologic investigations in this field, the diagnosis of such disorders can generally be made without difficulty by the aid of microscopic observations. The following case, however, was a striking exception in that it showed certain arterial lesions which differed in many respects from those previously described in vascular diseases. The alterations in question consisted essentially in a massive proliferation of peculiar endothelial cells, which later underwent necrosis. This frequently led to complete disintegration of the vessels involved. As the lesions were largely limited to the smaller arteries and arterioles of the pia, the process may be regarded as a productive-degenerative endarteritis of the small pial vessels. We do not mean to imply by this designation that the pathologic process which we are describing here was inflammatory, for evidences of inflammation were entirely lacking; we are merely following the customary practice of applying the term endarteritis to lesions showing proliferative changes of the lining cells of the small vessels.

In addition to the atypical histologic picture, several features of clinical interest were noted. There was a combination of pyramidal, extrapyramidal and pseudobulbar signs, with an unusual manifestation of tonic innervation in the left hand. The course of the illness was more continuous and the dementia was deeper than that ordinarily observed in cerebral arteriosclerosis. The results of the serologic tests were negative. The clinical picture was complicated by the presence of a paraplegia in flexion. This was found to be due to an encapsulated tumor of the cauda equina. The tumor was evidently an independent

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process, for it bore no apparent relation to the widespread vascular changes. In view of the uncommon nature of the observations, we are reporting the case in considerable detail.

REPORT OF CASE

Weakness of left lower extremity following a fall. Gradual development of mental symptoms one year later, leading to profound dementia with signs of pyramidal, extrapyramidal and pseudobulbar involvement. Flexion paralysis of lower extremities. Death five years after the onset of mental symptoms. Extensive productive-degenerative lesions of the small pial vessels and a benign tumor of the cauda equina.

History.—L. M. S., a white woman, aged 52, was admitted to the Foxborough State Hospital on Aug. 17, 1924. There was nothing of significance in the family history. The patient was born in Latvia and came to this country twenty years ago. Her early history was normal. She was married about thirty years ago. There were no children and no miscarriages. Her husband was healthy. She had always been well until the winter of 1921-1922, when she slipped and fell backward on some ice. She was able to go home by herself, but the next day stayed in bed, complaining of pain in the back of the head and in the limbs, particularly the left leg. For about six months she remained in bed part of the time. During this period she was seen at the outpatient department of a general hospital, where the condition was called "lateral sclerosis." Although she gradually resumed her housework, she occasionally had "falling spells." These were not accompanied by convulsive movements or loss of consciousness. She continued to complain of pain in the left leg and left side of the abdomen, and there was apparently some weakness of the left lower extremity. Mental symptoms were first observed about a year after the accident. She became easily excited and sometimes appeared slightly confused. From time to time she was restless at night. She soon developed delusions of jealousy in regard to her husband and became very irritable. Finally, as a result of an attack on her husband during an outburst of rage, she was committed to the hospital.

Examination.—On admission, the patient was well developed and well nourished. The blood pressure was 250 systolic and 140 diastolic. The speech was somewhat slurred and nasal. There were coarse tremors on coordination tests. The deep reflexes were exaggerated, and the gait was ataxic. The patient showed emotional instability. She expressed delusions in regard to her husband going out with other women. Her memory was definitely defective, and her grasp of general information was deficient. She had no insight, and her judgment was poor. The urinalysis and other laboratory examinations showed nothing abnormal. The Wassermann reaction of the blood was negative.

Course.—During the next few months the patient became more and more uncertain on her feet, falling several times. On June 30, 1925, following a severe fright, twitching movements in the body and face were noted, and within a few hours she developed paralysis of the left arm and leg. She became more unstable emotionally and showed increasing intellectual dilapidation. She was incontinent and helpless, and for a short time had some difficulty in swallowing. In June, 1926, she had a left-sided convulsive seizure. Subsequently, generalized convulsive seizures occurred every few months.

On June 25, 1927, the patient was reexamined. The fundi were normal. The visual fields could not be tested adequately. The pupils were equal and reacted a little sluggishly to light and in accommodation. The facies was fixed and

parchment-like (fig. 1). The patient smiled frequently in a peculiarly slow and stiff manner. Although the muscles of the jaw appeared stiff, and the tongue could not be protruded, there was no marked difficulty in swallowing. The pharyngeal reflexes were somewhat diminished. The head was immobile, exhibiting a loss of normal associated movements. Both upper extremities were flexed and held against the sides of the body. The left arm was spastic and almost completely paralyzed, very slight voluntary movements being possible at the wrist, elbow and shoulder. The fingers were held in an unusual position, with the middle, ring and little fingers extremely flexed, and the index finger and thumb extended. Thus, the left hand seemed to be continually pointing at some object. There were no contractures, for the fingers could be moved passively without great difficulty. When the hand was released, it slowly regained its original posture. Movements of the head and neck produced no change in the fingers. The tonus of the right arm was normal. It could be moved freely, although it was very weak. There were no tremors or incoordination. In the upper extremities, the deep reflexes were more active on the left than on the right. Hoffmann's sign was positive on both sides. There was a flexion paralysis of the lower extremi-

Fig. 1.—Photograph of the patient, showing masklike facies and paraplegia in flexion.

ties (fig. 1). Owing to the presence of contractures, the knees could only be extended to a right angle. The patellar and achilles reflexes were somewhat exaggerated, and a nonsustained ankle clonus was obtained on the right. There was practically no response to stroking the soles of the feet. Rossolimo's sign was strongly positive on both sides. The abdominal reflexes were absent. There was some general wasting of the musculature. The left arm and leg were slightly larger than the right, the skin appearing thickened, swollen and slightly cyanosed. A defense reflex, consisting in the typical flexion withdrawal of the limb on painful stimulation, was observed in both lower extremities. It was easier to bring out on the left side, and after it had been elicited a few times it could be obtained by succeeding stimuli of much weaker intensity. A sensory examination was impossible on account of the demented state of the patient. The speech was indistinct, flattened out and somewhat nasal in tone, but there were no indications of aphasic disturbances. At times the patient laughed and wept in an uncontrollable manner. There was incontinence of urine and feces.

A lumbar puncture was performed on Aug. 11, 1927. It yielded a small quantity of xanthochromic fluid, which coagulated within a few minutes. The fluid showed an increased protein content, but it contained no cells. The Quecken-

stedt procedure revealed a complete block. The Wassermann reactions of the blood and spinal fluid were negative. The colloidal gold curve showed slight changes (1222) in tubes 9 to 12.

Following a series of convulsive seizures on Oct. 29, 1927, conjugate deviation of the eyes to the right was observed, with the right pupil widely dilated and the left somewhat miotic. The head was turned to the right, and the mouth was pulled over to the same side. On Feb. 11, 1928, a definite grasp reflex was obtained by gentle stroking of the fingers of the right hand. The patient became unresponsive to questions, but did not appear to be unconscious. She gradually grew weaker, and decubital ulcers developed. On March 2, 1928, signs of bronchopneumonia were found, and death occurred five days later.

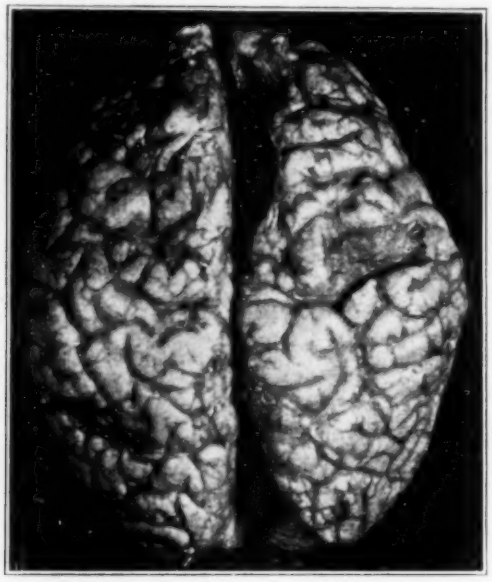

Fig. 2.—Large defect in the medial part of the right frontal lobe and smaller superficial foci of destruction elsewhere.

Gross Pathologic Changes.—Necropsy was performed one hour after death. There were some grayish patches in the cardiac muscle and signs of bronchopneumonia in the lungs. The ascending aorta showed a few small yellowish patches on its inner surface, and the coronary arteries were slightly thickened.

The brain weighed 945 Gm. It exhibited numerous focal losses of substance, which looked like organized softenings. The largest of these was situated in the right frontal region. It involved mainly the medial surface, extending almost to the frontal pole anteriorly, the corpus callosum below and the parietal lobe posteriorly (fig. 2). There was a large organized, yellowish-brown focus in the right parietal lobe. There were smaller areas of loss of substance in the right parieto-occipital region and the upper part of the left rolandic region. On section, most of the zones of destruction were found to be superficial, generally involving all of the cortex, but leaving the underlying white matter comparatively intact. Occasionally, however, organized softenings were encountered deeper in the white substance of the parietal lobes. These were more numerous on the right.

The cortex of the left temporal lobe was indistinctly outlined in places. Several smaller foci were observed in the thalamus and putamen on both sides. The pons was abnormal in form, and contained a brownish focus about the size of a lentil near the aqueduct. Several small softenings were found in the medulla oblongata. On the surface of the left cerebellar hemisphere there was a large superficial loss of substance which extended to the white matter. The right cerebellar hemisphere exhibited a similar lesion. The basal vessels were somewhat thickened. On removing the spinal cord, a red-brown mass was found in the lower

Fig. 3.—Section from the lumbar region of the spinal cord, showing dilated blood vessels with proliferation of large translucent cells. The walls of the vessels are markedly thinned out in places; van Gieson's stain; × 80.

lumbar region. It consisted apparently of thickened dura and a soft tumor lying between the strands of the upper portion of the cauda equina.

Microscopic Examination.—Throughout the central nervous system extensive lesions of the blood vessels were found. In describing them it would seem advisable to trace the sequence of histologic events, for the changes were greatly varied in the later stages of the process. In the beginning, however, the pathologic picture was uniform. The earliest changes consisted in swelling and proliferation of the lining cells of the small vessels. They appeared translucent and swollen, sometimes attaining a size several times larger than normal (fig. 3).

Their nuclei were large and well stained. Their cytoplasm was slightly granular, but otherwise clear and colorless. As a result of active proliferation, they formed irregular masses of cells, which often completely filled the lumina of the involved vessels (figs. 3 and 4). When this occurred in the small arterioles, the structures making up the walls of the vessels seemed to disappear, leaving only a dense accumulation of large bubble-like cells. As a rule, the media and adventitia of the larger arterioles and small arteries were still recognizable, for the proliferation was frequently less intense in vessels of that caliber. Even here, however, the lumina were often much narrowed or completely obliterated (figs. 3 and 4).

The next stage of the process was ushered in by degenerative changes in the proliferating endothelial cells. They lost their rounded forms, and their nuclei became shrunken and finally disappeared. The fine granules vanished from the

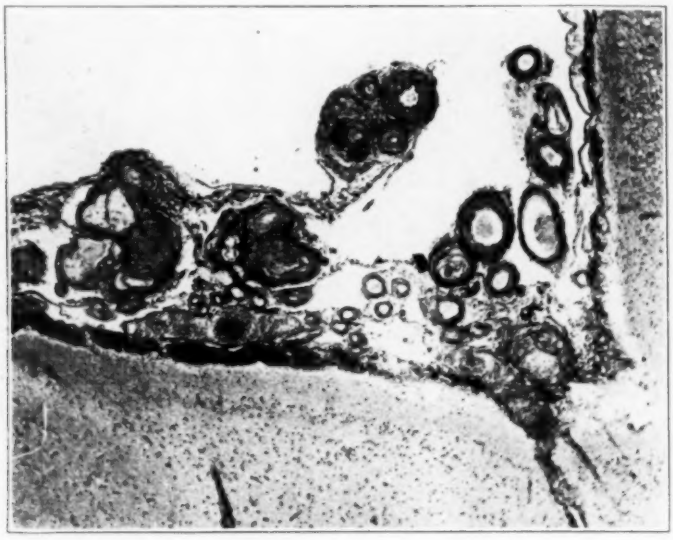

Fig. 4.—Section of the brain showing two meningeal blood vessels on the left and one in the angle on the right, with lumina completely closed by proliferated endothelial cells. To the right of the two first mentioned vessels, the organization of the involved vessels by connective tissue can be observed. One vessel has been converted into a solid strand of connective tissue. In the upper part of the section, the media of an arteriole shows fatty changes; van Gieson's stain; × 40.

cytoplasm, which soon broke down into a somewhat fragmented, amorphous mass that stained bright orange-yellow with sudan III. During this period the media was particularly severely involved. In sections stained by van Gieson's method, it stood out distinctly from the actively proliferating intima and the brilliant red adventitia by reason of its yellowish-brown color and structureless appearance. Where this was observed, the vessels were sometimes deformed and slightly thickened, as though their elasticity had been diminished and a slight compensatory thickening of the adventitia had taken place. Following this, the media became honeycombed with spaces containing necrotic material. At the same

time the intima was breaking down, and thrombosis was beginning to occur. As all the structures making up the vascular walls were often completely disintegrated, the lesions frequently looked more like small necrotic areas than like thrombi.

Even after thrombosis had taken place, the endothelial proliferation did not entirely cease. At this point serial sections showed that numerous collections of the cells described were still actively proliferating in all directions through the necrotic foci. During this period the affected vessels apparently offered little resistance to the blood stream, for blood elements were frequently observed in their broken-down walls, as well as in the surrounding nerve tissue. In this manner crescentic or circular hemorrhages which remained in close relation

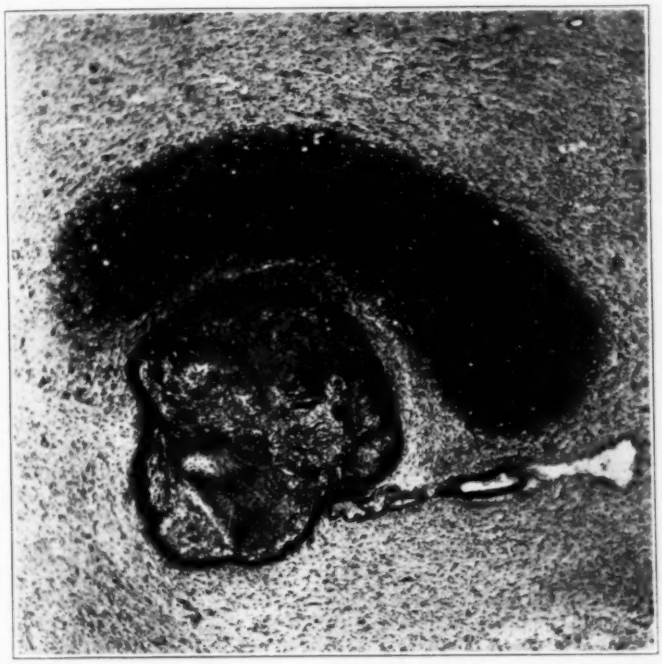

Fig. 5.—Large blood vessel in the white matter of the brain with a hemorrhage into the surrounding nerve tissue. The walls of the vessel are necrotic, and the lumen is closed by a thrombus; van Gieson's stain; × 40.

to the necrotic vessels were produced (fig. 5). Where the involvement was most marked, the vascular walls seemed to be completely replaced by proliferating intimal cells mixed with broken-down material (fig. 3). When such vessels were stained by van Gieson's method, all that could be seen was a brown structureless mass composed of clotted blood and cellular elements. At this stage toluidine blue preparations revealed a beginning growth of fibroblastic cells through the necrotic foci. Sections treated with van Gieson's stain soon showed an increasing number of connective tissue fibrils growing into these areas. With the conversion of the involved vessels into solid strands of connective tissue, the process came to a definite end (fig. 4).

Apart from the changes described, the adventitia exhibited little activity. With tannin-silver stains only a mild adventitial proliferation was found. There was no tendency for recanalization to occur. Inflammatory reactions were lacking in the perivascular spaces and in the walls of the blood vessels, as well as in the meninges and nerve tissue. The absence of calcification should also be emphasized. Except where the elastica was directly involved in the necrotic process, it did not show any obvious alterations. No changes were observed in the veins.

In view of the unusual nature of the vascular lesions, some observations of their microchemical reactions were made. It was noteworthy that the newly formed intimal cells showed little affinity for the commonly used stains. Thus, toluidine blue, thionin, hematoxylin-eosin, ammoniacal silver solutions and van Gieson's solution stained only the nuclei, the cytoplasm remaining uncolored and slightly granular. The most striking observations were made in sections treated with sudan III. In the early stages of the process the proliferating cells did not take up any of the sudan III, but as soon as regressive changes occurred, they became orange-yellow. Even after these cells had completely broken down, the necrotic products continued to assume a bright yellow tint, hence resembling fat thrombi. The fact that this color was doubly refracting would indicate that it was produced by cholesterol.

After the media became involved, it appeared yellowish-brown in van Gieson preparations and deep black with Bielschowsky stains. When toluidine blue was used, the media took on a pale green tint. During this period it stained bright yellow with sudan III. At this stage fatty degeneration was the most prominent feature of the pathologic process. Nevertheless, it was only a temporary phase, for the sudan III failed to affect the older necrotic foci. By studying serial sections it was found that different parts of the same vessel reacted differently to the sudan III; the fresher the necrosis was, the greater was the affinity for the stain. No fatty changes were observed in the adventitia.

As regards the distribution of the vascular lesions, they were found with greatest regularity in the smaller arteries and arterioles of the pia. They occurred in both the brain and the spinal cord, but were particularly widespread and severe in the brain, where few of the small pial vessels were intact (fig. 4). The lesions were not, however, always strictly limited to the pia, but sometimes followed the course of the vessels into the cerebral cortex. The cerebellum showed a similar type of involvement.

In addition to these changes, the pia-arachnoid was thickened and fibrotic. Numerous areas of necrosis were scattered throughout the brain. They occurred most frequently in the form of large, but superficial, striate defects, which generally did not extend beyond the cortex. Attempts at reparation proceeded mainly from the connective tissue. Neuroglial proliferation remained within moderate bounds. In the necrotic regions there were large amounts of lipoid material, the greater portion of which was lying free in the tissues. Most of the ganglion cells showed considerable lipoid accumulations. Elective disease of the cortical laminations was not observed. Bielschowsky stains did not reveal anything of note in the neurofibrillar structures. Several small and large striate softenings were found on the surfaces of the cerebellar hemispheres. Throughout the basal ganglia numerous small areas of necrosis were encountered in relation to vascular alterations of the type described.

The blood vessels of the spinal cord exhibited changes similar to those observed in the brain. In addition, however, alterations of a somewhat different nature were met with in the meninges about and above the tumor of the cauda equina.

In that area there were many cystic spaces containing blood cells (fig. 6). At first sight this gave the impression of a hemangioma-like mass, but here, as in other parts of the central nervous system, endothelial proliferation and thrombosis occurred in some arteries and arterioles. Essentially the same process that has been described could be traced in many of these vessels by comparing sections from different levels of the lumbar segments. Some vessels were replaced by cystlike spaces containing amorphous material and colorless red blood cells; others underwent connective tissue organization. In this region the dura was markedly thickened. It was folded on the ventral aspect of the spinal cord and contained a long narrow cyst. This extended upward to the middorsal segments, exerting considerable pressure even at that level. From this spot downward, all parts showed extreme involvement. As a rule only a few severely changed

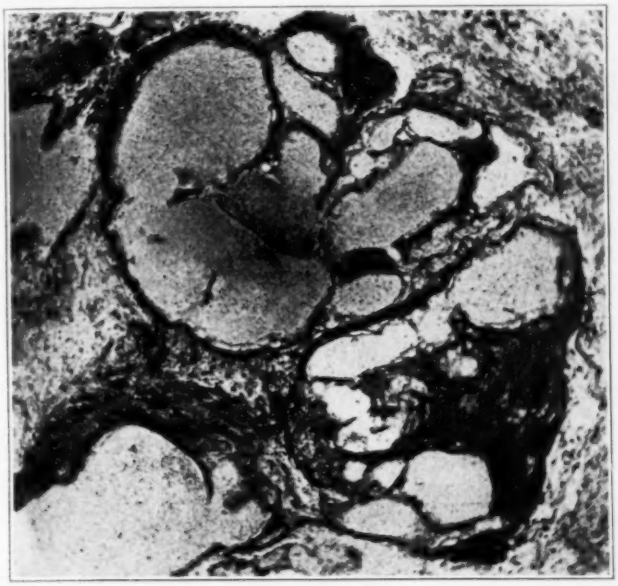

Fig. 6.—Section through the leptomeninges in the upper part of the cauda equina. The blood vessels are greatly dilated, with thin necrotic walls. In the lower portions of the section, large cells can be seen intermingled with necrotic material; van Gieson's stain; × 40.

ganglion cells remained in sections taken from below that point. The normal structures were no longer recognizable in the lumbar segments. Gliogenous scars were frequently observed in the gray matter. Large deposits of lipoid substances were scattered through the white substance, the various tracts being about equally affected.

As the tumor of the cauda equina apparently bore no relation to the vascular changes, only a short description of it will be given. It consisted of oval or almost round nuclei, which were bound together by numerous longitudinal and transverse fibers. Corresponding to the gross appearance, this network seemed loose and soft. No nerve fibers were found in the tumor. It was richly supplied with blood vessels, most of which showed hyaline degeneration. The paren-

chyma of the tumor appeared yellowish-brown in van Gieson stains and bluish-red with hematoxylin-eosin. It did not extend beyond the dura, to which it was adherent. It was regarded as a perineural fibroblastoma.

As to microscopic changes elsewhere, some of the large basal vessels showed slight thickening of the type usually seen in arteriosclerosis. In the kidneys, mild arteriosclerotic changes of a benign nature were found.

Summary.—The primary stage of the process consisted in an unusual type of swelling and proliferation of the lining cells of the small blood vessels. They formed large, bubble-like elements with almost clear, but slightly granular, cytoplasm (fig. 3). As a result of their active growth, narrowing or complete closure of the involved vessels occurred. The next stage was marked by the breaking down of these newly formed cells and the formation of thrombi. Even after this had taken place, some of the cells continued to proliferate in all directions through the thrombosed areas. Eventually, however, they all underwent fatty degeneration. They became irregular in shape, their nuclei shriveled up and disappeared, and the cytoplasm became fragmented. At the same time partial or complete disintegration of the vascular walls occurred. Thus, the lesions often looked more like necrotic foci than like thrombosed vessels. During this period some vessels became greatly dilated (figs. 3 and 6). Others allowed blood to escape into the surrounding tissues in the form of ringlike or crescentic hemorrhages (fig. 5). Finally, fibroblastic cells grew into the broken-down foci, converting them into solid strands of connective tissue (fig. 4).

COMMENT

When the histologic changes that have been described are analyzed, it becomes evident that they deviate in many respects from those previously observed in vascular disorders of the central nervous system. From a differential diagnostic point of view the only conditions that would seem to come into question are vascular forms of syphilis, endarteritis of nonsyphilitic etiology, arteriosclerosis and possibly Buerger's disease.

Syphilitic vascular processes of an exudative or infiltrative nature are excluded by the fact that there was no trace of inflammatory components in the case under discussion. This also applies to Buerger's disease, for leukocytic infiltration of the walls of the blood vessels is generally regarded as one of the essential features of the early stages of that disorder.

Numerous authors have described a productive form of endarteritis of the small cortical vessels which occurs in syphilis, as well as in severe toxemias and infections. According to Jakob,[1] who has devoted con-

1. Jakob, A.: Normale und pathologische Anatomie und Histologie des Grosshirns, Leipzig, Franz Deuticke, 1929, vol. 2, pt. 1.

siderable attention to the syphilitic variety, the main vascular changes consist in endothelial and adventitial proliferation, with budding and new vessel formation. Similar observations were made by Winkelman and Eckel [2] in endarteritis of nonsyphilitic origin. The only feature common to the process depicted by us and endarteritis of the small cortical vessels was the endothelial proliferation. Even in this respect, however, the resemblance was slight, for the latter disorder does not exhibit endothelial cells of the type observed here, nor does it show anything comparable to the extensive necrosis which these cells regularly underwent. Furthermore, it seldom leads to gross extravasation of blood. The adventitial proliferation, budding and new vessel formation characteristic of both syphilitic and nonsyphilitic endarteritis were lacking in the case described in this article. It may also be pointed out that we were unable to find any changes suggestive of syphilis in the inner organs.

Clinically, too, the picture differed considerably from that of endarteritis of the small cortical vessels. Jakob [1] stated that the syphilitic variety of endarteritis tends to run a prolonged course. Remissions often occur, and a duration of ten or more years is not uncommon. Hallucinatory episodes are fairly frequent, but in general marked psychotic symptoms tend to remain in the background. The Wassermann reaction may be either positive or negative. Hence the negative reaction obtained with the blood and spinal fluid of our patient does not absolutely exclude syphilis. Nevertheless, the clinical picture just outlined bears no resemblance to that presented by our patient, whose illness was characterized by an early and progressive dementia. As to the clinical manifestations of the nonsyphilitic type of endarteritis, the patients of Winkelman and Eckel [2] showed indications of a severe toxemia or infection. They were usually stuporous or delirious. The course of the disease was rapid and stormy, leading to a fatal termination within a few weeks or months. Visual and auditory hallucinations were prominent features. None of these symptoms, however, were observed in the case reported here.

More detailed consideration must be given to the possibility that the lesions were arteriosclerotic. The lack of fibroblastic proliferation in the early stages and the absence of changes in the elastica differentiate the pathologic process in question from the type of arteriolosclerosis recently described by Klemperer and Otani.[3] The only other type of sclerosis requiring attention is that designated by the term

2. Winkelman, N. W., and Eckel, J. L.: Endarteritis of the Small Cortical Vessels in Severe Infections and Toxemias, Arch. Neurol. & Psychiat. **21**:863 (April) 1929.

3. Klemperer, P., and Otani, S.: Malignant Nephrosclerosis (Fahr), Arch. Path. **11**:60 (Jan.) 1931.

atherosclerosis. This is characterized by swelling, proliferation, thickening and sclerosis of the intima. These alterations lead finally to necrosis and calcification. Since the present case showed swelling, proliferation and degeneration of the intima, the assertion might be made that it possessed much in common with atherosclerosis. This similarity, however, would seem to be only superficial, for when the changes observed by us are compared with those found in the latter condition, many essential points of difference are revealed. In atherosclerosis the proliferation takes place in the subendothelial connective tissue; in the case under discussion, the proliferating elements were endothelial cells. The former disorder generally affects only the larger vessels, whereas here the changes were limited to the smaller arteries and arterioles. We have been unable to find anything recorded in the literature of atherosclerosis that resembled the massively proliferating cells that we have described, particularly as regards the manner in which they completely filled the lumina of many of the vessels involved. Another unusual feature in our case was that even after thrombi had formed in the broken-down vessels, some of the endothelial elements continued to grow through the necrotic foci. So far as we have been able to determine, such an occurrence has never been reported in atherosclerosis.

The fatty changes also differed from those found in atherosclerosis in at least two fundamental points. Fortunately this subject has been studied experimentally, particularly by Russian investigators.[4] Thus Anitschkow has discarded the concept of degeneration in arteriosclerosis. He regards the process as a lipoid infiltration or impregnation. In experimentally produced arteriosclerosis of the aorta in rabbits and guinea-pigs, he found that fatty substances first made their appearance as a subintimal lipoid infiltration; the lipoid deposits were not in the cell bodies themselves, but were always situated in the intercellular spaces. Reactive phenomena in the aortic wall did not occur until later. This is similar to human atherosclerosis, the earliest stage of which is generally looked on as a process of lipoid infiltration or deposition. In our case, however, swelling and proliferation of the endothelial cells constituted the primary stage of the pathologic process. take the form of a simple lipoid infiltration, but were rather an expres- Fatty changes were not observed until these cells had enlarged and multiplied excessively. Furthermore, the changes in question did not sion of a regressive metamorphosis leading to complete cellular destruc-

4. Anitschkow: Ueber die experimentelle Atherosklerose der Aorta beim Meerschweichen, Beitr. z. path. Anat. u. z. allg. Path. **70**:265, 1922. Anitschkow and Chalatow: Zentralbl. f. allg. Path. u. path. Anat. **24**:1, 1913. Starokodowsky and Scobolew: Zur Frage der experimentellen Atherosklerose, Frankfurt. Ztschr. f. Path. **3**:912, 1909.

tion. The deeper portions of the walls of the blood vessels were not primarily involved, for the media sometimes remained intact even after large portions of the intima had completely broken down. As a rule, however, it underwent necrosis soon after the intima. Unfortunately, the exact sequence of events could not be determined in the media, but as it disintegrated rapidly, with large amounts of lipoid substances making their appearance, it is probable that here, too, the process was a degeneration rather than an infiltration.

In still other respects the lesions described were unlike those found in atherosclerosis. Thus, splitting of the internal elastic membrane and calcification are considered characteristic features of the latter. In our case, however, there were no indications of such changes.

In view of these facts, it seems doubtful whether the pathologic process observed in this case can be regarded as similar to those previously described in vascular disorders. Even the distribution of the lesions was unusual. They occurred with great regularity in the brain and spinal cord, but were not found elsewhere. The greatest involvement was in the smaller vessels of the pia, where scarcely an arteriole was intact. The shorter cortical branches were more affected than the longer vessels supplying the white matter, thus accounting for the widespread, but superficial, areas of destruction scattered over the surfaces of the cerebral and cerebellar hemispheres. In contrast to both syphiltic and nonsyphilitic forms of endarteritis of the small cortical vessels, the vessels of the cortex in this case were much less altered than those of the pia. Furthermore, the lesions were not strictly confined to the smallest arteries, for vessels of somewhat larger caliber were occasionally involved. The excessive endothelial proliferation, leading as it did to severe injury of the walls of the blood vessels, was undoubtedly responsible for the marked tendency to thrombosis, which was one of the characteristic features of the process.

From a clinical standpoint, too, the case was atypical. The slow but continuous progression of the disease, with profound dementia coming on at a comparatively early date, would be considered unusual in cerebral arteriosclerosis, in which more circumscribed mental defects are the rule and partial remissions are common. In the patients of Winkelman and Eckel [2] with endarteritis of toxic or infectious origin, gross hemiplegias did not occur. Patients suffering from pure forms of endarteritis syphilitica of the small cortical vessels generally present clinical pictures similar to those seen in very chronic or stationary types of dementia paralytica, to which the case reported here obviously bears no resemblance.

In view of the presence of a tumor of the cauda equina, considerable caution must be exercised in attempting to correlate the clinical symptoms with the anatomic changes resulting from the vascular disorder.

Paralysis of the flexor type has been described by Gordon [5] and others in patients showing cerebral lesions only, but in our case the alterations of the spinal cord above the tumor were probably responsible for the paraplegia in flexion. Even without taking into consideration the observations in the lower extremities, there was a confusing mixture of pyramidal, extrapyramidal and pseudobulbar signs, which were undoubtedly produced by changes incident to the vascular disease. Thus, the left arm was almost completely paralyzed, the speech was pseudobulbar, and the facies was masklike. A grasp reflex was elicited in the right hand, and the fingers of the left hand were constantly fixed in a pointing position. The latter phenomenon deserves special attention on account of its rarity. It has been observed by Goldstein and Bornstein,[6] Cohn [7] and others in patients with lesions of the striopallidal system. In the case presented here, there were small softenings scattered throughout the basal ganglia, but the most extensive destruction of nerve tissue took place in the area of distribution of the right anterior cerebral artery. Critchley [8] recently pointed out that forced grasping and groping and phenomena of tonic innervation frequently occur in patients with lesions of this vessel or of its branches. Although the posture referred to was an example of tonic innervation, definite conclusions concerning its significance as a localizing sign in our case would seem unwarranted on account of the multiplicity of the changes.

According to Goldstein and Bornstein,[6] the pathologic fixation of the hand in a pointing position really owes its origin to the fact that a functional grouping of muscles takes place in the central nervous system whereby purposeful modes of behavior are subserved. Hence, when lower mechanisms are released from the influence of the rest of the nervous system, the phenomena that make their appearance are not only more primitive, but also purposeful. The views of these authors would seem to receive support from the present case, for our observations indicate that the position assumed by the hand in the act of pointing has its basis in a central mechanism that behaves like a functional unit. Otherwise it would be necessary to regard the phenomenon in question as a consequence of accidental variations of muscular spasm in the different fingers. It is highly improbable, how-

5. Gordon, A.: Flexion Paralysis of Spinal and Cerebral Origin, J. Nerv. & Ment. Dis. **62**:354 (Oct.) 1925.

6. Goldstein, K., and Bornstein, W.: Ueber sich in pseudospontänen Bewegungen äussernde Spasmen und über eigentümliche Stellungen bei "striären" Erkrankungen, Deutsche Ztschr. f. Nervenh. **84**:234, 1925.

7. Cohn, H.: Weitere Beobachtungen über Haltungs- und Bewegungs-Störungen bei Schädigung des Stammganglienapparates, Ztschr. f. d. ges. Neurol. u. Psychiat. **125**:327, 1930.

8. Critchley, M.: The Anterior Cerebral Artery, and Its Syndromes, Brain **53**:120, 1930.

ever, that such a posture could persist indefinitely, as it did in our patient, if it were produced by merely accidental factors.

In regard to etiology, little of a positive nature can be said with any degree of certainty. There was nothing to suggest any relation between the encapsulated tumor of the cauda equina and the widely scattered vascular changes. It is possible that the cystlike spaces in the lower portion of the spinal cord owed their origin to the common tendency for hemorrhages to occur near tumors of the central nervous system, particularly since such a tendency would probably be greatly enhanced by the coexisting vascular disorder. The injury that apparently marked the onset of the illness may also have had something to do with the formation of these spaces. Although the question of trauma as an etiologic factor in tumors of the spinal cord is an interesting subject in itself, it does not lie within the scope of this article.

When vascular lesions occur as late sequelae of injuries to the nervous system, they are generally considered to be secondary to traumatic changes in the tissues surrounding the vessels. In this case, however, the arterial disease was undoubtedly primary. We have been unable to discover in the literature any record of alterations following trauma that resembled the observations reported here. It should be noted that the patient's fall was related in point of time to spinal symptoms only. Mental symptoms were not observed until about a year after the accident. This would indicate an extremely long period of development of secondary changes. In view of these facts, it seems probable that the vascular condition was independent of the trauma.

Since it is known that certain toxic substances are apt to affect the small vessels of the central nervous system, the question may be raised whether the changes described were produced by a disorder of that type. However, the patient did not exhibit any of the usual symptoms of a toxemia. One would therefore be obliged to assume that some unknown toxin of a very chronic but severe nature was operative in this case. With the knowledge available at present, such an assumption would be pure speculation.

The nature of the vascular disease discussed here would seem to be almost as obscure as its etiology. Histologically, there was a combination of productive and degenerative changes which began in the endothelial cells of the intima, but frequently spread to the media. Theoretically, one might think that the association of arteriosclerosis and endarteritis syphilitica of the small cortical vessels could lead to the occurrence of such productive-degenerative lesions. It is very improbable, however, that two independent disorders would merge with each other completely enough to produce alterations of a uniform character in practically all parts of the central nervous system. Furthermore, it seems unlikely that syphilis would bring about such severe changes

without showing some of its usual manifestations in other parts of the central nervous system or elsewhere. The features that have been brought out suggest the possibility that we are dealing with a hitherto undescribed type of disorder. Nevertheless, a definite conclusion on this point would seem unjustified on the basis of a single case. Final evaluation of the pathologic process must await further observations of histologic pictures similar to that described in this article. Until then, the question whether these alterations represent a new pathologico-anatomic entity or not must remain undecided.

SUMMARY

A clinically atypical case is reported in which unusual vascular lesions of a productive-degenerative nature were found. The changes were limited to the smaller arteries and arterioles of the central nervous system. The smaller vessels of the pia were involved with greatest regularity.

The first alterations consisted in swelling and proliferation of the endothelial cells, whereby masses of large, rounded elements with translucent, but slightly granular, cytoplasm were formed. This resulted in complete or partial blocking of the lumina of the affected vessels. Following this, the newly formed cells underwent severe fatty degenerative changes, which often spread to the media. Complete disintegration of the walls of the vessels frequently ensued, with the occurrence of thrombosis and hemorrhages.

The end-stage of the process consisted in connective tissue organization of the involved vessels. There was no tendency to recanalization, and splitting of the elastica interna was not observed. Calcification did not take place.

Clinically, the case showed an early and progressive dementia. There was a combination of pyramidal, extrapyramidal and pseudobulbar signs, with an unusual manifestation of tonic innervation in the left hand. The clinical picture was complicated by the presence of a paraplegia in flexion. This was found to be due to alterations produced by a tumor of the cauda equina. There was no apparent relation between the vascular lesions and the tumor, which was regarded as a perineural fibroblastoma.

SPINAL CORD CHANGES IN LYMPHO-GRANULOMATOSIS *

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The present investigation is based on reports of forty-three cases of Hodgkin's disease published in the literature, in which a clinical history is given, with observations made at autopsy or operation. Three cases which had personally been studied were added. The purpose of this study was, first, to obtain statistical data on the histopathologic changes of the spinal cord in lymphogranulomatosis from a verified material which is relatively large as compared with the rare involvement of the spinal cord in this disease. Second, the effect of x-ray treatment on the granulomatous masses invading the spinal canal was to be studied, with preference for those cases in which they had previously been verified by laminectomy.

As to the frequency of involvement of the spinal cord in Hodgkin's disease, it may be quoted from Ginsburg,[1] part of whose material was at my disposal at the autopsy, that from 1914 to 1925, at the Montefiore Hospital in New York (a hospital for chronic diseases), thirty-six cases of lymphogranulomatosis had been under observation, in three of which involvement of the spinal cord had been verified by biopsy or by autopsy, and in two of which such involvement had been suggested by the neurologic examination. Among the last 511 autopsies of the department of pathology of Northwestern University (statistics through the courtesy of Dr. J. P. Simonds) two cases of lymphogranulomatosis had been examined, one of which had shown invasion of the spinal canal. Shapiro[2] stated that among fourteen cases of Hodgkin's disease examined in the pathologic laboratory of the Cook County Hospital during 1929, two cases had shown disease of the spinal cord. In other words, 14 per cent of the clinical cases of the hospital for chronic diseases had shown disease of the spinal cord,

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* From the Institute of Neurology, Northwestern University Medical School.

1. Ginsburg, S.: Hodgkin's Disease, with Predominant Localization in the Nervous System; Early Diagnosis and Radiotherapy, Arch. Int. Med. **39**:571 (April) 1927.

2. Shapiro, P. F.: Changes of Spinal Cord in Hodgkin's Disease: Report of Two Cases with Unusual Skin Manifestation in One, Arch. Neurol. & Psychiat. **24**:509 (Sept.) 1930.

and the same number, 14 per cent, was found among the autopsy material of a large city hospital.

The clinical history and the observations at autopsy in the three cases that will be described in detail are fairly representative for the other cases of the corresponding three groups of the material in the literature.

REPORT OF CASES

CASE 1.—H. P., a man, aged 35, in 1922 had enlarged cervical lymph nodes, puffiness of the face and swelling of the feet and legs. Between 1923 and 1929, he received intermittent and irregular x-ray treatment. Except for persistent itching of the skin, he felt well, with minor intermissions. In March, 1929, he had pain and tenderness between the shoulders, which at times radiated into the arms and ribs. In August, 1929, while hiking, his legs began to feel weak; the weakness progressed rapidly, and after two weeks there was a paralysis of both

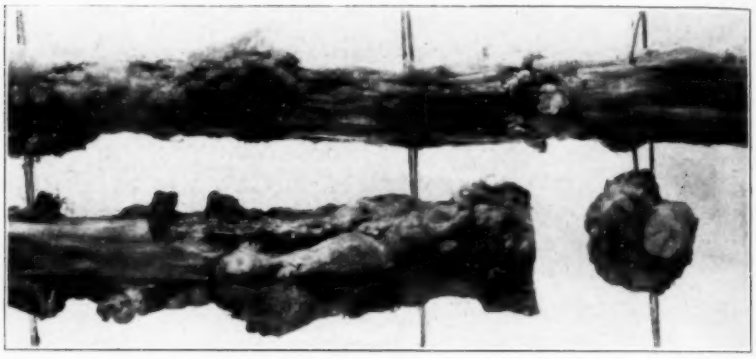

Fig. 1 (case 36).—Photograph of spinal cord and transverse section of mid-dorsal region to demonstrate epidural masses.

legs, with moderate spasticity in the arms and complete loss of all kinds of sensations below the nipple line. A laminectomy from the eighth cervical to the second dorsal vertebra revealed only slight edema of the spinal cord, reddening beneath the opened space and numerous vessels at the posterior surface. On October 16, bed sores over the buttocks developed. The patient died on October 21.

Autopsy.—There were: nodular spleen, enlarged lymph nodes in the mediastinal, peribronchial, left cervical, axillary, inguinal, mesenteric and retroperitoneal regions and extension of retroperitoneal masses through the intervertebral foramina into the spinal canal between the third and ninth dorsal vetebrae (fig. 1).

Microscopic Examination.—The outer posterior aspect of the dura mater was covered with a massive lymphogranulomatous tissue. The dura was thickened. The subarachnoidal space was free from cellular infiltration and showed no thickening of the pia-arachnoid (fig. 2). In transverse section, the spinal cord appeared sievelike, containing wide spaces, which were surrounded by the swollen glia fibers (Holzer stain). The myelin sheaths were swollen and distorted, but there was not much demyelinization in the midthoracic segments (Weil stain). Axons were preserved, but swollen (Davenport stain). There was no increase

in fibrous glia, but the cytoplasm of the astrocytes stained with cresyl violet and showed vacuolation. The anterior horn cells were relatively well preserved.

Microscopic Diagnosis: Epidural lymphogranulomatosis with edema and myelopathy.

CASE 2.—A. C., a woman, aged 34, in June, 1916, had a sense of heaviness in the left upper quadrant, with some enlargement of the abdomen, which grew in size during the next four years. In 1920, she had tonsillitis followed by enlargement of the glands of the neck, and later of those of the axillae, elbows and groins. During the second half of the year, there was extreme weakness with a feeling of numbness in both legs. Deep x-ray treatment was administered. In February,

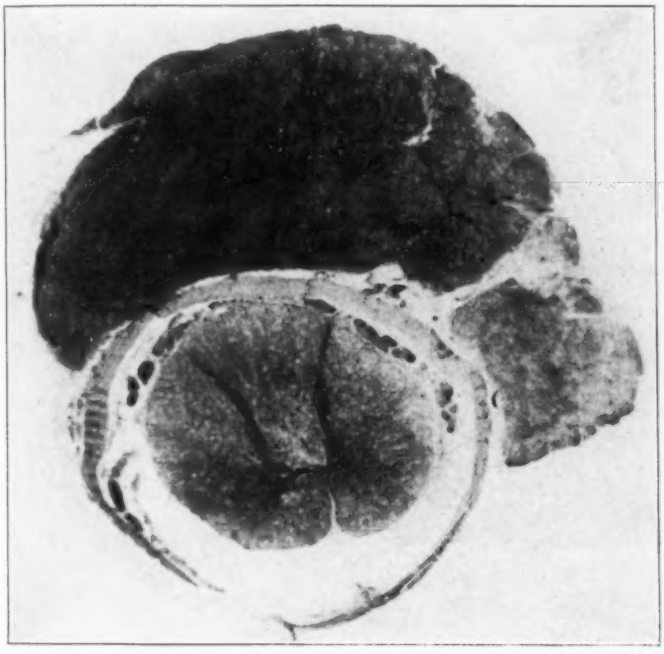

Fig. 2 (case 36).—Transverse section of spinal cord; Weil stain; to demonstrate epidural lymphogranulomatous masses.

1923, she was unable to walk and had pains in the sacral region. Spastic paralysis of both legs developed, with tenderness on percussion of the lower cervical and upper dorsal vertebrae. There was a level of hyperesthesia at the second dorsal vertebra; below this, sensation for pain, touch and temperature were normal, but there was an absence of vibratory sensation from the iliac crest downward, with loss of sense of position in the toes of both feet. In April, 1924, bronchopneumonia developed and was followed by death.

Autopsy.—There was a generalized lymphogranulomatosis of the lymph nodes that have been mentioned and of the nodes of the abdominal cavity. Epidurally, scattered fibrous-fatty masses were found, which were prominent at the level of the second and third dorsal vertebrae.

Microscopic Examination.—At the level of the second and third dorsal vertebrae there was partial demyelinization of nearly the whole of the white matter, most marked in the lateral and anterior columns (fig. 3). In the demyelinized areas fat-containing granular corpuscles were found (fig. 4) and an increase in fibrous glia. There was a loss of axons, with swelling of those remaining. Most of the anterior horn cells were intact, with only isolated atrophic forms. In sections above and below this level, secondary ascending and descending degeneration was seen.

Microscopic Diagnosis: Scar tissue of epidural lymphogranulomatosis; myelopathy of the upper dorsal segments.

Case 3.—In the fall of 1929, C. H., a young man, experienced tenderness and swelling of the lymph nodes in the neck, axilla and groin with loss of weight, soon after a period of chills and fever. In February, 1930, he had cough and a feeling of nausea. He lost 18 pounds (8.2 Kg.) within ten days and altogether 50 pounds (22.7 Kg.). In March, there was itching of the skin and pain in the throat. On May 25, roentgenograms of the chest showed a markedly thickened

Fig. 3 (case 39).—Transverse section through spinal cord; Weil stain; to demonstrate paling of myelin sheaths in lateral and anterior columns.

pleura and retraction of the left side of the chest, with enlargement of the hilus on both sides. A blood count revealed: 18,000 white cells, of which 64 per cent were polymorphonuclear, 27 per cent lymphocytes, 3 per cent mononuclears and 6 per cent eosinophils, and 2,980,000 red cells.

Deep x-ray therapy was applied to the chest and inguinal region. The patient then felt well until July 17, when he caught a cold and felt weak. There were incontinence of urine and exaggeration of all the deep reflexes. On July 26, paralysis of the palate developed and also bilateral optic neuritis. The arms were weak, and the legs were paralyzed, with a bilateral Babinski sign and absence of the abdominal reflexes. Sensation for pin prick was diminished up to the groin; there was an area of hypesthesia above, up to the clavicles; prick sensibility was normal over the neck and face. Sensation for touch was normal throughout. The patient died on July 30.

Autopsy.—There were: wide-spread lymphogranulomatosis; bilateral pulmonary congestion and edema, with scattered encapsulated tubercles; marked fibrous thickening and ossification of the parietal pleura from the third to the seventh rib, and a retropharyngeal abscess. The spinal dura did not show gross abnormal-

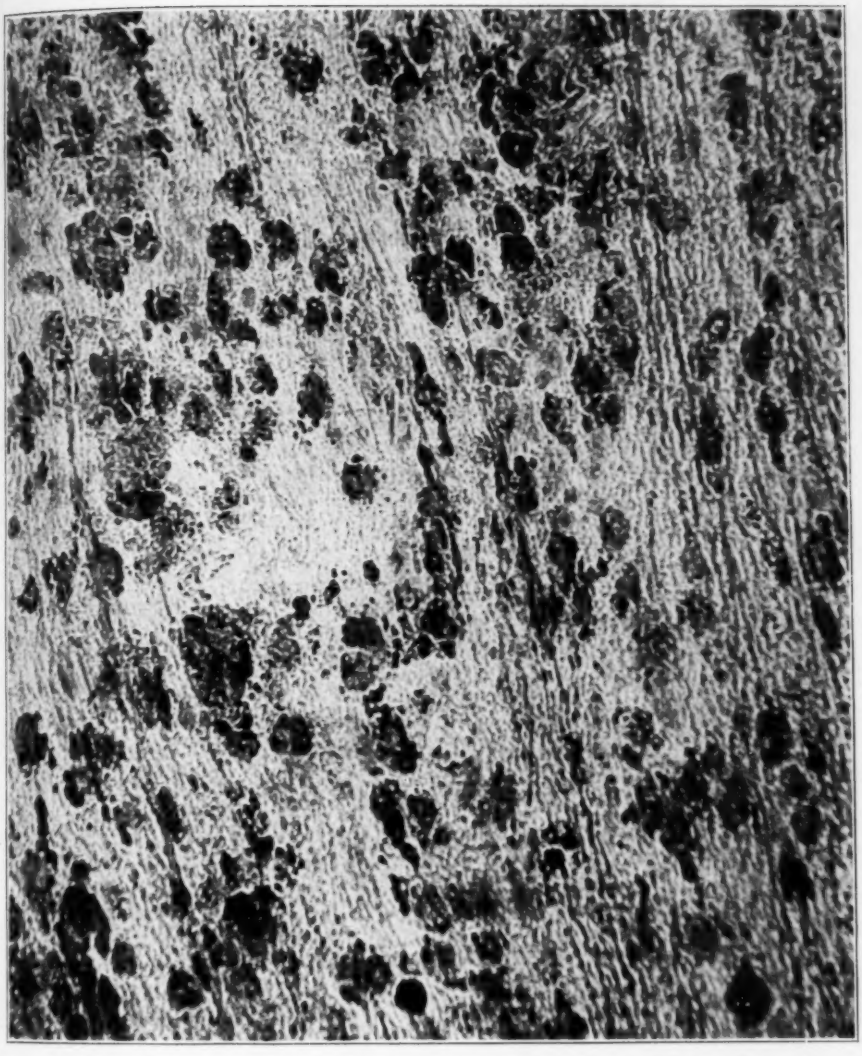

Fig. 4 (case 39).—Longitudinal frozen section of spinal cord; sudan III stain; enlargement, × 240; to demonstrate fat-laden gitter cells in lateral columns.

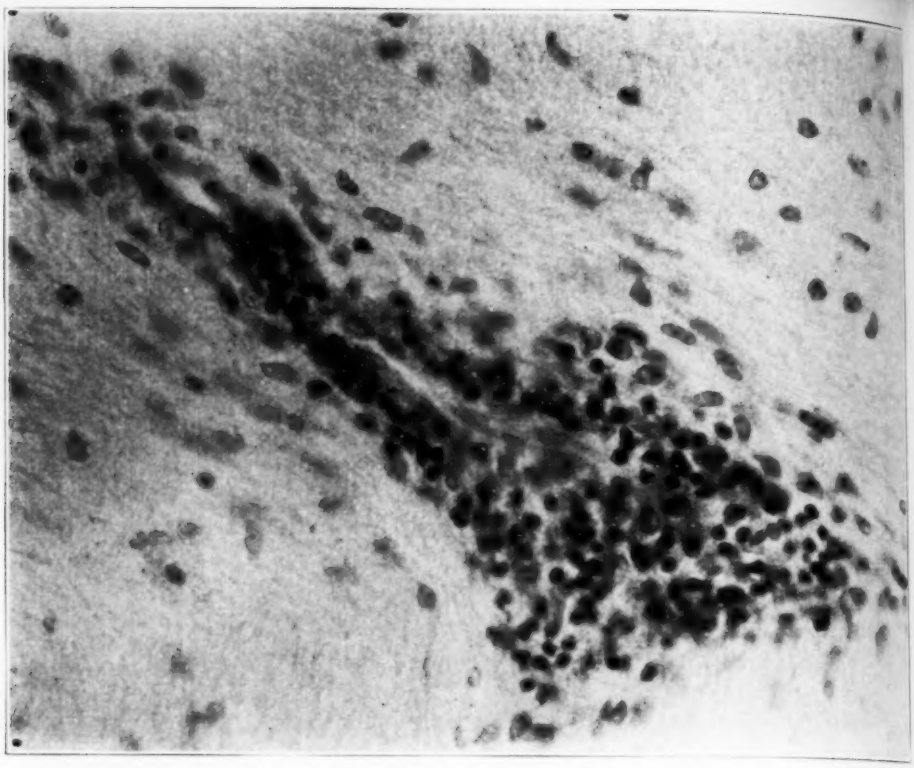

Fig. 5 (case 41).—Section through pons; cresyl violet stain; Leitz objective, 4 mm.; ocular, × 6; to demonstrate perivascular infiltration.

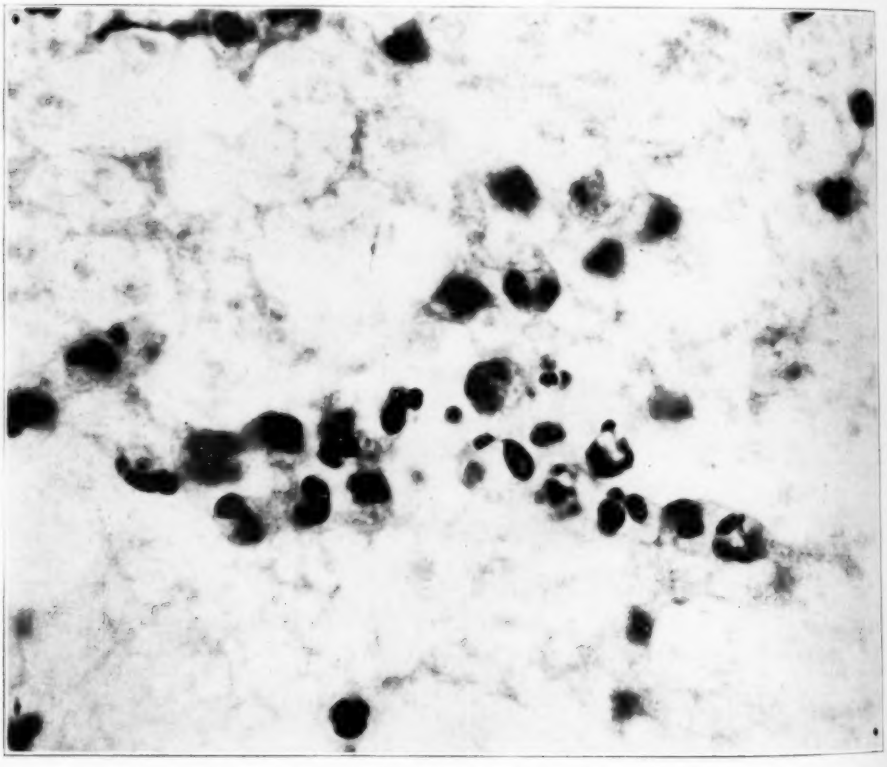

Fig. 6 (case 41).—Section through dorsal spinal cord; cresyl violet stain; Zeiss objective, 3 mm., apochromatic; ocular, × 10; to demonstrate character of perivascular infiltration.

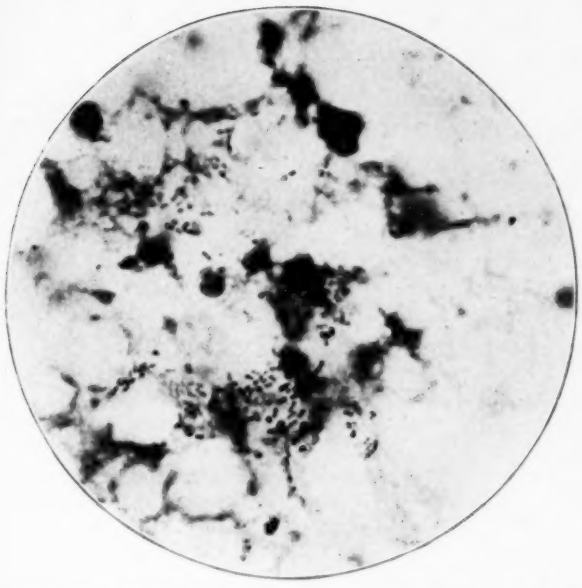

Fig. 7 (case 41).—Section through dorsal segment of spinal cord; Unna-Pappenheim stain; Zeiss objective, 2 mm.; ocular, × 10; to demonstrate diplococci.

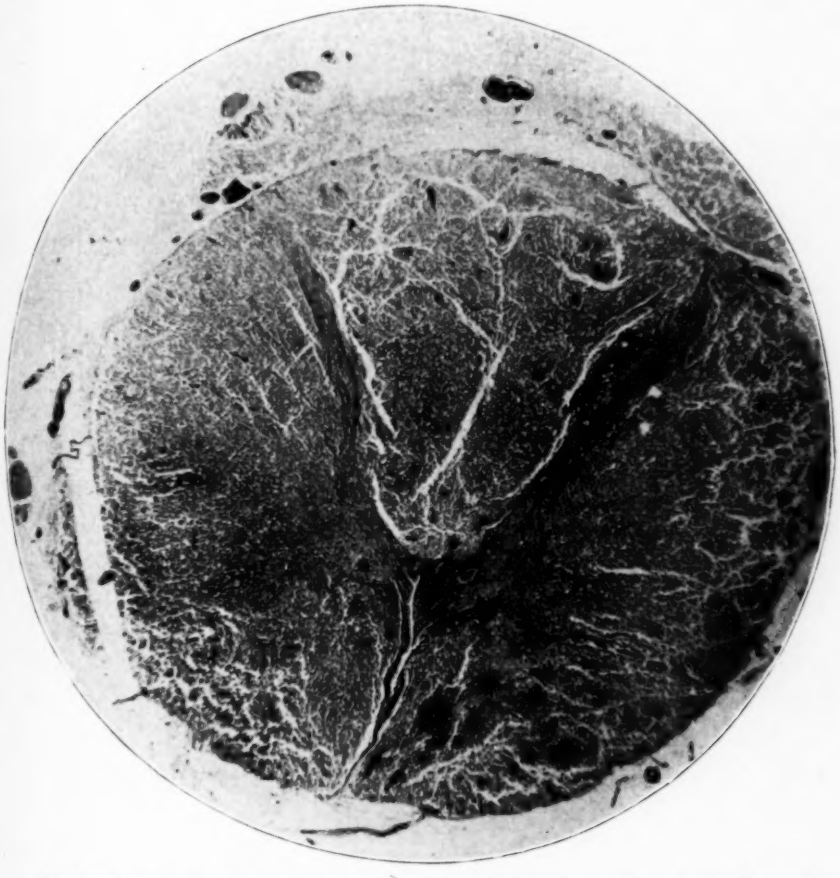

Fig. 8 (case 41).—Transverse section through dorsal segment of spinal cord; Weil stain; Leitz objective, 1 mm.; ocular, × 4; to demonstrate foci of hemorrhage.

ities; the spinal cord showed an uneven surface, and at places the substance protruded over the surface of the ruptured pia-arachnoid and was softened; there was recent blood in the terminal portion of the cauda equina. The cervical cord was very lumpy and symmetrically enlarged. In the pons and medulla oblongata were two well circumscribed gray-brown areas which were not softened.

Microscopic Examination.—There was a diffuse perivascular cellular infiltration in sections of the hemispheres, the pons (fig. 5) and the medulla oblongata. It consisted of polymorphonuclear leukocytes, lymphocytes and frequent segmentation of the nucleus, and a moderate number of monocytes. There were edema around the blood vessels and partial demyelinization. There was a diffuse small round cell infiltration of the pia-arachnoid at the convexities. The leptomeninges of the spinal cord showed only mild infiltration with small round cells. In sections through the midthoracic region there was a marked cellular infiltration, mostly around the central arteries and in the lateral columns. It was not confined to the perivascular spaces, but extended diffusely into the white matter. It consisted of the same cells that have been described in the brain; no plasma cells or eosinophilic cells were seen in these infiltrations (fig. 6). The segmentation of the nuclei was more marked than in the sections of the brain. In a focus in the lateral columns, a colony of diplococci, resembling pneumococci, was found (fig. 7). The whole section of the spinal cord was faintly stained with the Weil stain for myelin sheaths, without revealing, however, any marked demyelinization. The myelin sheaths were distorted and swollen; this was true also of the axons in sections stained by the Davenport method. Numerous foci of recent hemorrhages were seen in the gray matter (fig. 8). Fat-laden gitter cells were scattered throughout, or accumulated perivascularly. There was no increase in fibrous glia in sections stained by the Holzer method; the cytoplasm of the astrocytes stained diffusely with cresyl violet and showed marked vacuolation. Many anterior horn cells were severely affected, showing atrophy and shadow formation.

Microscopic Diagnosis: Encephalomyelitis and meningitis (diplococci).

According to the observations at autopsy, the forty-six cases may be divided into four groups:

1. Lymphogranulomatosis of the epidural space or of vertebrae.

2. Cases that clinically had shown paraplegia, in which x-ray treatment had been given and in which at autopsy lymphogranulomatous scar tissue had been found epidurally or in the region of the intervertebral foramina.

3. Cases of infectious myelitis. In both cases there was an additional encephalomeningitis. Case 1 of group 1, which also presented encephalitis in addition to the epidural lymphogranulomatosis, was tabulated in group 1. Case 42 which did not show involvement of the spinal cord, and which was not considered in the statistics in tables 2 to 5, was added in order to demonstrate the occurrence of encephalitis in lymphogranulomatosis.

4. Syringomyelia. Case 33 also belongs to this group; it showed cavity formation throughout the whole dorsal and lumbar cord.

TABLE 1.—*Autopsy Observations in Forty-Six Cases of Lymphogranulomatosis*

Group 1—Lymphogranulomatosis of Epidural Space or of Vertebrae

Authors	Clinical History	Observations at Autopsy or at Operation
1 Askanazy, M.: Verhandl. deutsch. path. Gesellsch. **24**: 78, 1921	Woman 59; for 2 mo. pain in neck and paralysis of arms; died after onset of fever and meningeal symptoms	Brain: leptomeningitis; ecchymoses; perivascular cellular infiltration; scattered neuronophagia. Spinal cord: granulomatous tissue at C 5, epidurally
2 Blakeslee, G. S.: Arch. Neurol. & Psychiat. **20**: 130, 1928	Man 26; Hodgkin's disease for 5 yr.; progressive destruction of vertebrae from 2 to 4; paraplegia for 2 mo.	Operation: mutton-tallow material extradurally at the level of vertebrae D 2 to 4
3 Cain, Rochet, and Horowitz: Bull. Soc. méd. d. hôp. de Paris **45**: 1498, 1929	(a) Man 23; Hodgkin's disease for 3 yr.; paraplegia and cachexia for a few months	Extradural lymphogranulomatous masses at C 6 to D 2
	(b) Man 25; 2 mo. after febrile herpes labialis flaccid paraplegia	Epidural granulomas at D 7 to 9; total transverse demyelinization, with fields of empty spaces
4 Carslaw, J., and Young, J. S.: Glasgow M. J. **108**: 193, 1927	Man 24; Hodgkin's disease for 5 yr.; pneumonia for last 5 mo.: for 2 mo. transverse lesion of spinal cord	Epidurally, granulomatous masses in upper dorsal cord; diseased vertebrae D 1 to 4; spinal cord softened at this level
5 Dietrich: Verhandl. d. deutsch. path. Gesellsch. **24**: 78, 1921	Paraplegia of legs	Lymphogranulomatosis of dorsal vertebrae
6 Duering, M.: Deutsches Arch. f. klin. Med. **127**: 76, 1918	Man 43; Hodgkin's disease for 5 yr.; for 4 yr. paresthesias in legs; pain in back; paresis in legs, with incontinence of bowels; for 1 yr. complete paraplegia of legs	Lymphogranulomatosis of spinal column at D 9 to L 2; epidural granulomatous tissue in lower dorsal region; demyelinization of spinal cord mostly in lateral columns; numerous tissue spaces and gitter cells
7 East, C. F. T., and Lightwood, R. C.: Lancet **2**: 807, 1927	Man 43; Hodgkin's disease for 2 yr.; since 5 mo. weakness of upper arms; for 2 mo. numbness below D 10; retention of urine; then paraplegia of legs	Lymphogranulomatous tissue in spinal canal invading intervertebral foramina at D 1, 2, 6, and 7
8 Eichhorst, H.: Deutsches Arch. f. klin. Med. **61**: 519, 1898	Youth 17; 3 wk. before death signs of a transverse lesion of spinal cord	Epidural granulomatous growth at vertebrae D 5 to 7
9 Elsberg, C. A.: Arch. Neurol. & Psychiat. **20**: 137, 1928	Paraplegia of legs; x-ray treatment	Operation: lymphoid deposits in epidural space
10 Ginsburg, S.: Arch. Int. Med. **39**: 571, 1927	(a) Man 57; for 3 yr. persistent pruritus with Hodgkin's disease; for 1 yr. paraplegia of legs	Laminectomy: epidural lymphogranuloma between vertebrae D 3 to 7; erosion of lamina of vertebra D 6
	(b) Woman 32; after 3½ yr. of Hodgkin's disease severe pain in dorsal and cervical spine developed, followed by paraplegia of legs and incontinence	Laminectomy: epidural lymphogranulomatous masses at D 2 to 5
11 Holmes, G. W.: Am. J. Roentgenol. **16**: 107, 1926	Man 33; since 1 yr. pain in back, lower abdomen and legs; x-ray treatment	Laminectomy: lymphogranulomatous masses epidurally in lumbar region
12 Judin, S.: Arch. f. klin. Chir. **150**: 317, 1928	Woman 33; Hodgkin's disease for 4 yr.; x-ray treatment for 3 yr.; paraplegia of legs for 1 mo.	Laminectomy: destruction of vertebra C 4 with epidural lymphogranulomatosis at this level, at D 1 to 3 and at cauda equina
13 Koelichen, M.: Rev. neurol. **1**: 545, 1927	Man 29; Hodgkin's disease for 6 yr.; intermittent x-ray treatment; few months before death paraplegia of legs with sphincter involvement	Epidural lymphogranulomatous tissue at D 1 to 3 and at cauda equina
14 Luce, H.: Deutsche Ztschr. f. Nervenh. **78**: 347, 1923	Youth 17; Hodgkin's disease for 4 yr.; accident 1 yr. ago and 3 mo. later paraplegia	Vertebrae C 7 to D 4 destroyed, fractured; epidural masses at D 1 to 2
15 von Muellern, K., and Grossmann, B.: Beitr. z. path. Anat. u. z. allg. Path. **52**: 276, 1912	Man 28; Hodgkin's disease for 2 yr.; pain in back for 2 mo.	Lymphogranulomatosis of vertebrae, with epidural masses and compression of spinal cord, in dorsal region
16 Naffziger, H. C.: Arch. Neurol. & Psychiat. **20**: 136, 1928	Woman; for 5 yr. Hodgkin's disease; x-ray treatment; disease of vertebrae from D 2 to 4; for 6 mo. paraplegia of legs; complete block since 2 mo.	Laminectomy: mutton-tallow material epidurally
17 Neubuerger, K., cited from Walthard (no. 33)	Man 20; sudden onset with lancinating pain in shoulders and total paraplegia within a few hours	Laminectomy: granulomatous masses epidurally
18 Nonne, M.: Deutsche Ztschr. f. Nervenh. **47-48**: 478, 1913	Woman 38; for 6 mo. pain in lumbar region with paraplegia of legs for 4 wk.; laminectomy at from D 5 to 6; cachexia; death	Laminectomy: granulomatous at posterior aspect of spinal cord. Autopsy: granulation tissue epidurally in dorsal region

TABLE 1.—*Autopsy Observations in Forty-Six Cases of Lymphogranulomatosis —Continued*

Group 1.—Lymphogranulomatosis of Epidural Space or of Vertebrae—Continued

Authors	Clinical History	Observations at Autopsy or at Operation
19 Osler, William, and McCrae, T.: Principles and Practice of Medicine, 1925, p. 985	Paraplegia occurring in Hodgkin's disease	Lymphogranulomatous growth in spinal canal
20 Weber, F. P.: Internat. Clin. (ser. 30) **1**: 126, 1926	Youth 18; Hodgkin's disease for 4 yr.; lumbar pain since 1 yr. ago; paraplegia of legs for 6 mo.	Epidurally lymphogranulomatous tissue down to cauda equina
21 Weber, F. P., and Bode, O.: Lancet **2**: 806, 1927	For 4 mo. severe pain in left shoulder; wasting of muscles of upper extremities	Diffuse lymphogranulomatous infiltration of epidural spaces of dorsal aspect of spinal cord
22 Poynton, F. J., and Harris, K. E.: Lancet **2**: 903, 1930	Man 23; for 5 mo. pain in back and stiffness of legs	Purplish-gray masses infiltrating dura mater for a length of 4 cm. in region of D 2 to 4
23 Ryle, J. A., cited from Weber (no. 20)	Hodgkin's disease for 3 yr.; x-ray treatment; sudden paraplegia of lower extremities with incontinence	Granulomatous masses on the frontal aspect of vertebral bodies; softening of spinal cord in dorsal segments
24 Schaeffer, H., and Horowitz, A.: Presse méd. **38**: 403, 1930	(a) Woman 25; Hodgkin's disease for 2 yr.; x-ray treatment; for 4 mo. paraplegia of legs with complete anesthesia up to D 10; septicemia following decubitus (b) Young man; 3 yr. diseased; improved under x-ray treatment; for 2 mo. spastic paralysis of legs	Epidural lymphogranulomatosis at lower dorsal segments with complete demyelinization of spinal cord at this level and vacuolation; epidural masses of young granulomatous tissue at from C 6 to D 1
25 Shapiro, P. F.: Arch. Neurol. & Psychiat. **24**: 509, 1930	Woman 32; Hodgkin's disease for 1 yr.; x-ray therapy; for 4 wk. paralysis of legs with incontinence of urine	Epidural granulomatous tissue at from D 3 to 4; at the same level demyelinization and intense "Luecken" formation of spinal cord; below and above secondary degeneration
26 Shore, L. R., and Young, W. A.: Lancet **2**: 915, 1925	Woman 26; for 1 yr. pain in right leg	Infiltration of the bodies of vertebrae D 11 to L 2 with lymphogranulomatous masses
27 Sicard, J. A., Belot, J.; Coste, and Gastaud: J. de radiol. et d électrol. **9**: 377, 1925	Woman 28; Hodgkin's disease for several years; improved under x-ray treatment	Granulomatous masses invading the spinal column through the intervertebral foramina; destruction of lower cervical vertebrae
28 Simons, A.: Deutsche Ztschr. f. Nervenh. **59**: 289, 1918	Youth 18; sudden paraplegia of legs and constipation; following laminectomy fever developed; x-ray treatment; died 3 mo. after operation	Laminectomy; large granulomatous masses epidurally at from D 2 to 6. Autopsy; granulomatous masses have disappeared; only white, milky connective tissue remains
29 Suckling, C. W.: Lancet **1**: 246, 1885	Neurologic symptoms pointing to transverse lesion of spinal cord	Multiple granulomatous growths epidurally
30 Taylor, A. S.: Arch. Neurol. & Psychiat. **20**: 130, 1928	Man 26; symptoms of compression of spinal cord in lower cervical and dorsal region	Laminectomy: epidurally lymphogranulomatous masses on cervical spinal cord
31 Tidy, H. L., cited from Weber (no. 20)	Man 46; paraplegia of legs in Hodgkin's disease	Lymphogranulomatous growths on posterior aspect of spinal cord from D 6 to 10
32 Urechia, C. I., and Goia, I.: Presse méd. **35**: 179, 1927	Woman 48; Hodgkin's disease for 9 mo.; paralysis of legs for 3 wk.; x-ray treatment	Nodular infiltration of inner surface of dura mater of lumbar and sacral region with granulomatous masses; irregular foci of vacuolation in lumbar spinal cord
33 Walthard, K. M.: Ztschr. f. d. ges. Neurol. u. Psychiat. **97**: 1, 1925	Woman 53; sudden onset with pain in back and complete paraplegia of legs within 30 hr.; level of anesthesia from D 3 downward; decubitus; pyelonephritis	Epidural granulomatous masses at D 3; complete degeneration of spinal cord; foci of hemorrhagic softening with thrombi formation; destruction of bodies of vertebrae from D 8 to 12, and granulomatous masses at this level epidurally
34 Warrington, W. B.: Liverpool Med.-Chir. J. **31**: 52, 1911	Man 46; Hodgkin's disease for 3 yr.; paraplegia of legs for 1 yr.	Destruction of the bodies of vertebrae from D 8 to 12; epidural lymphogranulomatous masses
35 Welch, J. E.: Proc. New York Path. Soc. **10**: 161, 1910	Man 32; Hodgkin's disease	Collar tissue of granulomatous masses epidurally at from D 6 to 8
36 Weil, A.: Case of Dr. J. P. Simonds	Man 35; Hodgkin's disease for 7 yr.; 5 yr. x-ray treatment; 5 mo. pain between shoulders; 2 mo. paralysis of legs with sensory level at D 4	Invasion of spinal canal through intervertebral foramina by granulomatous masses extending all along dorsal spinal cord epidurally; edema of dorsal segments with vacuolation

TABLE 1.—*Autopsy Observations in Forty-Six Cases of Lymphogranulomatosis —Continued*

Authors	Clinical History	Observations at Autopsy or at Operation
Group 2.—Cases with Paraplegia Clinically, X-Ray Treatment and Lymphogranulomatosis Scar Tissue Epidurally or in Region of Intervertebral Foramina at Autopsy		
37 Forrest, D.: Lancet **2**: 809, 1927	Man 34; Hodgkin's disease for 3 yr.; spastic paraplegia of legs 3 mo.; x-ray treatment	Enlargement of left lumbar and iliac glands; pressure on lumbar artery; degeneration of Goll's column in cervical and dorsal segments; small patch with loss of myelin in lateral pyramidal tract; pallor in periphery of spinal cord; in S 1 marked degeneration of pyramidal tract
38 Shapiro, P. F.: Arch. Neurol. & Psychiat. **24**: 509, 1930	Woman 30; Hodgkin's disease for 17 mo.; 2 courses of x-ray treatment; for 2 mo. flaccid paralysis of legs; septicemia following sacral ulcers	At midthoracic level of spinal cord degeneration of posterior columns and peripheral zone of spinal cord; intensive vacuolation of posterior and periphery of lateral columns; hemorrhage in pons
39 Weil, A., and Davison, C.: Arch. Neurol. & Psych. **22**: 966, 1929	Woman 34; Hodgkin's disease for 8 yr.; 1 yr. paraplegia of legs with sensory level at D 2; deep x-ray therapy	At from D 3 to 4 fatlike masses causing compression of spinal cord epidurally; spinal cord at this level demyelinized throughout, with numerous fat-laden gitter cells; above and below secondary degeneration
Group 3.—Infectious Myelitis and Encephalitis		
40 Allen, G. A., and Blacklock, J. W. S.: Glasgow M. J. **103**: 115, 1925	Woman 44; 2 yr. ago "nervous breakdown"; 1 yr. later Hodgkin's disease; for several months paralysis of legs with retention of urine; shortly before death left hemiparesis	Subdural and subarachnoid spaces contain pus with staphylococci and streptococci.; Marchi and Weigert degeneration in both pyramidal tracts; some diffuse degeneration of myelin sheaths of juxtagrigeal white matter extending half way to the surface; infectious myelitic below middorsal region
41 Weil, A.: Case of Dr. R. Grinker	Young man; Hodgkin's disease for 1 yr.; for 6 mo. cough and cachexia; for 2 mo. bronchopneumonia; x-ray therapy; for 2 wk. cold, incontinence, paralysis of palate, bilateral optic neuritis, weakness of arms, paralysis of legs; hypesthesia up to groin	Purulent bronchitis; retropharyngeal abscess; recent hemorrhages in brain and spinal cord; cellular infiltrations throughout, perivascular and in tissue; leptomeningitis
42 Hecker, H. V., and Fischer, W.: Deutsche med. Wchnschr. **48**: 482 and 520, 1922	Man 32; Hodgkin's disease for 2 yr.; a few months before death epileptiform convulsions	In centrum ovale on both sides of brain at the level of the heads of the caudate nuclei soft, hemorrhagic foci; perivascular infiltration by lymphocytes and plasma cells; no eosinophilic cells
Group 4.—Syringomyelia		
43 Forrest, D.: Lancet **2**: 809, 1927	Youth 14; Hodgkin's disease for 10 mo.; spastic paraplegia for 1 mo.	No epidural masses; syringomyelia in lower cervical spinal cord
44 Turnbull, cited from Weber (no. 20)	Youth 14; Hodgkin's disease with spastic paraplegia of legs	Syringomyelia at from D 3 to 9

TABLE 2.—*Distribution of Forty-Six Cases of Lymphogranulomatosis*

Group	Observations at Autopsy	Cases	Per Cent of Total	Male Sex	Female Sex	Age, Yr.	Per Cent of Total
1	Lymphogranulomatosis of dura mater or of vertebrae	39	85	24	14	14–20	18
						21–30	32
						31–40	29
						41–50	13
						51–60	8
2	Scar tissue in spinal canal (clinically paraplegia; patient given x-ray treatment)	3	7	1	2	34, 34, 30	..
3	Infectious myelitis	2	4	1	1	44—	..
4	Syringomyelia	2	4	2	..	14, 14	..

TABLE 3.—*Thirty Cases of Paraplegia with Autopsy Reports*

Duration of Hodgkin's Disease, Yr.	Cases	Per Cent of Total	Duration of Paraplegia, Mo.	Cases	Per Cent of Total
1–2	12	40	1–2	16	53
3–5	14	46	3–6	10	33
6–8	4	14	7–12	4	14
		X-Ray Treatment in Nine Cases			
1–2	5	56	1–2	4	44
3–5	2	22	3–6	5	56
6–8	2	22	....	..	..

TABLE 4.—*Paraplegia and Time of Onset Before Death*

	Cases	Duration, Mo.	Per Cent
Paralysis of legs	43	1–3	83
		4–6	7
		7–12	10
Paralysis of arms	2	....	..

TABLE 5.—*Location of Epidural Lymphogranulomatosis*

Vertebrae	Cases	Per Cent of Total
Cervical	6	16
Seventh cervical to fourth dorsal	1	3
First to sixth dorsal	12	32
Seventh to twelfth dorsal	10	26
Dorsal	6	16
Dorsolumbar	1	3
Lumbosacral	2	4

COMMENT

Tables 1 to 5 are self-explanatory. They demonstrate the following facts: The involvement of the spinal cord begins at the end-stage of a case of Hodgkin's disease that may have lasted from one to eight years. Signs of a complete spinal cord lesion develop rapidly, after a short period of prodromal signs, from one to six months before death and within a period of a few days or weeks at the maximum. It does not seem likely that deep x-ray therapy will prolong life after the lymphogranulomatosis has invaded the spinal canal, except in cases in which an early laminectomy has been performed. From clinical, experimental and autopsic evidence combined (case 28) it has been proved that x-ray treatment is able to reduce considerably the size of the epidural lymphogranulomatous tissue. Therefore, the presence of only small masses of granulomatous or scar tissue epidurally at autopsy, following prolonged deep x-ray therapy, cannot be taken as evidence against the probability that the symptoms of a complete transverse spinal cord lesion which had been established clinically had been produced by the epidural or vertebral lymphogranulomatosis.

The theory that in lymphogranulomatosis a hypothetic toxin is formed which acts destructively on the spinal cord "par distance" without the formation of any local foci could not be supported by the

analysis of forty-six cases. In 92 per cent of the total, local lymphogranulomatous tissue was found either epidurally or involving the vertebrae. In 4 per cent an infectious encephalomyelitis explained the clinical symptoms. The question whether the inflammatory process in the latter cases was or was not produced by the same agent that was responsible for the general lymphogranulomatosis cannot be answered definitely. The absence of the typical cells in the perivascular infiltrations (eosinophilic, Sternberg's and plasma cells) and the demonstration of diplococci in case 41 speak rather in favor of the theory that the infection was secondary to bronchopneumonia.

The mechanism of the myelopathy in groups 1 and 2 can easily be explained by the mechanical obstruction of blood vessels and lymphatics supplying the spinal cord through the lymphogranulomatous tissue, either within the intervertebral foramina or outside the spinal canal. The granulomatous tissue may originate from retroperitoneal or mediastinobronchial lymph nodes or from diseased vertebrae. It can easily be understood that the interruption or diminution of vascular supply of the spinal cord, if continued over a longer period of time, will produce a diffuse myelomalacia, which will be the more severe the more spinal arteries are involved. The frequency of the involvement of the dorsal segments of the spinal cord, 74 per cent of the total, is easily understood if one considers that the blood supply of this region is taken over by the spinal branches of the intercostal arteries, and if one considers the enlargement of all the mediastinal and interthoracic lymph nodes. If to the invasion of the intervertebral foramina is added an invasion of the spinal canal itself, which interferes with the collateral blood supply through anastomoses with higher and lower segments, the resulting anemia will produce the myelomalacia, which will be anemic softening if the blood supply to a given region has been interrupted entirely. The addition of stasis of the lymphatic fluids at the segments involved, together with the anemia and the cachectic changes of the plasma, will aggravate the interference with the normal nutrition of the nerve tissues. Another example showing that this type of mechanical obstruction of the blood supply and lymphatic circulation is responsible for the disease of the spinal cord is given in cases in which the deep cervical lymph glands were first and mainly involved. The first complaints of the patients were of pain in the neck, radiating into the arms. Weakness and final paralysis of the arms followed, with wasting of the muscles. Symptoms of compression of the spinal cord developed only at the end-stage of the disease, and at autopsy lymphogranulomatous masses were found invading the spinal canal through the intervertebral foramina.

Recently, Shapiro [2] claimed that a hypothetic "toxin" in Hodgkin's disease was able to produce the typical histologic picture of pernicious

anemia—subacute combined degeneration. No other instance could be found in the literature, and his statements do not support his claim.

A woman, aged 30, had suffered from persistent cough and dyspnea for seventeen months. A diagnosis of Hodgkin's disease had been made and several courses of x-ray therapy given. Two months before death flaccid paraplegia of the legs developed, with a sensory level at the tenth dorsal vertebrae. The woman died following a septic ulcer. The autopsy revealed lymphogranulomatosis of the peribronchial, peritracheal and peri-aortic lymph nodes. Microscopic examination of the spinal cord showed at the midthoracic level numerous "Luecken" and fat-laden gitter cells, with marked degeneration of the myelin sheaths and nerve fibers. The author states: "The changes severely affected the entire posterior column. In the lateral columns the peripheral zone, including the dorsal and ventral spino-cerebellar tract and the spinothalamic tracts with the dorso-lateral fasciculus were almost as severely involved. The intermediate zone (pyramidal and rubro-spinal tracts) were only moderately affected, the central zone of propria fibers even less. The anterior columns were intact. Other levels of the cord showed practically the same changes

As a photographic proof of the condition, there was added a photomicrograph of a frozen section stained with sudan III showing numerous fat-laden gitter cells. The histologic picture that has been described is seemingly not that of subacute combined degeneration as seen in pernicious anemia. The "Luecken" were not the "Lueckenfelder" produced by the coagulation necrosis of the spinal cord tissue in the latter disease. They resembled the vacuolation, the "Luecken," which are seen in cases of lymphogranulomatosis in which there is an interference with blood supply and lymphatic circulation due to a pathologic process outside the spinal cord.

When this case was presented before the Chicago Neurological Society (May, 1930) the suggestion was made that one possibly was dealing with a myelomalacia of such a type rather than with the subacute combined degeneration of pernicious anemia. Unfortunately, Dr. Shapiro was unable to send the microscopic preparations from this case to me for study because they had been lost. The preceding treatment with the x-rays in Dr. Shapiro's case makes it impossible for the pathologist to say that no granulomatous tissue had been present during life within the intervertebral foramina or outside the spinal canal, interfering with circulation in the spinal arteries. For the same reason, because an intensive course of roentgen therapy had been given, Shapiro is not justified in concluding in his first case (no. 25 of table 1) that the epidural granulomatous mass, 30 mm. long and 15 mm. thick, "had not produced the severe degeneration of the underlying cord by any direct compression."

The many examples of improvement in the clinical symptoms of a lesion of the spinal cord following x-ray treatment also speak against the assumption that a hypothetic toxin was destroying the spinal cord.

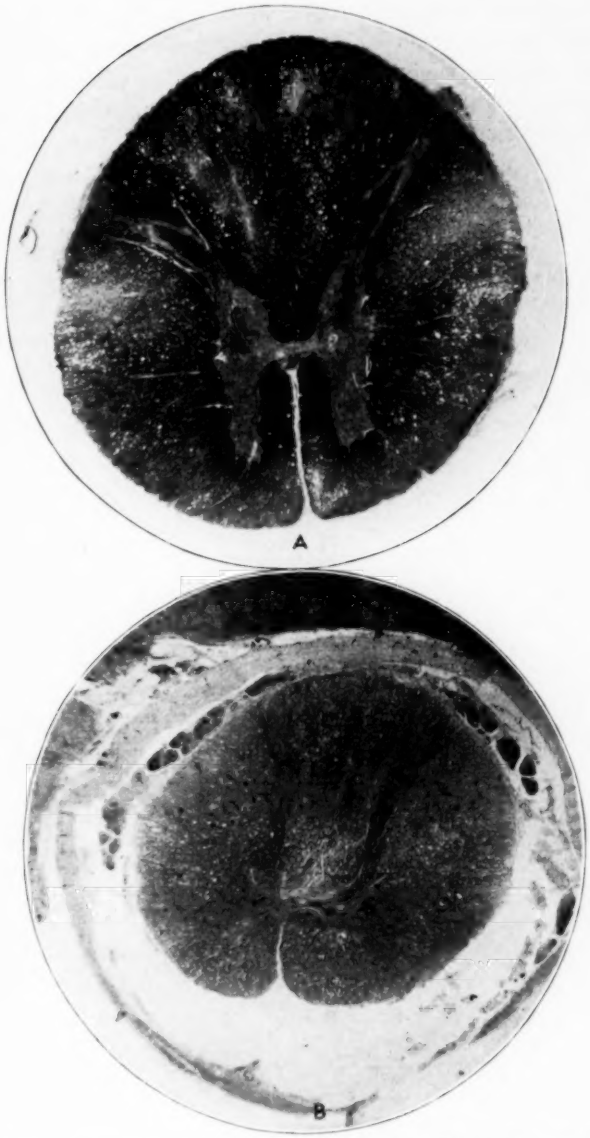

Fig. 9.—*A*, transverse section through spinal cord in a case of pernicious anemia in a woman of 56 years; duration of disease, four years; *B* (case 36), transverse section through spinal cord in a case of Hodgkin's disease in a man, aged 35; duration of disease, seven years; x-ray treatment, five years. Both sections were stained with Weil stain and photographed with the same optic system: Zeiss objective, 1-1.5 mm.; ocular, × 4 (reduced one-half in reproduction); same extension of the camera. The figure demonstrates the histologic picture of pernicious anemia in comparison with the myelopathy in a case of epidural lymphogranulomatosis.

Such destruction as that occurring in subacute combined degeneration of the pernicious anemia type could not have been repaired. On the other hand, every evidence points to the fact that the benefit from the x-ray treatment was brought about by a reduction in size of lymphogranulomatous masses invading the spinal canal. One might ask why subacute combined degeneration of the spinal cord has been claimed only once, by Shapiro, if 86 per cent of all cases of lymphogranulomatosis do not show disease of the spinal cord, and if in the remaining

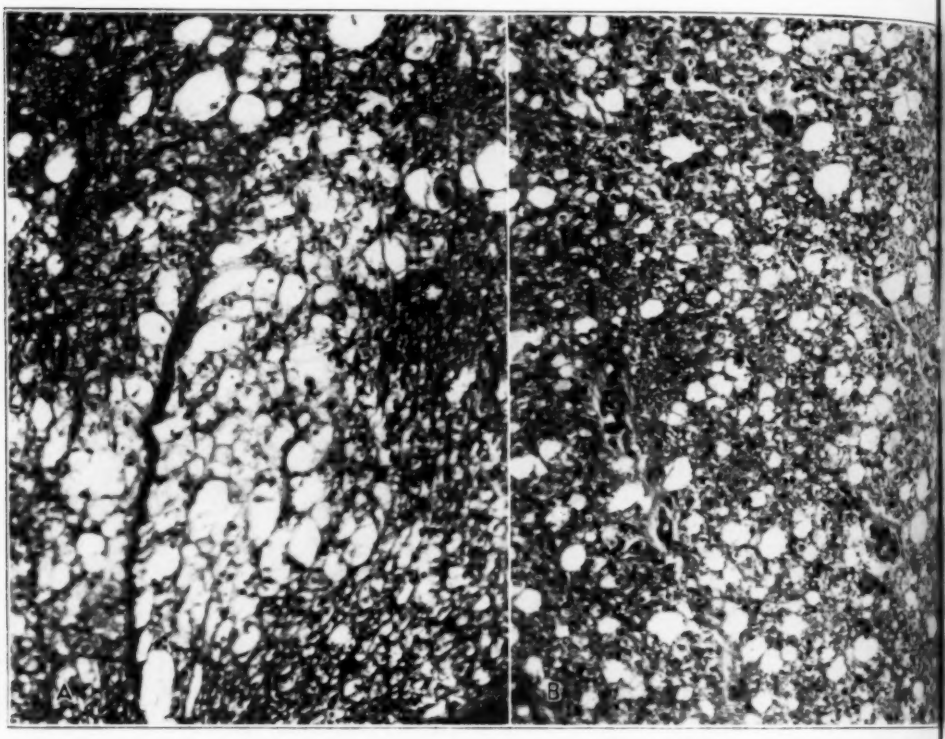

Fig. 10.—Same cases as in figure 9 *A* and *B*; van Gieson stain; Leitz objective, × 10; ocular, × 10 (reduced one-half in reproduction); to demonstrate the "Lueckenfelder" in pernicious anemia (*A*) and the intense vacuolation, the "Luecken," in the case of epidural lymphogranulomatosis (*B*).

14 per cent granulomatous masses were demonstrated in 92 per cent as being responsible for the destruction of the spinal cord.

In order to avoid further misunderstanding it may once more be emphasized that Davison and I[3] did not claim that subacute combined degeneration does not occur outside of pernicious anemia.

3. Weil, A., and Davison, C.: Changes in the Spinal Cord in Anemia: A Clinicomicroscopic Study, Arch. Neurol. & Psychiat. **22**:966 (Nov.) 1929.

We dealt only with "changes in the spinal cord in anemias," and we wished to demonstrate that anemia itself, i.e., lack of hemoglobin and oxygen, was not responsible for the condition of subacute combined degeneration, a histologic picture that is seen only in the pernicious types. It was concluded that one and the same toxin acted destructively on the spinal cord and the hematopoietic system, though both changes might occur at different periods and not simultaneously. In the meantime experimental investigation has made it probable that a similar hypothetic toxin is produced in certain avitaminoses, and from former experience we know that it also may be seen in pellagra in man.

Two pairs of photomicrographs are added in order to emphasize again the difference between the histologic picture of the "Luecken-felder" in pernicious anemia and the "Luecken," the vacuolation of the edematous spinal cord, in epidural lymphogranulomatosis.

CONCLUSIONS

1. Reports were collected from the literature of forty-three cases of lymphogranulomatosis in which the spinal cord had been diseased and in which observations at autopsy or at operation had been recorded. Three personal cases that had been studied histologically were added.

2. In 85 per cent of all the cases there was an invasion of the spinal canal by epidural lymphogranulomatous tissue. In 7 per cent which had shown paraplegia clinically and in which there had been treatment with x-rays only scar tissue could be demonstrated in the spinal canal, together with severe disease of the retroperitoneal and intrathoracic lymph nodes. In two cases, 4 per cent, there was an infectious encephalomyelitis, which could explain the clinical symptoms. In two cases, both of boys aged 14, a syringomyelia was found.

3. In the differential diagnosis of symptoms of disease of the spinal cord in a case of Hodgkin's disease of several years' standing, one should consider: (1) invasion of the spinal canal by lymphogranulomatous tissue (92 per cent), (2) an infectious myelitis and (3) syringomyelia. The idea that a hypothetic toxin might produce the histologic picture of subacute combined degeneration (pernicious anemia type) should be abandoned. The therapy should be directed to early x-ray treatment and laminectomy.

4. The dorsal segments of the spinal cord were involved in 80 per cent of all the cases, while in only 16 per cent the cervical region was affected and in 4 per cent the lumbosacral region alone.

5. A comparison of cases in which treatment with x-rays had been given with cases in which this treatment had not been given did not show any prolongation of life in the former case; in 86 per cent of all cases that came to autopsy, the patients died within from one to six months after the onset of the paraplegia.

ABSTRACT OF DISCUSSION

DR. G. B. HASSIN: In Dr. Weil's cases were the changes present at the level of the epidural mass also found above and below it? In my opinion it would be proper to designate the changes described by Dr. Weil as fenestration or rarefaction of the cord, caused by the dropping out of swollen nerve fibers from an edematous parenchyma. In myelomalacia, the glia is also destroyed and the entire aspect of the cord is changed, which is not the case here. In subacute degeneration of the cord, changes such as those described by Dr. Weil occur, but they are due to a toxemia, while in lymphogranulomatosis they are of mechanical origin. One is not justified in denying the toxic origin of subacute degeneration of the cord, because its pathology is similar to that of multiple sclerosis, an essentially toxic disease process.

DR. ARTHUR WEIL: I am pleased that Dr. Hassin agrees that in lymphogranulomatosis a hypothetic toxin cannot be made responsible for the changes in the spinal cord, but merely mechanical obstruction of circulation through the invading lymphogranulomatous masses. The idea of the toxic origin of subacute combined degeneration is in perfect harmony with former publications (Weil and Davison). We are still ignorant of the true nature of this toxin. In recent experiments the theory has been advanced that a metabolic disturbance in an avitaminosis might be the etiologic factor.

PLANTAR REFLEXES IN NORMAL ADULTS*

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Although the Babinski phenomenon has been the subject of much study, the normal plantar reflex has received little attention. Textbooks describe no uniform method of eliciting this response, nor do they agree on a description of the reflex. Purves-Stewart,[1] McKendree[2] and Monrad-Krohn[3] considered flexion of the big toe only as the normal reaction, while Wechsler,[4] Church and Petersen[5] and Jelliffe and White[6] described the reflex as flexion of all the toes. Oppenheim[7] spoke of dorsal flexion of the foot as well as of the toes. Textbooks also disagree as to the way in which this reflex should be elicited. Wechsler[4] called attention to the possibility of bringing out a doubtful response by rotating the head away from the side stimulated; McKendree[2] suggested flexing the knee, while Purves-Stewart[1] expressed the belief that the hip, too, should be partially flexed. Only Oppenheim[7] emphasized the importance of distracting the patient. There is no standard method of examining the plantar reflex, nor is there any widely accepted way of reading the response.

The present study was undertaken with the hope of establishing uniform conditions for eliciting this phenomenon by investigating the responses under recorded and controlled circumstances. My associates and I examined 160 normal adults, studying their plantar reflexes under arbitrarily selected "standard" conditions; we then modified these conditions in a definite manner and noted the ways the responses varied.

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* Submitted for publication, April 27, 1931.

* One of a series of studies on normal subjects from the Graduate School of Medicine, University of Pennsylvania, under the direction of Dr. T. H. Weisenburg.

1. Purves-Stewart, James: Diagnosis of Nervous Diseases, ed. 5, New York, E. B. Treat & Company, 1921, p. 315.

2. McKendree, Charles A.: Neurological Examination, ed. 1, Philadelphia, W. B. Saunders Company, 1928, p. 85.

3. Monrad-Krohn, G. H.: Clinical Examination of the Nervous System, ed. 4, New York, Paul B. Hoeber, Inc., 1928, p. 95.

4. Wechsler, Israel: Text Book of Clinical Neurology, ed. 1, Philadelphia, W. B. Saunders Company, 1927, p. 37.

5. Church, Archibald, and Petersen, Frederick: Nervous and Mental Diseases, ed. 5, Philadelphia, W. B. Saunders Company, 1906, p. 36.

6. Jelliffe, Smith E., and White, William Allen: Diseases of the Nervous System, ed. 1, Philadelphia, Lea & Febiger, 1915, p. 52.

7. Oppenheim, Hermann: Text Book of Nervous Diseases, ed. 5, translated by Alexander Bruce, Edinburgh, Darien Press, 1911, vol. 1, p. 58.

METHODS OF STUDY

Selection of Subjects.—Most of the persons examined were patients in the Philadelphia Orthopaedic Hospital and Infirmary for Nervous Diseases. Excluded from this study were the following groups: sufferers from organic diseases of the spinal cord or of the motor tracts in the brain; children; orthopedic cases in which there were diseases of the spine or the legs; patients in whose cases the diagnosis was doubtful. A hundred and fifty-one persons were available; 10 volunteers, most of them medical students, were added to this list, and the reflexes were studied on the 322 feet of the 161 subjects. Neurologic examination of all these adults had been made, and all were "neurologically negative."

Instruments.—To be certain that variations in response were not due to alterations in the intensity of stimulation, we sought an instrument that would apply a constant pressure. We adopted the McCouch stimulator, which consists of a flat spring in an adjustable handle; by sliding a sleeve along the handle, the part of the spring exposed could be lengthened or shortened. This instrument was described and illustrated by Waggoner and Ferguson;[8] they used it to examine the reflex in infants, and attached a wax point to the end of the stimulator. The tougher skin of adults would not respond to this tip, and we used a thin wire at the end of the spring. At its loosest this device applies a pressure of 80 Gm.; when the minimum amount of spring is exposed, the pressure is 250 Gm. Waggoner and Ferguson found significant differences

Stimulator devised by Dr. Grayson P. McCouch.

between these responses, but with adults a difference was seldom found. We set the instrument at a calibration that applied a stimulus of 165 Gm., and used it at this reading in all "standard" experiments.

To study pinprick as a stimulus, we used an algesimeter that consisted of a sharp pin carried on the end of a coiled spring. This was controlled by a knob that could be set in any of several positions. We kept the device placed so as to deliver pinprick at a pressure of 63 Gm.

Recording the Results.—To simplify recording, we used a series of pairs of letters based on the fact that the little toes usually moved together as one unit, and the big toes moved as another. Flexion was indicated by "D" (down); extension by "U" (up); no movement by "Q" (quiet), and fanning by "F." The first initial of the pair referred to the big toe; the second to the minor toes. Thus, the report "QD" would mean that the big toe remained quiet and the lesser toes flexed. The ten possible responses were coded as follows:

QQ: No movement of any toe.
DD: Flexion of all the toes.
DQ: Flexion of the big toe; the other toes do not move.
QD: Flexion of the minor toes; the big toe quiet.
DU: Flexion of the big toe; extension of the other toes.
QU: Extension of the lesser toes; no movement of the big toe.

8. Waggoner, R. W., and Ferguson, W. G.: The Development of the Plantar Reflex in Children, Arch. Neurol. & Psychiat. **23**:619 (April) 1930.

UD: Extension of the big toe; flexion of the other toes.
UQ: Extension of the big toe, no movement of the minor toes.
UF: Extension of the big toe; the lesser toes fan.
UU: Extension of all the toes.

The response indicated "UF" is the classic Babinski sign.

Standard Conditions.—The standard conditions for performing the examination were: patient supine, head away from side stimulated; knee extended; patient distracted; stimulus made with McCouch stimulator at intensity of 165 Gm.; stroke made on fibular side of foot, starting at heel, moving deliberately along sole to end of foot. All movements of all the toes were recorded, and the foot was observed after the stimulator had left it to see if there were any secondary responses. After the reaction with this standard technic had been noted, the process was repeated with the subject's head turned the other way; the reflex was then examined with the knee in flexion. The study was repeated with the tibial side of the sole. Then, standard conditions were reestablished, but the algesimeter delivering a pinprick at 63 Gm. of pressure was used as the stimulator. In some cases further observations were made using the pin at 63 Gm. as a stimulator in the form of a series of single pricks under the "ball" of the foot (metatarsal heads). Observations were made as to the movements of the ankle and of the superficial muscles of the thigh and leg, but the present report is limited to a study of toe movements.

THE PLANTAR REFLEX UNDER STANDARD CONDITIONS

As the stimulator is drawn along the sole of the foot, a movement of the toes is sometimes observed just as the instrument is leaving the heel; the most noticeable response, however, occurs just as the "ball" of the foot is being irritated. Occasionally a third movement is seen after the stimulator has left the foot. There are, therefore, two sensitive zones on the plantar surface; the response from the first zone we termed "calcaneal," and the reflex from the ball of the foot we have designated as the "metatarsal arch response." Movements that occur after the instrument has left the foot are here referred to as "secondary" reactions.

The literature on the subject of the normal plantar reflex is confusing. Babinski [9] himself spoke of the stimulus as "pricking the sole of the foot" and described the response as "flexion of the thigh on the pelvis, of the leg on the thigh, of the foot on the leg, and of the toes on the metatarsus." Freidman [10] realized that extension of the big toe might be normal, but said that when it did occur in health it was accompanied by extension of the other toes. In infants the reflex is often of the extensor type, although Wolff [11] has maintained that in babies all

9. Babinski, Joseph: On the Cutaneous Plantar Reflex, Compt. rend. Soc. de biol. **48**:207, 1896.

10. Freidman, Edward D.: On a Possible Significance of the Babinski Reflex, J. Nerv. & Ment. Dis. **51**:146 (Feb.) 1920.

11. Wolff, Lotta: Response to Plantar Stimulation in Infancy, Am. J. Dis. Child. **39**:1176 (June) 1930.

the toes extended and that this is not, therefore, a Babinski sign. Waggoner and Ferguson,[8] however, seemed to be satisfied that the response is comparable to a genuine Babinski sign. They confirmed an observation of Tournay,[12] that at the moment of birth the reflex is flexor. Burr [13] called attention to the inconstancy of the infantile plantar reaction.

The responses that occurred in the normal adults whom we have studied as the stimulator was passing the ball of the foot (the metatarsal arch responses) were, in the 322 feet, distributed as follows:

QQ 59	QD 68	UQ 9
DD 83	DU 40	UF 0
DQ 10	QU 21	UU 28
	UD 4	

The response symbolized "DD" is the presumably normal plantar reflex. This downward movement of all the toes occurred in only a fourth of the cases. In 41 feet the big toe extended; this means that when the "ball" of the foot was stimulated, extension of the big toe occurred in 12 per cent of the normal adults examined. The genuine Babinski sign, coded as "UF," did not occur once; this suggests that fanning rather than extension is the indicator of a Babinski sign. A hasty neurologic examination will often result in recording as a positive Babinski phenomenon responses such as those symbolized by "UD," "UQ" or "UU." This error, no doubt, is responsible for some of the doubt cast on the validity of this reflex.

To assume that these observations indicate that an extension of the big toe might be normal would be unjustified. The tabulation records responses to irritation of the metatarsal arch only; it does not consider the first movements of the toes. Many of the textbooks, such as that of McKendree,[2] suggest that only the first movement is of clinical significance. In about a third of our cases this metatarsal arch response followed a calcaneal response, and most of the responses of the ball of the foot of extensor type followed calcaneal reactions of flexor pattern. For example, of the 28 feet that showed extension of all the toes ("UU"), 21 showed a preliminary flexor movement. If, instead of listing the metatarsal arch responses, one tabulated the first movements, the distribution would be different. So corrected, the tabulation would have to read:

QQ 49	QD 62	UD 3
DD 152	DU 20	UQ 2
DQ 17	QU 10	UU 7

12. Tournay, Maurice: Plantar Reflex in Infants, Encéphale **27**:718 (Nov.) 1926.

13. Burr, Charles W.: Reflexes in Early Infancy, Am. J. Dis. Child. **21**:592 (June) 1921.

By this method of recording, about half the feet show the expected flexion of all the toes, and only 3 per cent show extension of the big toe. Most of the feet that did show upward movement of the hallux, did, as in Freidman's [10] cases, show extension of the minor toes as well.

To describe the normal plantar reflex as flexion of the toes is therefore inadequate. A careful examiner should record whether or not there was response at the calcaneal zone, and should describe the movements of all the toes. The expression "Babinski sign absent" or "plantar reflex, normal" should not be acceptable. There is no normal plantar reflex; in this study only half the subjects showed the flexion of all the toes that is supposed to be normal.

Secondary Responses.—In 68 of the 322 feet examined, movement of the toes occurred after the stimulator had left the feet. Most of these secondary responses occurred when the metatarsal arch response was of the flexor type, and most of the secondary movements were extensor. Of the 83 patients whose ball-of-the-foot response was of "DD" type, 23 showed secondary reactions of some extensor form. Of the 68 persons whose metatarsal arch response was of "QD" type, 29 showed some form of extensor reaction as a secondary movement.

When a calcaneal response preceded a metatarsal arch reaction, the former was usually flexion, the latter extension. The same pattern is extended along the foot, and many of the patients who exhibited flexion at the ball of the foot showed extension as a secondary reaction. This suggests that, in many cases, extension is an overreturn of the flexing toes.

Distraction.—Just as distraction may reinforce a knee jerk, so one might imagine that the plantar reflex might be made more valid by taking away the patient's attention. Oppenheim [7] suggested distracting the patient by tracing a letter on his hand and asking him to identify it. We placed a key, coin or similar object in the subject's hand, and asked him to feel it and call out its name. In most cases this precaution seemed unnecessary, although some of the medical students who volunteered were so much interested that distraction was essential. In most of the adults examined, no significant differences were found between the response when the patient was attending and the reaction when he was distracted.

Turning the Head.—Of the textbooks I consulted, only Wechsler's [4] emphasized a position of the head in examining the plantar reflex. In this he followed the suggestion of Walshe,[14] who pointed out that rotating the head toward the side under examination would, by increasing hypertonus, reduce the time of extension, whereas turning the head to

14. Walshe, F. M. R.: Variations in the Form of Reflex Movements, Brain **46**:281 (Oct.) 1923.

the side opposite would make the extension movement, if any, more prominent. A doubtful Babinski sign, Walshe believed, can be made definite by turning the occiput toward the paralyzed side. In our work, under "standard" conditions, the subject's head was turned away from the side stimulated; after determining this response, the head was turned and the reflex again examined. Of the 322 feet, only 28 showed a different reaction after the head had been rotated. This suggests that in ordinary clinical practice the position of the head is not important in examining the plantar reflex. McCouch [15] pointed out that the modification of tone with the position of the head is not effective as long as cerebral control remains uninhibited, and that this negative conclusion is not necessarily valid for patients with disease of the motor pathway.

The question of tone as a factor in the plantar reflex is interesting. Freidman [10] considered the normal response to be evidence of reciprocal innervation. If the Babinski response is associated with increase of extensor tone, one would expect that drugs that cause this increase would convert a flexor response into an extensor one. This was reported in a case of parkinsonism by Elliott and Walshe,[16] who described the case of a patient with paralysis agitans in whom a flexor reaction could be changed into a Babinski phenomenon by the injection of $\frac{1}{1000}$ grain (0.0006 Gm.) of scopolamine. Zador [17] has pointed out that physostigmine, by increasing flexor tone, tends to diminish an extensor response, whereas scopolamine, by decreasing tone, might make prominent a doubtful Babinski sign. Associated with the problem of extensor and flexor tone is the question of relative chronaxie; this will be discussed later.

Bending the Knee.—Of the 322 feet tested under standard conditions, bending the knee brought about a shift toward extension in 20 instances and toward flexion in 37 cases; in the remaining 275 feet, bending the knee was not associated with any change in the response. The conclusion seems to be that in determining the plantar reflex the attitude of the knee is not important.

Tibial Side of the Foot.—Jelliffe and White [6] suggested that the stimulus may be applied to either border of the foot, but most clinicians consider that the stroke must be made along the outer edge of the sole, wthout giving thought to the reason for this instruction. We repeated our examinations by stimulating the tibial side of the foot, and found that in 286 of the 322 cases this was followed by prompt withdrawal of the foot. In most cases flexion of the toes accompanied the withdrawal.

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15. McCouch, Grayson P.: Personal communications to the author.

16. Elliott, T. R., and Walshe, F. M. R.: Babinski Response in Toxic States, Lancet **1**:65 (Jan. 10) 1925.

17. Zador, Julius: Effect of Certain Drugs on Tonicity, Monatschr. f. Psychiat. u. Neurol. **64**:336 (Aug.) 1927.

Most persons accept an irritation along the outer edge of the sole, but pull the foot away when the inner side is stimulated. This is due to the arrangement of the arches of the foot: Normally, the inner edge is raised and is spared the contact with the shoe and the ground that hardens the outer edge of the sole. As a result, the skin on the tibial side is more sensitive, which accounts for the differences in the withdrawal reaction. In some cases we applied a very hot test tube to the outer edge of the foot, and withdrawal with flexion of all the toes was observed. The reaction of withdrawal can be elicited by supplying a sufficiently high ratio between intensity of stimulus and toughness of skin. It is the degree of skin sensitiveness that accounts for withdrawal when the inner edge of the foot is stroked.

Significance of Withdrawal.—When withdrawal occurs, the clinician often wonders whether to accept this reaction as significant or to repeat the test. Many neurologists believe that withdrawal is a "reflex of defense," and isolated extension of the big toe, they think, is a sort of residuum or symbol of withdrawal of the whole foot. My observations do not confirm this; in almost every case, withdrawal was accompanied, not by extension of the toes, but by flexion. Babinski [9] himself described "flexion of the leg on the thigh and foot on the leg" as part of the normal plantar reflex, a movement that surely brings about withdrawal. Collier [18] spoke of the plantar reflex as a part of a complex movement in which the whole limb takes part. My work on stimulation with a pin suggests that flexion of the toes, not extension, is a defense reflex. Waggoner and Ferguson [8] found that a more intense stimulation might convert an infantile Babinski into a flexion reflex.

Withdrawal of the foot cannot be considered symbolic of a Babinski sign. It means merely that excessive irritation was produced, because either the stimulus was too intense or the skin was too sensitive. When this response is elicited, the clinician should repeat his examination, using a lighter stimulus.

Response to a Painful Stimulus.—To study the response to a nocuous stimulus, we used the algesimeter, delivering a pinprick at a pressure of 63 Gm. Recording first the response to a standard stimulus, then the reaction to drawing this pin along the sole of the foot, we noted no change in 218 of the 322 feet. In the remaining 104 instances, we observed a shift toward flexion in 66 and toward extension in 38. Rapidly drawn across the sole of the foot, a pin does not produce pain; in fact, it is a less intense stimulus than the standard stimulator, because its surface area is so much less. The rapid stroke does not allow the pin to penetrate. In the investigation of nocuous stimuli, observations about the pin as a stroking instrument are valueless; under such condi-

18. Collier, James: Plantar Reflexes, Brain **22**:271 (Feb.) 1899.

tions a pin is not a nocuous stimulus at all. Clinically, a pin might be used to study the plantar reflex quite as well as a blunter instrument.

After trying other methods, we concluded that a single pinprick under the ball of the foot would be a serviceable nocuous stimulus. By the time I had reached this conclusion, some of my patients were no longer available; this record is, therefore, limited to a study of 80 subjects—160 feet. The algesimeter was set at 63 Gm. of pressure; the pin was inserted under the head of the first metatarsal, and the response of the big toe was noted. The pin was then inserted under the ball at a lesser toe—the least calloused portion of the arch was selected—and the movement of the toes just above the point of insertion was recorded. These responses were then compared with the reflex when the standard stimulator was used. The results were as follows:

In the 160 feet, the big toe under standard stimulus extended in 18, flexed in 93, and did not move in 49 cases. When a pinprick was used, the 18 feet that originally showed extension now presented flexion in 10 cases and repeated the extensor movement in 8. Of the 49 feet that did not show the movement of the big toe under the standard stimulus, 11 showed no movement when a pin was used, 7 showed extension and in 31 feet the response to the pin was flexor. Of the 93 feet that exhibited flexion of the big toe to the standard stimulus, 71 repeated this when a pin was used. A nocuous stimulus converted a flexor response into an extensor one in less than a seventh of the cases; in more than half of the subjects, an extensor movement of the big toe was converted into flexion.

Of the 160 feet, the lesser toes exhibited flexion to the standard stimulus in 78, extension in 40 and no movement in 42. Pinprick resulted in a great majority of flexion reactions; of the 40 feet whose lesser toes showed extension to the standard stimulus, 28 exhibited flexion to pinprick.

If the insertion of a sharp pin into the sole of the foot is a valid nocuous stimulus, one must conclude that flexion is the normal response to harmful stimuli. The Babinski sign cannot, therefore, be a defense reaction.

THEORIES OF THE PLANTAR REFLEX

Before any hypothesis offering to account for the plantar reflex can be accepted, it must satisfy the following postulates. It must explain: (1) Why the normal response in human beings is usually flexion, while in primates below man it is usually extension. The fact that these primates have a well developed motor pathway system must be kept in mind. (2) Why in infants a Babinski sign is commonly observed. (3) Why in human adults the extension reflex occurs in disease of the pyramidal tract even when the extrapyramidal tracts are severed.

In cerebral lesions, the Babinski reflex occurs only when the leg centers are implicated. The first observation of this was made in 1910 by Potts and Weisenburg.[19] Their recognition of the fact that the arc of this reflex must be involved in the lesion before an extensor response could occur explained the absence of this sign in many cases of cerebral palsy, an observation that had previously puzzled clinicians. Another case of jacksonian epilepsy without a Babinski sign was reported by Tournay.[20] He assumed that the motor centers are "exhausted" by the convulsion, and that when the leg area is not implicated it is not "exhausted" and the plantar reflex remains normal. "Exhaustion" is an indefinite term, and in its very vagueness Tournay's hypothesis is less satisfactory than the more direct one offered by Potts and Weisenburg.

Many of the theories seek phylogenetic explanations. Rudolph [21] asked how myelinization of the pyramidal pathways can account for the normal reflex and destruction of this tract for the Babinski sign when, as his own researches have shown, subhuman primates who have an intact, myelinated tract present an extensor reflex. Phylogenetically, the reflex shows a march from (1) flexion, as in the mongoose, to (2) extension, as in the monkey, to (3) flexion in the human adult. Rudolph pointed out that at the moment of birth the baby has: (1) a flexion response, but during infancy shows (2) extension, and in adult life exhibits (3) flexion. That the human being at birth has a flexion response was described by Tournay [22] and confirmed by Waggoner and Ferguson.[8] Rudolph suggested that this march of flexion-extension-flexion is an instance of ontogeny recapitulating phylogeny. Another phylogenetic explanation was offered by Rabiner and Keschner.[23] They expressed the belief that man needs a flexed big toe as a fulcrum in walking; in lower primates this is unnecessary. In their opinion, an extrapyramidal pathway, presumably the rubrospinal, carries the impulse that is responsible for extension, whereas the corticospinal tract mediates flexion. In lower primates the extrapyramidal is the more influential of the motor systems; hence in these animals extension of the big toe is the normal position. In man, an upper motor neuron lesion suppresses the pyramidal pathway and allows the rubrospinal tract to regain

19. Potts, Charles S., and Weisenburg, T. H.: Tumor Limited to the Arm Center, Rev. Neurol. & Psychiat. **8**:577, 1910.

20. Tournay, August: Plantar Reflexes in Jacksonian Epilepsy, Arch. Neurol. & Psychiat. **13**:592 (May) 1925.

21. Rudolph, G. M.: Phylogenetic Significance of the Plantar Response, J. Neurol. & Psychopath. **2**:337 (Feb.) 1922.

22. Tournay, Maurice: Plantar Reflexes in Infants, Encéphale **27**:718 (Nov.) 1926.

23. Rabiner, Abram, and Keschner, Moses: Mechanism of the Babinski Phenomenon, Arch. Neurol. & Psychiat. **16**:313 (Sept.) 1926.

dominance, thus establishing the clinical Babinski sign. McCouch [15] properly asked how this can explain extension of the big toe in a spinal man when the rubrospinal tract is severed as effectively as the pyramidal pathway. Freidman [10] also used a phylogenetic explanation, calling attention to the assistance offered to a tree-climbing primate by an extended big toe; he conceived a Babinski phenomenon as a return to the tree-climbing stage.

French physiologists, particularly Claude [24] and Bourguignon,[25] have sought the explanation of the plantar reflex in differences in chronaxie. In 1927, Bourguignon [25] reported that the normal average chronaxie of the muscles flexing the toes was 55 sigma, whereas the average extensor chronaxie was 29 sigma. In apoplexy he found these figures reversed. Clinicians are familiar with the "pseudo-Babinski sign" in which all the leg muscles except the extensors degenerate so that the only reflex obtainable is the extensor one. Under these circumstances a Babinski sign can appear in poliomyelitis. Such a reaction occurred in a case of lumbosacral radiculitis reported by Rouquier and Couretas; [26] in this patient, electrical tests showed that the extensors were less impaired than the flexors. Bourguignon [27] believed that this "pseudo-Babinski sign" has the same significance as the genuine reflex, in that the response in each case is due to differences in extensor and flexor chronaxie. In a case of carbon monoxide poisoning with a Babinski sign, Bourguignon and Desoille [28] found that extensor chronaxie exceeded flexor.

If differences in chronaxie accounted for differences in response, the question would be changed but not answered. One still would not know why the differences in chronaxie existed.

SUMMARY AND CONCLUSIONS

1. In adults there is no one type of response that can be considered the normal plantar reflex. In most cases all the toes flex, but extension of the toes, even of the big toe, is compatible with a normal motor system.

2. Isolated extension of the big toe with fanning of the other toes does not occur in normal adults.

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24. Claude, Henri; Bourguignon, G., and Baruk, H.: Babinski Sign in Dementia Praecox, Rev. neurol. **1**:1078 (June) 1927.

25. Bourguignon, Georges: Peripheral Conditions of the Plantar Reflex, Rev. neurol. **1**:1081 (June) 1927.

26. Rouquier, A., and Couretas, D.: Babinski's Sign Without Pyramidal Tract Disease, Rev. neurol. **2**:167 (Aug.) 1926.

27. Bourguignon, Georges, and Desoille, Henri: Babinski's Sign, Compt. rend. Acad. d. sc. **181**:161 (July 20) 1925.

28. Bourguignon, Georges, and Desoille, H.: Intermittent Claudication Following Carbon Monoxide Poisoning, Rev. neurol. **1**:360 (March) 1927.

3. In eliciting the plantar reflex, the positions of the patient's head and knee are not important, and distraction is not usually necessary.

4. When withdrawal of the whole foot occurs, the patient should be reexamined with a lighter stimulus.

5. A pin drawn along the sole of the foot is a convenient instrument for studying the plantar reflex. It is not a nocuous stimulus.

6. A pin inserted into the ball of the foot is a nocuous stimulus; it tends to produce flexion of all the toes. The Babinski sign is an extension, and cannot, therefore, be a reflex of defense to a harmful stimulus.

7. No theory has adequately explained the plantar reflex; no such theory can be accepted unless it accounts for: (*a*) the infantile Babinski sign, (*b*) the fact that the response in human adults is usually flexion and (*c*) the clinical Babinski sign of disease of the pyramidal tract.

8. In recording the plantar reflex, the clinician should describe the responses that occur in the lesser toes as well as in the big toe; secondary movements should be reported as well as primary ones. The statement "Babinski sign present" or "absent" is an inadequate description of the plantar reflex.

DENIS-AYER METHOD FOR THE QUANTITATIVE ESTIMATION OF PROTEIN IN THE CEREBROSPINAL FLUID*

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The quantitative method in use for eleven years at the Massachusetts General Hospital and for the past four years at the Boston City Hospital consists essentially in the measurement, by means of a suitable colorimeter, of the turbidity produced by adding a solution of sulphosalicylic acid to the cerebrospinal fluid. The method was described by Denis and Ayer.[1] We have made two minor modifications in the original method: (1) in the preparation of a protein standard solution, and (2) in the dilution of spinal fluid used when the protein content is very low, thereby eliminating the need of a second protein standard. The original method required the use of a special colorimeter. This is no longer necessary. These modifications and the fact that the normal values given in the original paper (from 35 to 100 mg. per hundred cubic centimeters) are entirely too high are the reasons for publishing in detail the method as now used.

METHOD

Into a test tube 0.6 cc. of spinal fluid is measured. To this are added 0.4 cc. of distilled water and 1 cc. of a 5 per cent solution of sulphosalicylic acid. The contents of the tube are then mixed by inversion (but not by violent shaking) and, after being allowed to stand at least five minutes, are read against a standard protein suspension prepared at the same time as the unknown. The standard is made by adding to a test tube 3 cc. of a solution containing 30 mg. of protein per hundred cubic centimeters and 3 cc. of a 5 per cent solution of sulphosalicylic acid.

Standard.—Twenty cubic centimeters of normal human blood serum is diluted to 200 cc. with a 15 per cent solution of sodium chloride in a volumetric flask and filtered. This filtrate is the concentrated standard.

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1. Denis, W., and Ayer, J. B.: Method of Quantitative Determination of Protein in Cerebrospinal Fluid, Arch. Int. Med. **26**:436 (Oct.) 1920.

The total nitrogen of this filtrate is determined by the macro-Kjeldahl method with 40 cc. The nonprotein nitrogen is determined in the original undiluted serum by the micro-Kjeldahl method of Folin [2] and this figure divided by ten is subtracted from the total nitrogen to obtain the protein nitrogen. The protein nitrogen multiplied by 6.25 gives the protein content of the concentrated standard.

The concentrated standard is diluted with distilled water to make the dilute standard containing 30 mg. per hundred cubic centimeters.

The standards are preserved with a few crystals of thymol and kept on ice except when in use. In this way we have kept the concentrated standards for more than six months and the dilute standards for more than twelve months without appreciable change in the protein content.

COMMENT

In the directions given we have stated that 0.6 cc. of cerebrospinal fluid should be used for the determination. While this is the amount found most convenient for use with the great majority of normal or approximately normal fluids, it will produce too great turbidity for

TABLE 1.—*A Comparison of the Spinal Fluid Protein as Determined by the Denis-Ayer and by the Micro-Kjeldahl Methods*

	Denis-Ayer Method: Protein (Mg. per 100 Cc.)	Micro-Kjeldahl Method: Protein (Mg. per 100 Cc.)
1	17	14
2	63	61
3	64	57
4	151	147
5	216	197
6	250	214

accurate reading in fluids with a greatly increased protein content. With such fluids it is necessary to use 0.3, 0.2 or even 0.1 cc. of spinal fluid, and to add 0.7, 0.8 or 0.9 cc. of water (in order to bring the volume of the diluted fluid to 1 cc.). In fact, in fluids of extremely high protein content, such as may be encountered in cases of compression of the cord, meningitis, etc., it is sometimes necessary to make a preliminary 1 : 10 dilution with water, as even 0.1 cc. of such fluids may contain too much protein to be read against the standard. For fluids with very low protein values, such as normal ventricular fluid, it is preferable to use 1 cc. of cerebrospinal fluid and no water. By thus varying the amount of spinal fluid used, only the one standard solution containing 30 mg. of protein per hundred cubic centimeters is necessary for all determinations.

The colorimeter originally recommended was the small Duboscq-Pellin biologic, or the small Bausch and Lomb-Duboscq biologic. These special colorimeters with small cups were necessary because of the small amount of fluid (2 cc.) available. We have found that the standard

2. Folin, O.: J. Biol. Chem. **38**:87, 1919.

5 cm. Bausch and Lomb-Duboscq colorimeter (or any standard colorimeter) can be used, the only disadvantage being the triple quantities of spinal fluid, water and sulphosalicylic acid necessary because of the larger colorimeter cups. Thus, in a series of spinal fluids, by using 1.8 cc. of spinal fluid, 1.2 cc. of distilled water and 3 cc. of sulphosalicylic acid solution for the unknown, and 6 cc. each of the protein standard and sulphosalicylic acid for the standard, we obtained with

TABLE 2.—*A Comparison of the Spinal Fluid Protein as Determined by the Denis-Ayer and the Macro-Kjeldahl Methods*

	Denis-Ayer Method: Protein (Mg. per 100 Cc.)	Macro-Kjeldahl Method, Using 2 Cc. of Spinal Fluid: Protein (Mg. per 100 Cc.)
1	950 (on 0.6 cc. of 1:10 dilution)	900
2	1,362 (on 0.4 cc. of 1:10 dilution)	1,569
3	1,860 (on 0.3 cc. of 1:10 dilution)	1,802
4	1,780 (on 0.3 cc. of 1:10 dilution)	1,881

TABLE 3.—*A Comparison of Protein Values of the Spinal Fluid as Determined by the Denis-Ayer Method Using Different Colorimeters*

	Duboscq-Pellin Biologic: Protein (Mg. per 100 Cc.)	Bausch and Lomb-Duboscq Biologic: Protein (Mg. per 100 Cc.)	Standard 5 Cm. Bausch and Lomb-Duboscq (Using Triple Amounts): Protein (Mg. per 100 Cc.)	Standard 5 Cm. Bausch and Lomb with Attachments for Use with Small Amounts of Fluid: Protein (Mg. per 100 Cc.)
1	18	..	..	18
2	21	..	22	..
3	23	..	..	23
4	27	..	28	..
5	27	..	25	..
6	30	..	..	30
7	30	..	..	30
8	31	31	31	..
9	32	32	32	..
10	39	..	..	38
11	43	43	43	..
12	45	..	46	47
13	50	..	50	..
14	50	48	48	..
15	54	..	53	..
16	57	..	59	58
17	60	..	..	61
18	109	..	108	..
19	150	150	146	..
20	154	148	154	..

the standard size colorimeter values which duplicated exactly those obtained with the small Duboscq-Pellin model. These comparisons are shown in table 3, column 3.

Small detachable cups and plungers are now available for the standard 5 cm. and the large Bausch and Lomb colorimeter. This makes it possible to combine the advantages of the larger colorimeter with the use of a small volume of solution. These attachments consist of a pair of all-glass cups of 1 cc. capacity, solid glass plungers with a threaded adapter and cup-holders for 1 cc. cups. They are easily inter-

changeable with the standard cups and plungers. A special diaphragm with a smaller opening is used in the eye piece. Since most laboratories are equipped with the standard size colorimeter, we recommend the use of these attachments both because they are less expensive and because the turbidity comparisons are more easily made. In table 3 we present values obtained with the various colorimeters, and it will be seen that the comparative results are satisfactory.

Whatever the type of colorimeter used, an even lighting of the two cups is necessary before beginning each set of determinations. When the standard solution (equal quantities of standard protein solution and sulphosalicylic acid solution) placed in the two cups can be accurately matched against itself, an even lighting is assured. Care must now be exercised not to move the position of the colorimeter until the set of determinations has been completed.

Denis and Ayer stated that the method is "accurate to within 5 per cent." The possible error of 5 per cent applies to the actual amount of protein present, and not to comparative readings between different fluids. Ten complete determinations on the same fluid gave five readings of 34 mg. and five of 35 mg. of protein per hundred cubic centimeters. The exact magnitude of the error inherent in the method has not been determined, since there is no more accurate method to use as a check on individual samples of normal fluid. Denis and Ayer checked the method by macro-Kjeldahl determinations on large composite samples of spinal fluid. For checking individual normal fluids it might seem that the determinations of protein nitrogen by the micro-Kjeldahl method would suffice. Normal spinal fluid, however, contains much more nonprotein nitrogen than protein nitrogen. Nonprotein nitrogen averages from 12 to 18 mg. per hundred cubic centimeters, while protein nitrogen averages from 3 to 6 mg. In a normal fluid, with 25 mg. of protein, the total nitrogen might amount to 20 mg. of which 16 mg. is nonprotein nitrogen and only 4 mg. protein nitrogen ($4 \times 6.25 =$ 25 mg. of protein per hundred cubic centimeters). To obtain the latter figure it is necessary to determine separately the total nitrogen and the nonprotein nitrogen, and then to subtract the latter from the former. A combined error of 1 mg. of nitrogen in the two determinations could introduce an error of 25 per cent in the calculation of the protein. A comparison of results by the Denis-Ayer and micro-Kjeldahl methods in a short series is given in table 1. It will be seen that these agree as well as can be expected.

All methods dependent on the estimation of the amount of protein precipitated lose accuracy when applied to solutions containing large amounts of protein. When the protein content of spinal fluid exceeds 400 mg. per hundred cubic centimeters, a greater degree of accuracy can be obtained by the more complicated Kjeldahl procedure. For all

practical purposes, however, a sufficiently accurate figure can be obtained by the method of Denis and Ayer, even when the spinal fluid contains several thousand milligrams per hundred cubic centimeters, as in the complete Froin syndrome. A comparison of determinations by the macro-Kjeldahl and by the Denis-Ayer method is given in table 2.

Considerable amounts of pigment do not materially affect the results, but gross bacterial contamination sufficient to produce visible turbidity will give too high protein readings.

The method of Denis and Ayer is as accurate as any that we have seen described, has a wider range, a greater speed of execution and is more economical of fluid. The original difficulty in preserving the standard protein solutions has been eliminated. A special colorimeter is no longer necessary.

CALCULATIONS

$$\frac{\text{Reading of the Standard}}{\text{Reading of the Unknown}} \times \frac{30 \text{ (mg./100 cc. in standard)}}{\text{(cc. of spinal fluid used)}} = \text{mg. protein per 100 cc.}$$

With the standard set at 8 (which we have found convenient), and with the use of 0.6 cc. of spinal fluid, this is simplified to:

$$\frac{400}{\text{Reading of the Unknown}} = \text{mg. protein per 100 cc.}$$

It is convenient to construct a table so that the protein values may be read off at a glance once the colorimeter reading has been made.

Normal Values.—Ayer and Foster [3] and Fremont-Smith and Ayer [4] have published tables of values in normal and pathologic states. In the latter paper there is also a discussion of the difficulty of establishing absolute normal levels, and of the origin of the protein normally present.

We consider the following as normal values: ventricular fluid, from 5 to 15 mg. per hundred cubic centimeters; cisternal fluid, from 15 to 30 mg., and lumbar fluid, from 20 to 45 mg. Very rarely, we have found higher protein in the lumbar fluid—up to from 60 to 70 mg. per hundred cubic centimeters—for which no cause could be found. It is possible that in such cases there was a pathologic process of the central nervous system which was unrecognizable clinically, or that normal persons occasionally have more protein than 45 mg. per hundred cubic centimeters in the spinal fluid.

SUMMARY

A method for the determination of the protein content of the cerebrospinal fluid, accurate within approximately 5 per cent, is described. The technic is simple and requires only a small amount of fluid and a minimum of time (ten minutes).

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3. Ayer, J. B., and Foster, H. E.: Quantitative Estimation of Total Protein in Spinal Fluid, J. A. M. A. **77**:365 (July 30) 1921.

4. Fremont-Smith, F., and Ayer, J. B., in Dana, C. L., and others: The Human Cerebrospinal Fluid, Association for Research in Nervous and Mental Diseases, New York, Paul B. Hoeber, Inc., 1926, vol. 4, chap. 6.

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Spasmodic torticollis may be defined as hyperkinesis of the musculature of the neck, of all the large and small, superficial and deep muscles that make up its complex motor system. According to Meige [1] and Barré,[2] the smaller, deep muscles of the neck (the anterior and posterior groups) contract first; the larger muscles, the trapezius and the sternocleidomastoid, act later, accentuating and completing the movements of the former. Thus the muscular contractions of the neck do not occur simultaneously, but successively. Grossly, they usually show in the large muscles—sternocleidomastoid, splenius and trapezius—but they may predominate in the smaller muscles and result in brisk rotatory movements of the neck. The movements are often unilateral; they may be symmetrical, when, for instance, both trapezii or both sternocleidomastoids are involved. They may manifest many other varieties, depending on the predominance of the groups of muscles affected.

Thévenard [3] considered spasmodic torticollis a tonus disorder with involvement of only those muscles of the neck the function of which is to assure a normal attitude of the head; when the disturbance is generalized and extends to the musculature of the entire body, it is termed dystonia. The majority of authors (Sterling,[4] Schmidt,[5] Wimmer,[6] Maliwa,[7] Barré,[2] Goodhart, Wechsler and Brock [8]) looked on

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1. Meige, H.: Rev. neurol. **1**:1013, 1929.
2. Barré, J. A.: Rev. neurol. **1**:984, 1929.
3. Thévenard, A.: Les dystonies d'attitude, Thèse de Paris, Paris, Octave Doin, 1926.
4. Sterling, V.: Rev. neurol. **1**:937, 1929.
5. Schmidt, W.: Deutsche med. Wchnschr. **48**:1607, 1922.
6. Wimmer, R. J.: Rev. neurol. **2**:904, 1930.
7. Maliwa, Edward: Med. Klin. **18**:1522, 1922.
8. Goodhart, S. P.; Wechsler, I., and Brock, S.: Remarkable Extrapyramidal Involuntary Movements, Arch. Neurol. & Psychiat. **21**:1299 (June) 1929.

spasmodic torticollis as a partial or initial manifestation of dystonia musculorum deformans (torsion spasm) or of a generalized athetosis (Foerster [9]). In one of his latest discussions [1] Meige defined the condition as a dyskinesia of the muscles of the neck, which may be observed also in other parts of the body. With the advent of knowledge of postencephalitic states, the dystonias came to be recognized as organic lesions of the brain (Thomalla,[10] Wimmer [11]). It was but logical to consider also as such spasmodic torticollis, which, as was pointed out, is most likely a partial manifestation of dystonia. Though Babinski [12] long ago advocated the organic nature of spasmodic torticollis, direct proofs furnished by pathologic studies were few (cases of Cassirer,[13] Wimmer [6]). Most of the proofs were indirect, supplied mainly by clinical, mostly postencephalitic, cases in which spasmodic torticollis preceded, followed or was associated with a parkinsonian state. Such cases, to which belongs the one here recorded, are necessarily of great interest, anatomically, pathologically and clinically.

REPORT OF A CASE

CASE 1.—*History.*—Mrs. R., aged 22, one of a family of thirteen children, with a good family history, was admitted to the neurologic service (Dr. Hassin) of the Cook County Hospital on Jan. 7, 1930, because of "jerkings" in the head. For the last five years she had suffered from "tremors" in both upper extremities. Additional, inconstant complaints were headaches, vertigo, stuttering, nocturia, excessive salivation and a loss of 30 pounds (13.6 kg.) in weight. From February to April, 1929, she had been treated at the Research and Educational Hospitals of the University of Illinois, from which she was discharged with the diagnosis of epidemic encephalitis. One month after discharge, jerkings of the head appeared, in the form of sudden muscular contractions. They were more marked in the waking hours and while walking or when the patient's attention was centered on them; in sleep they ceased, but the patient could fall asleep only by lying on her right side, in which position she could prevent the head from turning.

Examination.—The patient was well nourished; speech was slow and monotonous; the face was expressionless; the head was inclined to the right and exhibited clonic-tonic movements during which the face and the chin were also turned to the right. When the face was held in the midline or turned to the left, it would return to the former position after a few jerkings. The left sternocleidomastoid muscle was hypertrophied at the junction of its upper and middle thirds, and felt hard to the touch. The right sternocleidomastoid also felt firm, but did not protrude as did the left. The head could be kept still by the patient pressing the right hand against the chin.

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9. Foerster, O.: Ztschr. f. d. ges. Neurol. u. Psychiat. **73**:1, 1921.
10. Thomalla, C.: Ztschr. f. d. ges. Neurol. u. Psychiat. **41**:311, 1918.
11. Wimmer, A.: Étude sur les syndromes extra-pyramidaux; spasme de torsion progressif infantile, Rev. neurol. **28**:952, 1921.
12. Babinski, J.: Rev. neurol. **8**:142, 1900.
13. Cassirer, R.: Klin. Wchnschr. **1**:53, 1922.

The extremities on the left side were rigid, and the forearm was semiflexed. Both the forearms and hands exhibited slight pronation and supination movements, which seemed to be more marked on the right side. Passive movements in the extremities showed a definite cog-wheel resistance in the elbows and knees, especially on the left side. Coordination in the upper and lower extremities was good; intention tremor was absent; the reflexes, deep and superficial, were lively; pathologic reflexes were absent, and sensibility, the cranial nerves, the viscera and the organs of the chest were normal.

Laboratory observations of the spinal fluid and blood, and the chemical examination of the latter and of the urine gave negative results.

The results of the clinical examination may be summarized as follows: tonic-clonic movements of the neck to the right; a masklike face; rigidity, especially of the left extremities; tremor of the hands, more pronounced on the right, and absence of involvement of the pyramidal tract or cranial nerves and of sensory disturbances. The clinical picture was that of a parkinsonian state of five years' duration, mainly unilateral, complicated by a spasmodic torticollis of eight months' standing.

Course.—As the patient's condition grew worse, she insisted on an operation. The left spinal accessory was divided, but the twitchings did not subside, and the patient was returned to the neurologic ward in as unfavorable a condition as before the operation.

Reexamination, made five and again seven months after the operation, revealed the same parkinsonian state: a slow, monotonous, stuttering speech; a masklike face; a semiflexed left forearm and hand; a slight forward bend of the body; tremor of the hands, and cog-wheel phenomena. The head, as well as the chin and nose, was constantly inclined to the right and on being turned to the left immediately turned back to the right; it still exhibited jerkings to the right, where the shoulder was elevated. The left sternocleidomastoid muscle was much less prominent and much less tense than at the last examination before the operation. Faradic and galvanic stimulations of the right sternocleidomastoid muscle turned the occiput of the head toward the right shoulder, and the chin and nose toward the opposite side. The left sternocleidomastoid, though firm to the touch, did not respond to the faradic current, while galvanic stimulation of this side caused a lively anodal and a rather poor cathodal contraction.

COMMENT

The case under discussion resembles greatly those described by Guillain and Girot,[14] Thévenard [3] and others. Thévenard's patient, six years after an attack of epidemic encephalitis, exhibited irresistible rotations of the face toward the left shoulder. Two years later, the face became entirely rotated toward the left and he was unable to turn it to the right. The right sternocleidomastoid showed a marked relief with considerable prominence of its sternoclavicular insertions. In contrast, its fellow muscle on the left was effaced, and the trapezius showed no abnormal features. This abnormal attitude was much relieved by the antagonistic gesture, a slight support of the right cheek by the right index finger. The gesture was sufficient to make the rotation to the left disappear.

14. Guillain, G., and Girot, L.: Rev. neurol. **1**:198, 1926.

but the head was still somewhat inclined to the right shoulder. In complete rest the rotation of the head subsided, but in walking it increased. Passive rotation met with no resistance. As in our patient, the muscles were involved that serve the purpose of keeping the head in a normal attitude, and a torticollis complicated a parkinsonian state which was mainly unilateral. Thévenard gave the history of another patient who showed all kinds of transitions between spastic torticollis, athetosis and torsion attitudes. He also referred to several other cases of both torticollis and torsion spasm, some of which were complications of parkinsonian postencephalitic states.

On the other hand, cases are recorded in which an existing torsion of the muscles of the neck became aggravated by an intercurrent attack of encephalitis, as in the patient of Friburg-Blanc and Picard.[15]

Of great interest are the anatomic and pathologic features of spasmodic torticollis. The anatomic features pertain to the type of muscles that produce an abnormal attitude of the head. In our patient, the head was inclined to the right, and, as was pointed out, the chin and nose also were turned in that direction. Such an abnormal position could hardly be explained by the excessive action of the left sternocleidomastoid muscle alone, for while it turned the face and chin to the contralateral shoulder, it should also have inclined the head to the ipsolateral, that is, the left side. A simultaneous contraction of the right splenius and to some extent of the upper portion of the right trapezius evidently prevented the inclination of the head to the left. Probably many other muscles were involved here, for, as mentioned in the introductory comments, in spasmodic torticollis the entire musculature of the neck is implicated. According to Foerster,[16] for instance, in this condition—one deals along with the contractions of the contralateral sternocleidomastoid muscle and of the upper portion of the trapezius—with those of the ipsolateral splenius capitis and splenius cervicis, the longissimus capitis, the semispinalis capitis, the recti capitis postici major and minor and the obliquus capitis inferior. The principle of multiple muscular involvement in spasmodic torticollis is of great importance in the choice of the method of treatment for this morbid condition.

Pathologic Features.—These features are of especial interest, for spasmodic torticollis used to be looked on as a psychogenic disease, and even recently the psychogenic factor has been considered important (Laignel-Lavastine,[17] Wilson [18]). Meige differentiated torticollis tic

15. Friburg-Blanc, and Picard, J.: Rev. neurol. **2**:645, 1927; abstr., Arch. Neurol. & Psychiat. **20**:861 (Oct.) 1928.

16. Foerster, O.: Zentralbl. f. Chir. **53**:2804 (Oct. 30) 1926; footnote 9.

17. Laignel-Lavastine: Discussion in Rev. neurol. **1**:198, 1926.

18. Wilson, D. C.: Clifton M. Bull. **10**:177, 1924.

and torticollis spasm, considering the former mental and the latter organic. While one cannot deny that some cases of spasmodic torticollis are functional, especially those of a clonic type, such cases are probably rare. The consensus is that it is an organic disease process. Advocated by Babinski in 1900,[12] this theory found its confirmation in the cases of Cassirer [13] and Wimmer.[6] Cassirer's case, studied by Bielschowsky, showed swelling of the brain, including the corpus striatum, with the perivascular spaces dilated, the myelin swollen and the ganglion cells degenerated and packed with fat, which was also present in the glia cells; there were satellitosis and numerous gitter cells in the adventitial spaces, with capillary fibrosis in the putamen and the corpus striatum. Milder changes were present in the optic thalamus and cortex. The pyramidal tracts, which were unusually developed, showed no secondary degeneration. Cassirer came to the conclusion that spasmodic torticollis is an organic disease of the brain, and that for this reason treatment must be surgical. The changes found in his case much resembled those described in Thomalla's case [10] of torsion spasm. While the caudate nucleus presented no particular alterations, the liver exhibited a cirrhosis, as seen in Wilson's disease. Numerous clinical observations, of Maliwa,[7] Guillain and Girot,[14] Krebs [19] and others, showed that lesions of the midbrain, as seen in parkinsonian conditions, may manifest themselves as spasmodic torticollis. The latter may thus be symptomatic of epidemic encephalitis; it may be one of its sequelae, or it may appear as a fragment on an episode of the clinical syndrome of torsion spasm. Goodhart, Wechsler and Brock [8] considered the name torticollis dystonia appropriate. On the other hand, Sterling [4] characterized spasmodic torticollis as an initial stage of a dystonic process, the progressive generalization of which corresponds to the clinical type of torsion spasm; it is a localization of the torsion spasm in the muscles of the neck. Wimmer [6] classified spasmodic torticollis, parkinsonian states and general rigidity as dystonias which may show as any of the foregoing conditions. The evidence in favor of the organic nature of spasmodic torticollis became so strong that Meige himself [20] had to admit that the more he studied the manifestations of spasmodic torticollis, the more it became apparent to him that it is an organic process, most likely of the corpus striatum. However, the pathologic basis of this condition differs somewhat from that seen in parkinsonian states. In the latter, the lesion is mainly in the midbrain, in the substantia nigra, while in spasmodic torticollis it is mainly in the telencephalon, in the corpus striatum.

19. Krebs, E.: Rev. neurol. **1**:1033, 1929.

20. Meige, H.: Rev. neurol. **29**:288, 1922 (discussion of paper of André-Thomas and Long-Landry).

One must then assume that a telencephalic morbid process became superimposed on a lesion of the midbrain, which, having existed in our case for five years, extended to the region of the basal ganglia. This case also shows that in postencephalitic states the underlying pathologic condition is not stationary, but progressive. It constantly involves new areas, causing additional clinical symptoms and signs. The lesion is mainly degenerative, which renders the prognosis hopeless. The treatment can, therefore, be only symptomatic.

It is true that psychic or medicinal treatment has been successful in some cases (Meige [21]), but generally it is not. It is, moreover, costly, time consuming and difficult to carry out. The best way to reduce the distress is by interrupting the pathways that conduct the abnormal irritations from the brain to the affected musculature. Attempts to accomplish this by surgical intervention have been made repeatedly, and numerous methods have been devised—cutting the spinal accessory on one (Babinski [22]) or both sides (Sicard and Rabinau [23]); section of the muscles and nerves of the neck (Barker [24]); resection of the muscles (multiple myotomies of Kocher and de Quervain,[25] Mann [26]), or of the three upper cervical nerves and the suboccipital muscles (Leriche, quoted from Barré [2]), cutting the spinal accessory nerves, together with the posterior roots of the first three or four cervical nerves (Keen,[27] McKenzie,[28] Frazier,[29] Finney [30]) or both the anterior and posterior roots (Dandy [31]), or intradural resection of the three or four upper cervical anterior and posterior roots alone (Foerster,[16] Kaijser [32]). The results of surgical treatment are in many cases excellent (Finney, Foerster, Dandy, McKenzie, Keen). Thus, of Finney's thirty-two

21. Meige, H.: N. iconog. de la Salpêtrière, Paris **20**:1020, 1907.

22. Babinski, J.: Rev. neurol. **27**:367, 1921.

23. Sicard and Rabineau: Section bilateral du nerf spinal externe dans le torticolis spasmodique, Rev. neurol. **28**:290, 1915.

24. Barker, F. D.: An Interesting Neuritis, J. Comp. Neurol. **3**:112, 1893.

25. Quervain: Le traitement chirurgical du torticolis spasmodique d'après le methode de Kocher, Semaine méd. **16**:405, 1896.

26. Mann, L.: Berl. klin. Wchnschr. **57**:1174, 1920.

27. Keen, W. W.: A New Operation for Spasmodic Wry Neck, Namely, Division or Exsection of the Nerves Supplying the Posterior Rotatory Muscles of the Head, Ann. Surg. **13**:44, 1891.

28. McKenzie, K. G.: Surg., Gynec. & Obst. **39**:5, 1924.

29. Frazier, C. H.: Ann. Surg. **91**:848, 1930. The Immediate Effect of Rhizotomy on Spasmodic Torticollis, Arch. Neurol. & Psychiat. **23**:1291 (June) 1930.

30. Finney, J.: Ann. Surg. **81**:255, 1925.

31. Dandy, W.: An Operation for Treatment of Spasmodic Torticollis, Arch. Surg. **20**:1021 (June) 1930.

32. Kaijser, F.: Foerster's Operation bei Torticollis spasticus, Acta chir. Scandinav. **65**:576, 1929.

patients, twelve were cured completely and sixteen were improved. The results would have been still better if a modern technic had been used, for some patients had been operated on as long as twenty years before the time of writing. Equally good results have been recorded by the methods of Kocher, Foerster and others. Improvement was lasting and in many instances may be considered as amounting to complete cure as the observations covered a period of many years. In view of the hopelessness of securing relief by other methods, treatment for spasmodic torticollis by a competent surgeon should be the standard treatment, or at least should be undertaken when other methods have failed. The unsuccessful results in many cases (Secard and Descamp,[33] Patrick,[34] Dercum,[35] Schaller [36]) were probably due, as in our case, to improper surgical technic.

REPORT OF CASES

The following cases illustrate the situations that make surgical intervention imperative.

CASE 2.—The patient was seen by one of us (Dr. Hassin) in 1901, in Vienna, in the clinic of Krafft-Ebing. He exhibited spasmodic contractions of the muscles of the neck and shoulders. The head was constantly moved from right to left; the thumb of the left hand presented athetoid movements, and the muscular contractions of the left side of the trunk were so violent that the patient was bent to the left and backward. With the help of a special apparatus, the patient was able to keep quiet for a short time without being jerked backward. The jerkings and the muscular contractions were "slower than those seen in tic convulsif." The patient also exhibited, according to Krafft-Ebing, some signs of hysteria: globus, transient aphasia and emotional instability. He was treated with electricity by Erb in Heidelberg and by Ziemssen in Munich, and by "famous orthopedic surgeons" in Berlin and by Krafft-Ebing himself with hyoscine, extract of conium and suggestion. The case was demonstrated by Krafft-Ebing as one of hyperkinesia of the eleventh nerve. Nine years after this case was observed, the clinical picture presented by this patient was described by Ziehen [37] as a tonic torsion neurosis and by Oppenheim as dysbasia lordotica, known also as dystonia musculorum deformans, torsion spasm (Flatau and Sterling [38]) or Ziehen-Oppenheim's disease. In this patient the hyperkinesia of the eleventh nerve or spasmodic movements of the neck were but a part of the clinical picture of dystonia musculorum deformans and probably could have been relieved by an operation.

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33. Secard-Descamp: Torticolis mental de Brissaud; Insuccès du traitement, N. iconog. de la Salpêtrière, Paris **20**:459, 1907.

34. Patrick, H.: J. Nerv. & Ment. Dis. **44**:63, 1916.

35. Dercum, F.: A Case of Anomalous Torsion Spasm, J. Nerv. & Ment. Dis. **45**:420, 1917.

36. Schaller, W.: Spasmodic Torticollis, J. A. M. A. **60**:1421 (May 10) 1913.

37. Ziehen: Allg. Ztschr. f. Psychiat. **68**:281, 1911.

38. Flatau, E., and Sterling, W.: Progressive Torsionspasm bei Kindern, Ztschr. f. d. ges. Neurol. u. Psychiat. **7**:586, 1911.

Case 3.—An undertaker, aged 35, was under the observation of one of us (Dr. Hassin) in Chicago in 1924. He had been suffering from polyarthritis, infected teeth, gastro-intestinal disorders and habit movements. While driving his automobile, he was in the habit of pulling his hat down on his face; while eating he would jerk the muscles of his face and neck, and on other occasions he would throw his hands to the back of his head. These ticlike movements finally stopped and were followed by spasmodic contractions of the muscles of the neck. The head would be rotated to the right and remain in a state of rigidity, and then become relaxed; such movements would be repeated again and again. The patient could not resist them, nor could he assign any reason for their occurrence, except that he once fell asleep while leaning his neck against the back of a chair. The movements of the neck became more and more persistent; they continued day and night, and were not relieved by the so-called antagonistic gestures, which is unjustly considered as evidence that spasmodic torticollis is a functional disease (Barré). At that time I was still under the influence of Brissaud's teaching concerning mental torticollis and tried psychogenic treatment. The patient grew steadily worse and finally died in the hospital, where a physician made a diagnosis of chorea. The symptoms, however, as I was informed, were those of a tumor of the brain—the patient became blind, paralyzed and incontinent.

These cases illustrate how distressing spasmodic torticollis may be. If such patients were under our care now, we should insist on surgical treatment. Our patient is considering another operation, which will be carried out according to one of the methods mentioned.

ABSTRACT OF DISCUSSION

Dr. R. P. Mackay: I have been interested in hearing Dr. Hassin discuss the subject of spasmodic torticollis. Several patients with the condition have come to my attention, and one, observed recently at St. Luke's Hospital, illustrates several features that are important. Dr. Hassin made the remark that there is but one reason to consider spasmodic torticollis as due to an organic lesion, and that is its occasional occurrence in association with parkinsonism. I wish to point out other reasons for believing it to arise from organic disease of the brain. First, many of the contractions are asynergic or involve only fractions of a normal synergic movement. The patient at St. Luke's Hospital exhibited unilateral contraction of the platysma of the right side, without any distortion of the face. Muscular contractions in functional or hysterical conditions rarely, if ever, involve only a part of a synergic group of muscles. That is to say, such contractions originate very high in the cortex, at a point where total movements and not individual muscles are represented. It is difficult to see how either a normal or a hysterical person could produce a unilateral contraction of the platysma muscle without producing any contractions of the facial muscles, which normally are associated with the action of the platysma. Such fractions of normal movements must arise much lower in the nervous system than do so-called functional movements.

Another reason for thinking that these conditions have an organic origin is illustrated by the patient to whom I have referred. Not only did she have spasmodic torticollis, but other contractions of the same order developed. Not only was the head twisted about, but the arm became involved, the right half of the abdomen contracted independently of the left, and, finally in walking, she had a gait suggestive of dystonia. She became dissatisfied with our therapeutic efforts, and went to a prominent clinic in the middle west, where the case was looked on as one of dystonia musculorum.

A third reason for considering spasmodic torticollis as due to organic disease is found in the work of Dr. E. C. Rosenow who took organisms from infected

foci in patients with spasmodic torticollis and injected them into the subarachnoid spaces in the frontal region in rabbits. Within four or five days the rabbits exhibited symptoms of spasmodic torticollis. I observed them and was astonished to see how exactly they demonstrated the movements exhibited in man. Whatever one may think of the theory of the selective activity of bacteria, it is hard to disregard the spasmodic movements exhibited by these rabbits.

This case is interesting and possibly, as Dr. Hassin indicated, it is closely related to the group of dystonia musculorum.

DR. ALFRED P. SOLOMON: It is my opinion that when some of these patients are studied with analysis, a close relationship will be found between their tic and their mental conflicts. A more direct causal relationship will be observed if they are studied in the presence of the specific environmental factor that is assumed to be responsible for the spasmodic tic. I had opportunity to study repeatedly the patient described by Dr. Mackay, both in her home and in the hospital, in the presence of the responsible factor, in this instance, her husband. At these times the tic, primarily a spasmodic torticollis, became generalized, so as to involve at times very diversified groups of muscles. It was possible by using various forms of direct suggestion to cause the tics to disappear entirely for short periods. It is my impression that none of these patients with chronic cases deliberately exhibit spasm of a specific muscle. It seems that the habit developed merely as a desire to contract the muscles. A great variety of complex, purposeless movements are thus performed, some which cannot be imitated by normal persons, yet in this patient constant repetition seems to have permitted the compulsion to affect muscles not usually under higher cortical control. I have studied patients who have submitted to bilateral sternocleidomastoidectomies or who have worn mechanical restraints, and who, faced with the physical impossibility of contracting these muscles, have exhibited just as energetic spasms in previously unaffected groups of muscles. I have been unable to cure chronic cases completely by any manner of psychotherapy, but my studies on this condition have led me to believe that it is functional in origin.

DR. LEWIS J. POLLOCK: I think that the Society owes Dr. Hassin a debt of gratitude for bringing this subject before us for discussion. I do not think that there can be much doubt that many cases of so-called spasmodic torticollis are clearly of organic nature. We see cases of congenital athetosis in which the movements of an extremity are constantly associated with spasm of the neck, which only with great difficulty can be differentiated from the so-called functional tic. The same is true of many cases of acquired athetosis. Many cases of typical postencephalitic sequelae are associated with spasm of the neck. In other cases other integrated movements occur along with spasm of the neck. I have been particularly impressed with the masticatory movements and movements of the tongue. It is noteworthy that in many of the cases that are obviously organic in character, as was pointed out, other parts of the body may at times become involved in the dystonia.

Another thing that seems noteworthy is that the old methods of distinguishing tic from organic spasm, namely, the efficacy of the restraining gesture, should be taken under consideration. It seems strange to me that if the head is turned toward one side, the mere touch of the cheek is sufficient to bring the head back and hold it there, as if by a magnet. I have observed a number of patients with torticollis in whom the position of the head in relation to space had an effect on the spasm. I have seen a child with torticollis in whom the tic could immediately be brought on by having the child lie on his back, and it could immediately be relieved by placing the child on his abdomen. I can remember several cases in which labyrinthine function was defective. If some disorientation is brought about by labyrinthine disturbance, it is conceivable that a patient can correct or balance stimuli by muscle sense, producing a form of neck reflex. One must be somewhat guarded in the choice of surgical procedures if one is dealing with a release of integrated movements, because the question is whether or not section of the posterior root is indicated in lesions in the basal ganglia. In experimental

animals section of the posterior root is commonly followed by an increase of such reflex activities in the deafferented limb as are initiated elsewhere. When Dr. Davis performed a section of the posterior root in a severe case of paralysis agitans, tone was definitely diminished, whereas the previously existing tremor became greatly exaggerated into movements of considerable extent and some violence.

DR. G. B. HASSIN: Dr. Solomon is right in considering the clonic cervical contractions as tics, that is, as a functional condition; but the tonic variety, spasmodic torticollis, can hardly be classified as a tic. Treatment for spasmodic torticollis as a functional disorder is exceedingly difficult. One patient described by Meige showed improvement after six years of patient work, while a surgeon could accomplish the same result in a much shorter time. Meige himself admitted that the more he studied the subject of spasmodic torticollis the more he became convinced that this condition is organic. I would not say that all cases are organic. Nor are all cases of hemiplegia or paraplegia organic. From what Dr. Pollock said and from what I attempted to show, one may see that the subject is exceedingly intricate. The successes of surgical treatment are suggestive, especially the cutting of the spinal roots as performed by Foerster and successfully performed also by a Scandinavian surgeon, Kaijser. It was even suggested that the posterior roots alone be cut; it would be exceedingly interesting to compare these results with the views that Dr. Pollock tried to bring out.

I wish to thank Dr. Mackay for bringing forth additional facts in support of my views.

I must insist that the majority of cases of spasmodic torticollis are so distressing that surgical procedures should be considered first, in spite of the excellent psychologic theories.

THE HORMONAL CAUSES OF PREMENSTRUAL TENSION*

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My attention has been increasingly directed to a large group of women who are handicapped by premenstrual disturbances of manifold nature. It is well known that normal women suffer varying degrees of discomfort preceding the onset of menstruation. Employers of labor take cognizance of this fact and make provision for the temporary care of their employees. These minor disturbances include increased fatigability, irritability, lack of concentration and attacks of pain.

In another group of patients, the symptoms complained of are of sufficient gravity to require rest in bed for one or two days. In this group, particularly, pain plays the predominant rôle. There is still another class of patients in whom grave systemic disorders manifest themselves predominantly during the premenstrual period.

REPORT OF CASES

CASE 1.—A young, unmarried woman suffered from frequent convulsive attacks, which later occurred exclusively within ten days preceding menstruation. Neurologic investigation resulted in a diagnosis of idiopathic epilepsy. In view of the close chronologic coincidence of the attacks and menstruation, a sterilizing dose of roentgen rays was applied to the ovaries. Following the treatment, the patient had only one attack during one and one-half years. Then, suddenly, a repetition of attacks occurred within a ten day period. Four or five weeks later, a renewed series of attacks took place, followed by the occurrence of normal menstruation. After watching several menstrual periods, always preceded by epileptic attacks, roentgen treatment to the ovaries was repeated, and at present a period of remission has taken place.

CASE 2.—The patient was a sufferer from severe bronchial asthma, which was only slightly influenced by changes in climate. The most serious and frequent attacks regularly preceded the menstrual period. After due consideration, a sterilizing dose of roentgen ray was directed against the ovaries. For two and one-half years, complete amenorrhea existed and with it complete freedom from asthmatic attacks. Recently, this patient again had a severe asthmatic attack. After six weeks another severe seizure was noted, and was followed within a few days by the appearance of normal menstruation.

These two cases illustrate well the close connection between the ovarian function and systemic manifestations due to other organic systems.

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A study of the sexual cycle in lower animals and in human beings has shown that these estrual phenomena are dependent on the action of the anterior lobe of the pituitary which liberates a hormone that circulates in the blood and induces the growth of the ovarian follicles, thus producing the activation of the female tubular tract.[1] The hormones that produce these phenomena have been and can be recovered from the blood and urine, and in the case of the female sex hormone, have been studied quantitatively under normal and abnormal conditions.[2]

The group of women to whom I refer especially complain of a feeling of indescribable tension from ten to seven days preceding menstruation which, in most instances, continues until the time that the menstrual flow occurs. These patients complain of unrest, irritability, "like jumping out of their skin" and a desire to find relief by foolish and ill considered actions. Their personal suffering is intense and manifests itself in many reckless and sometimes reprehensible actions. Not only do they realize their own suffering, but they feel conscience-stricken toward their husbands and families, knowing well that they are unbearable in their attitude and reactions. Within an hour or two after the onset of the menstrual flow complete relief from both physical and mental tension occurs.

After encountering a number of patients with such strikingly similar complaints, I was led to investigate some of them to determine whether any abnormality in the secretion of hormones could be noted. The first patient on whom this examination was made offered a most striking explanation of the entire symptom complex.

CASE 3.—A woman, aged 32, had been married for six years and was the mother of two children. She had noticed an increasing nervous tension preceding menstruation, which was particularly manifest if the menses were overdue. Occasionally, eight weeks elapsed before menstruation occurred, under which circumstances hystero-epileptic manifestations occurred. Neurologic examination showed no abnormalities. The patient was ready to commit suicide, and from her own description it was evident that a family rupture was imminent, although she said that her husband was both considerate and kind. Both general and local pelvic conditions were normal.

At a time when this tension was at its height, 80 cc. of blood was aspirated from a vein. Within a few hours relief was experienced, but the relief was transitory, and a full recurrence of all manifestations was noted within two days. The blood of this patient showed twice the amount of female sex hormone that is normally found premenstrually.[3] It was decided to tone down the ovarian activity by roentgen treatment directed against the ovaries. With the onset of

1. Smith, P. E.: Am. J. Anat. **45**:205, 1930. Zondek, B., and Aschheim, S.: Arch. f. Gynäk. **130**:1, 1927.

2. Frank, R. T.: The Female Sex Hormone, Springfield, Ill., Charles C. Thomas, 1929.

3. Frank, R. T., and Goldberger, M. A.: Clinical Data Obtained with Female Sex Hormone Blood Test, J. A. M. A. **90**:106 (Jan. 14) 1928.

amenorrhea, complete subsidence of the symptoms occurred. After the full effect of the roentgen treatment had developed, the blood was again examined, and it was found that less female sex hormone than normal was now present in the circulation. The nervous disturbances of this patient have been relieved for three years.

In the case just cited, an excess accumulation of hormone caused the symptom complex complained of, and could be temporarily relieved by venisection and permanently improved by reduction in the amount of female sex hormone in the circulation.

The accompanying table gives a synopsis of the cases observed.

Cases of Premenstrual Tension

	Age	Regular Menses	Parity: Children	Parity: Abortions	Complaints	Relief with Onset of Menses	Treatment
R. P.	35	+	2	1	Severest tension; double oophorectomy advised elsewhere	Immediate	X-ray "toning"
B. H.	32	+	2	1	Severest tension; suicidal desire	Immediate	X-ray "toning"
F. B.	41	+	3	0	Severest tension; unbearable, shrew	Gradual	
L. H.	47	+	2	0	Severest tension; husband to be pitied	Immediate	Elimination
M. M.	28	+	0	0	Severest tension; suicidal desire	After 1 day	
A. B.	38	+	4	3	Severest tension; "almost crazy"	Immediate	X-rays advised
H. C.	35	+	1	1	Severest tension; psychoneurotic	Immediate	
B. M.	38	+	Unmarried		Severe tension; incapacitated mentally	Immediate	Elimination
K. R.	43	+	2	1	Severe tension; sexual tension also	Toward end of period	
M. L.	33	+	1	0	Severe tension; cardiac irregularity	Gradual	Elimination
A. W.	41	+	2	1	Severe tension; "impossible to live with"	Immediate	
B. N.	32	+	1	0	Moderate tension; despondent	Immediate	
E. M.	35	+	3	0	Moderate tension	Immediate	
C. R.	33	+	2	0	Moderate tension	Immediate	
S. S.	24	+	0	0	Moderate tension	Immediate	

In another illustrative case, the premenstrual tension was accompanied by premenstrual edema, which was particularly noticeable in the face, hands and feet. This, together with the fact that, premenstrually, the total amount of urinary secretion decreased to a striking degree, led me to investigate the entire urinary excretion throughout the cycle in this patient. It was found that there was a marked retention of female sex hormone compared with the quantity excreted by the normal woman, approximately only 300 mouse units of hormone being excreted throughout a complete menstrual cycle, although at least from 1,500 to 3,000 mouse units should be excreted during this time. Unfortunately, I am unable to give the corresponding level for hormone in the blood throughout the cycle in this patient. However, because of the striking regularity in the occurrence in the menses, the well marked premenstrual enlargement of the uterus and breasts, the fact that diffuse

subcutaneous hemorrhages preceded menstruation and that the menstruation was always profuse, I feel confident that the level of the hormone in the blood in this woman is high.

This case is quoted because it further emphasizes a contention that I have made for some time, namely that not only must the amount of hormone liberated by the ovaries be taken into consideration, but the amount excreted as well. In other words, a comparatively small amount of female sex hormone may produce striking effects in a given person if the renal excretory level is high, while a fully functioning ovary, which supplies an ample amount of female sex hormone to the normal person, may fail to produce full physiologic effect if the renal threshold of excretion is low and the hormone is consequently excreted as rapidly as it is formed.[4]

THERAPY

The group of patients with milder symptoms have been relieved by medical measures. In this group it has been possible to avoid the use of roentgen therapy, which in nervous, labile women may cause the severest neurovascular symptoms of the menopause. On the hypothesis that the excretion of the female sex hormone conforms physiologically to the ordinary principles of excretion, I have used calcium lactate, either alone or in combination with caffeine preparations, to increase the elimination of the hormone present in the circulation. Calcium lactate, which is also sedative in its action, is given in doses of 5 grains (0.32 Gm.) from three to five times a day. Theobromine sodiosalicylate, if tolerated by the stomach, is given three times a day. When neither of these remedies is well borne, an increased consumption of coffee has been prescribed. In addition to these measures, saline laxatives, preferably magnesium citrate, have been prescribed, because the female sex hormone is readily excreted through the bowel. A number of these patients note prompt relief following the medication. These measures should be prescribed only at the time of maximum tension, as they frequently produce loss of weight, which is harmful to emaciated patients.

It would thus appear that the continued circulation of an excessive amount of female sex hormone in the blood may in labile persons produce serious symptoms, some cardiovascular, but the most striking definitely psychic and nervous (autonomic). These periodic attacks are incapacitating and lead occasionally to extreme unhappiness and family discord. They can be directly ascribed to the excessive hormonal stimulus. At present, in the severest cases of this nature temporary or permanent amenorrhea, brought about by roentgen treatment, appears to be the proper procedure.

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4. Frank, R. T., and Goldberger, M. A.: Female Sex Hormone; Utilization of Hormone in the Normal Woman; Effect of Abnormal Kidney Permeability in the Production of Amenorrhea and Sterility, J. A. M. A. **94**:1197 (April 19) 1930.

CONCLUSION

I suggest that careful study of the changes occurring in the autonomic nervous system, particularly such reactions as lend themselves to accurate analysis, be undertaken by neurologists at that time of the cycle at which symptoms of tension are most manifest.

ABSTRACT OF DISCUSSION

Dr. Josephine H. Kenyon: The points brought out in this paper are interesting to us who are working with adolescent girls and healthy women. Premenstrual tension is an outstanding complaint of the presumably well women who present themselves periodically for examinations. We have had little effects from ovarian therapy by mouth; we have perhaps had better results from hypodermic medication, but any suggestion of other ways to combat the depression and emotional tension so commonly seen will be of value.

Dr. Edith R. Spaulding: This is certainly an important problem. I agree with Dr. Kenyon regarding the frequent occurrence of such conditions as Dr. Frank has described. One is reminded at once of the hysterical patient who is unable emotionally to cope with her whole sex life, and who shows uncontrollable tension during the premenstrual period. In many instances in that type of case, the feeding of ovarian extract produces an exacerbation of the emotional symptoms. This reaction, while not constant in all cases, seems to occur in the cases in which overstrong sexual emotions have found outlet in hysterical symptoms.

The treatment outlined by Dr. Frank suggests an interesting possibility in such cases. On the one hand, the patients can be helped psychologically to utilize their increased sexuality through gaining a better understanding of themselves and finding a more adult outlet for their emotions; on the other hand, in many cases, especially in unmarried women with deep-seated emotional difficulties, the lessening of the sexual drive offers a helpful therapeutic procedure.

Dr. Robert T. Frank: In case 3, every approach from a psychic standpoint was made and was unsuccessful. I have tried to look at these cases from an entirely impartial point of view. In fact, they obtruded themselves in a study of many hundreds of women, and I found the symptom complex so clearcut that I could no longer evade it. I have tried throughout these studies to make them on a qualitative and particularly on a quantitative basis, and I can give to them no other interpretation.

In the beginning, I was more interested in clarifying this condition from a symptomatic and therapeutic standpoint. I do not know whether this is a proper occasion to air again my entirely nihilistic beliefs on current endocrine therapeutics. Therapy for endocrine disturbances can be looked at from one of two points of view: from that of one who insists on having definite proof in his therapy, in other words, from the standpoint of the pharmacologist, or from that of one who tries out drugs and sees what the effect is. Both doubtless have their uses and are justifiable. One should take into consideration the fact that active endocrine preparations have been shown during the past few years to be extremely potent and toxic in direct proportion to their potency; for example, thyroxin, which must be given in milligram doses. Excessive administration of parathyroid extract is sometimes fatal. That overdoses of insulin cause insulin shock is known to every clinician. Solution of pituitary or epinephrine when given in overdoses may produce severe cardiovascular symptoms and collapse. On the other hand, such "things" as desiccated ovary, desiccated testis, thymus and anterior pituitary extracts can be given by the pound or bushel, and the only effect that I can note is a disturbance of a delicate stomach.

Clinical Notes

BUBBLE TECHNIC TO INCREASE THE EFFICIENCY OF LUMBAR SAC MEDICATION*

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We have felt for some time that the introduction of antimeningococcic serum into the lumbar sac is a relatively ineffective means of treating patients who have meningococcic meningitis, and that the method of introduction at the cistern, though obviously more efficient, still leaves room for much improvement.

Evidence points to the fact that the primary origin of meningococcic meningitis is septicemia. Choroiditis, ventriculitis and meningitis subsequently develop over the cortices and finally about the cord. When lumbar puncture is done and the injection of serum made, the treatment for the process in the sac and about the lower part of the cord is adequate. Even when the serum is mixed with spinal fluid in the syringe as it is introduced, the height to which the serum rises in the spinal subarachnoid space is questionable, and whereas the meninges about the lower part of the cord may have adequate and immediate contact with the serum, this area of inflammation is of less importance than that of the ventricles and cortical meninges.

If a rigid or, better still, a semirigid model of the cerebrospinal space is made, filled with colored solution and then a second colored solution introduced into the lower or lumbar end so as roughly to underlie the first, it is found that for the following reasons considerable time elapses before the solutions mix: 1. The system is closed and full. 2. The area of contact between the two solutions is limited to the space between the cord and the arachnoid. 3. The circulation over the cord is minimal as compared to that in the ventricles and over the cortices. Altering the position of the system or of the patient under treatment would aid but little to facilitate this mixing, because, as indicated, the system is at once closed and full. If in the model the conditions of a meningitis, in which there are dissimilar colloids (purulent spinal fluid and antimeningococcic serum) are simulated, the mixing takes place much less readily than with the simple colored solutions, as diffusion is less rapid. Thus, our impression is that the time taken for the serum to reach the point where contact is needed is unduly long. If in the model of the cerebrospinal space a bubble of air is introduced and then the ends of the system are alternately raised and lowered, a fairly rapid mixing occurs. The visualization of this process is simplified if one considers a carpenter's spirit level.

In an attempt to apply the principle outlined to the human subject, experimentation was carried out on a fresh adult cadaver. With the subject on the side and the head bent to approximate the under shoulder, 10 cc. of air was introduced into the lumbar sac and the upper end of the board on which the cadaver was lying was elevated on blocks 12 inches (30 cm.) high. Roentgenograms were taken of the cervical spine; the position was then reversed, so that the lower end of the board was elevated 12 inches, and a roentgenogram taken of the lumbar spine. This process was repeated with the head still held in the bent position, and roentgenograms were taken of the cervical and lumbar spines as before. The air introduced

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* From the Worcester City Hospital.

from below was demonstrable in the second of the cervical plates, and in both plates taken with the pelvis elevated the lumbar sac was well outlined by air. This demonstrates that the air was trapped by the bending of the neck and thus prevented from being lost over the cortices. In previous autopsies in cases of septic meningitis, it had been demonstrated that air injected ante mortem into the lumbar space without an attempt to prevent its entering the skull was lost in the meninges over the cortices.

To check the results of the roentgenographic studies, the brain was removed from the skull; the cephalic end of the board on which the body rested was elevated 12 inches, and the skull was filled with water; air was then injected into the lumbar sac, and it quickly appeared in the skull. The admixing effect of the air bubbles was evident in the particles of detritus that rose from the spinal canal into the skull.

Having demonstrated that the bend of the neck trapped the air in the cervical spine, that the air readily rose when the head of the cadaver was elevated only 12 inches, and that the passage of air bubbles was efficacious as a mixing agent, the conclusions were applied to clinical cases.

TECHNIC

With the patient lying horizontally, without a pillow, and with the head bent to touch the dependent shoulder, a lumbar puncture was done, and cloudy fluid was drained to a pressure of zero. Serum was made ready for injection in a 20 cc. syringe containing an ampule of serum and behind it (with the syringe tilted) from 7 to 8 cc. of air. The serum and the air were injected, and the head and the foot of the bed were alternately elevated 12 inches at one minute intervals for ten times; finally, with the foot of the bed elevated, two pillows were placed under the patient's head. The position was then reversed, the air passing into the meninges over the cortex, carrying with it a mixture of cerebrospinal fluid and antimeningococcic serum. In trained hands an efficient variation is the introduction of the serum into the cisterna magna with air bubbled through either at the same puncture or at a subsequent lumbar puncture.

SUMMARY

Recognizing the inefficiency of the ordinary treatment for meningococcic meningitis by the lumbar route, a relatively simple technical improvement is advanced. The principle involved is the admixture of serum and spinal fluid over the spinal cord by means of an air bubble after the manner of a "spirit level" and its conveyance over the cortices by the passage of this bubble into the skull.

CONCLUSIONS

1. By this technic, efficient admixture of serum and cerebrospinal fluid about the cord is obtained.

2. By the liberation of the bubble into the skull, the specific serum is conveyed to the areas of meningitis most in need of treatment, the cortices, even though the serum is given originally into the lumbar sac.

3. Patients treated by this means, though too few to enable us to draw any absolute conclusions, seem to show a more rapid response than do patients treated in the ordinary manner.

4. Patients treated by this means have shown neither subjective nor objective disturbances referable to the injection of the air.

5. In the limited number of patients treated, subarachnoid adhesions or block did not develop during the course of treatment.

Abstracts from Current Literature

LATE COCHLEOVESTIBULAR MANIFESTATIONS OF EPIDEMIC ENCEPHALITIS. GEORGES PORTMANN, Rev. d'oto-neuro-opht. **9**:241 (April) 1931.

This article is part of a symposium on encephalitis and was reported to the Fifth Congress of the French Societies of Oto-Neuro-Ophthalmology, held in Paris in June, 1931.

The virus of encephalitis epidemica has a particular affinity for the eighth nerve. By its anatomic and physiologic relations, the vestibular nerve occupies an important place in the study of this disease. The cochlear division is much less often involved. After describing the origin of the cochlear division of the eighth nerve and its course, together with the vestibular division to the brain stem, its endings in the anterior and lateral acoustic nuclei and its decussation, the author traces its pathway to the supranuclear centers and the cortex: the ventral and dorsal bundles fuse and pass upward along the internal side of the ribbon of Reil (lateral lemniscus). After a relay in the nucleus of the lateral ribbon of Reil, fibers go to the anterior and posterior quadrigeminal bodies and the subthalamic region; the cochlear division then traverses the posterior segment of the internal capsule and terminates in the median part of the first and second temporal convolutions.

Beginning as tendrils around the neuro-epithelium of the ampullae and maculae of the utricle and saccule, the vestibular nerve fibers unite into a trunk, which enters the brain stem at a higher level (bulbopontile furrow) than the acoustic division, and ends in the vestibular nuclei (the triangular, Deiters' and Bechterew's nuclei and the nucleus of the descending root). The triangular nucleus is in relation below and laterally with the terminal sensory nuclei of the vagus and glossopharyngeal nerves. Deiters' nucleus is composed of large cells with many dendrites and occupies the internal segment of the inferior cerebellar peduncle. Bechterew's nucleus is situated above Deiters' nucleus, and at first lies in the lateral angle of the fourth ventricle between the restiform body and the descending gray substance of the root of the fifth nerve; higher up it lies between the masticator nucleus and the vesicular root of the trigeminus. The nucleus of the descending root is formed by gray matter and lies between the restiform body and the juxtarestiform body, or descending branch of the vestibular nerve. Some of the vestibular fibers go directly to the nucleus of the descending root. The others form two large roots, the ascending and the descending. Some few fibers of the ascending root go to Deiters' nucleus and to the triangular nucleus, while the greater part ascend to the roof nuclei. The fibers of the descending root traverse the internal segment of the restiform body and end, for the most part, in the triangular nucleus; a few go to the nucleus of the descending root. From the triangular nucleus, fibers go to Deiters' nucleus and to the nucleus of the descending root, but Deiters' nucleus sends no fibers to the other vestibular nuclei. The vestibulospinal bundle originates in Deiters' nucleus, descends in the reticulated substance and the anterolateral column of the cord and is distributed to the cervical and thoracic segments. It is thus in more intimate relation with the musculature of the neck and trunk than with that of the limbs. Deiters' nucleus also sends fibers upward to the nuclei of the third, fourth and sixth pairs. Fibers from the nucleus of the descending root form part of the posterior longitudinal bundle. These ascending fibers, mostly crossed, terminate in the nuclei of the third and fourth nerves; the descending fibers go only as far as the dorsal cord. Some fibers go to the vestibulospinal bundle.

The triangular nucleus furnishes ascending and descending fibers to the posterior longitudinal bundle; it sends fibers to the nuclei of the sixth pair and the hypoglossus and to the cerebellum, which terminate in the nuclei of the roof, the

globus and the embolus. Fibers also go to the vestibulospinal bundle. Bechterew's nucleus supplies only ascending fibers to the posterior longitudinal bundle, which terminate in the nuclei of the third and fourth pairs.

The great importance of the vestibular nuclei in the constitution of the posterior longitudinal bundle and their extensive and intimate relations with the motor oculi nuclei and the muscles of the neck, trunk and limbs may be seen. They probably are in relation with the nucleus of the tenth pair also, but this has not been demonstrated anatomically.

Vestibulocerebellar fibers arise from the primary nuclei, especially the triangular nucleus. Perhaps, also, fibers reach the cerebellum directly from the vestibular nerve. The cerebellovestibular connections are more numerous, but the relations of the two systems are very complex and need further study.

Winckler believed that the fibers from the saccule and utricle form a separate division of the vestibular nerve and that there is dissociation of the utricular from the saccular fibers, the latter being associated with the cochlear fibers. Both end in the acoustic tubercle and the anterior nucleus, from where fibers go to the posterior longitudinal bundle; others cross to the opposite side, some going to the cerebellum, others to the corpora quadrigemina, and eventually reach the parietal cortex.

Cochlear symptoms are very rare in late epidemic encephalitis. The most important is tinnitus. Deafness of the perceptive type is often the only symptom, and may be overlooked without a systematic examination. The hearing by air may be only slightly modified, but the bone conduction is lost. The upper limit of the tone scale is lowered, and tonal islands of deafness exist for forks of 3,072 double vibrations and the immediate neighborhood. Vestibular symptoms are found with great frequency: vertigo, disturbances of equilibrium, motor oculi disturbances and altered vestibular reflexes. Vertigo manifestations vary in severity, frequency and duration, and most often are not accompanied by nausea and vomiting. The vertigo may be systematized or not, or it may be present only in certain positions of the head, and it is frequently accompanied by headaches, fatigue, intellectual laziness and changes in character. Disturbances of equilibrium, manifested by uncertain gait, lateropulsion or retropulsion and falling, are more frequent than vertigo. Nystagmus, oculogyral spasms and abnormal positions of the eyes are constantly present. Nystagmus varies in kind and intensity. Oculomotor disturbances are represented by paralyses, strabismus, Parinaud's syndrome, forced movements and oculogyral crises.

A careful examination is often required to demonstrate functional labyrinthine disturbances. Tests of equilibrium are made by having the patient stand first on both feet, then with one foot before the other and, finally, on one foot, with the eyes both open and closed, and by noting the tendency to fall, which is always in the same direction. The patient walks with feet far apart and takes false steps to avoid falling. The test of the extended arms, the eyes being closed, shows deviation of one or the other arm. The results of the turning test are usually the finding of a normal reaction or a hypo-excitability. With the caloric test, varying results are noted, but, usually, there is hypo-excitability. There is also dissociation between the results from rotation and from the caloric test, and also between the reactions from the horizontal and the vertical canals, the hypo-excitability being more marked in the former. The galvanic test is used to measure the threshold of excitability, which is most often raised. Deficiency of the otolithic apparatus is noted in some cases, in which there is vertigo only in certain positions of the head. This is indicated also by forced positions of the eyes in different directions, nystagmus and past pointing. The utricular function is tested by displacement of the head in the vertical plane, saccular function by displacement in the transverse plane. These tests have been too seldom applied.

The beneficial effects of labyrinthine tests on certain muscular disturbances, such as pulsions, merry-go-round movements, ocular spasms and torticollis, have been frequently noted. Especially interesting are the experiments of Delmas-Marselet. He found that, "labyrinthine excitations, capable of provoking in the

parkinsonians a strong sense of vertigo, inhibited momentarily the elementary reflexes of posture and the hypertonia corresponding to them."

Occasionally an association of cochlear and vestibular syndromes is seen, but, even then, the vestibular symptoms are more marked.

The most extensive histologic research has been made by Anglade, although not enough attention has been given to the nuclei of the eighth pair. The pathologic changes in the later lesions of the mesocephalic cranial nerves may be summed up as "a more or less developed glial state, seated at the level of the nuclei or in the course of the nerve fibers."

In summary, the latent vestibular syndrome is the important part of late otitic manifestations in epidemic encephalitis and is characterized by a permanent, often dissociated, hypo-excitability and crises of vertigo of variable intensity, accompanied by transient hyperexcitability.

An explanation of the pathogenesis on purely anatomic grounds is not adequate. It does not account for the variability of the symptoms. It is suggested that modifications of the chronaxia, to which vasomotor disturbances are added, offer a better explanation. Lapicque gave the name chronaxia to the threshold of excitability of a nerve, measured in terms of the time of passage of a current of electricity. Bourguignon and Renée Dejéan have recently made precise measurements of the chronaxia of the vestibular nerve, and found that it is constant for the same subject and varies within only small limits from one to another. It is from 50 to 100 times greater than that of the spinal and cranial motor nerves and is allied to that of the sympathetic nerves. Bourguignon and Radovici showed experimentally that one of the conditions for the existence of a reflex is an isochronism of the sensory and motor nerves and the muscles concerned. Lapicque has shown that the sympathetic system functions according to the law of heterochronism. The vestibular nerve resembles, in this respect, a sympathetic nerve; nevertheless, if the difference in chronaxia between it and the motor nerves is too great, the reflex action will be diminished or abolished. The author suggests that the encephalitic virus raises the chronaxia of the vestibular nerve to such a degree that there is a hypo-excitability of the reflex. Further, the virus may persist in a latent state, and, during periods of its release through a lighting up of the focus, the crises of vertigo and sudden hyperexcitability are produced. There are two kinds of inexcitability of a nerve, that due to death of the axis cylinder and that due to a heterochronism of the different nerve segments.

During the acute stage of epidemic encephalitis, peripheral vasomotor manifestations are common. It is probable that such phenomena occur also in the labyrinth or its nervous pathways. Lermoyez's disease and Ménière's syndrome are extreme examples, respectively, of vasoconstriction and vasodilatation, and all degrees between these may occur. Vasomotor stasis can produce vertigo, which is essentially a phenomenon of irritation of the labyrinth or the vestibular nerve. Vasodilatation causes hypo-excitability, and vasoconstriction causes hyperexcitability. Vascular modifications also affect chronaxia.

Experimental and clinical facts strongly suggest that the otolithic apparatus is responsible for the abnormal position of the eyes. Two cases of blepharospasm are cited; in one of them, wearing dark glasses corrected it, but in the other, relief was only obtained by placing the head backward.

The syndrome of the eighth pair may constitute the sole picture of epidemic encephalitis, as Barré and Reys showed in 1921. Such cases are particularly difficult to diagnose. In other cases, it is only part of the clinical picture. It should not be forgotten that cochleovestibular disturbances are often a part of the clinical manifestations, and a careful neuro-otologic study is necessary to determine them; especially should it not be neglected in the presence of the subjective symptoms of vertigo and tinnitus.

The diagnosis of eighth nerve disturbances having been established, differentiation between encephalitis, brain tumor, multiple sclerosis and syphiltic neurolabyrinthis must be made. As in epidemic encephalitis, so also in multiple

sclerosis there is a pure labyrinthine type as well as a form associated with the pyramidal syndrome. In multiple sclerosis the vertigo is less frequent and not so violent; on the contrary, disturbances of equilibrium are more marked, and nystagmus is frequent. But on the whole, a differentiation must be made from the history and by the colloidal benzoin reaction, which, when positive, speaks for multiple sclerosis. Certain pathologists have assumed a lesional identity between multiple sclerosis and epidemic encephalitis.

In intracranial hypertension due to tumor, vertigo is found, whether or not the vestibular pathways are directly involved; it is found also at times in simple ependymitis and serous meningitis. Neither the vertigo nor the deviations of the body and limbs are characteristic. Opinions are divided as to whether a vestibular test can reveal hypertension. Eagleton and other American writers believe that it can, while Bárány, Barré and Alfandry think that it cannot. Alfandry found that vestibular disturbances were frequent in hypertension from various causes, but that there is no pathognomonic syndrome. The differential diagnosis is difficult, especially since certain symptoms of hypertension (papillary stasis) have been found in epidemic encephalitis.

Tumors of the cerebellopontile angle lie between the pons and the seventh and eighth nerves on the inside, the cerebellar hemisphere on the outside and the flocculus and the digastric lobe below, and the anterolateral boundary is formed by the internal face of the petrous bone with the internal auditory meatus and its contents. Cochleovestibular disturbances are usually the first signs of trouble noted by the patient. Vertigo, occurring in crises and rarely accompanied by vomiting, pallor, tinnitus, falling, disturbances of gait with lateropulsion toward the diseased side, abnormal position of the head and spontaneous nystagmus are some of the symptoms. The nystagmus is constant, horizontal, rotary or, rarely, vertical, with the quick component toward the side of the lesion. Examination of the labyrinthine function is very important. The ear on the diseased side is deaf, and there is no reaction to the caloric test; in the opposite ear the vertical canals do not react. To these signs may be added paralysis of the facial, glossopharyngeal, hypoglossal and trigeminal nerves. Such a group of findings makes the diagnosis easy.

Tumors of the bulbopontile axis begin insidiously with abdominal pain and vomiting. Disturbances of the associated movements of the eyes are a constant symptom. It is difficult to differentiate them from oculomotor disturbances due to epidemic encephalitis. If the lesion is in the cortex or the corticonuclear pathway, although voluntary motion is paralyzed, the eyes react to vestibular stimulation. On the other hand, the lack of reflex motility points to a pontile lesion. Vertigo is common but not characteristic. Nystagmus is often absent, but, when present, it may be horizontal, rotary or vertical. Lesions seated low down cause rotary nystagmus; those high up cause vertical nystagmus. Tests of vestibular function yield responses of great variability: nausea and vertigo from the cold caloric test; deviation of the arms but no nystagmus after rotation; modification of the excitability of the vertical canals only; absence of all responses, and normal excitability.

In tumors of the cerebellum there is great variability in the vestibular syndrome. Vertigo is constant and is most often rotary. Past pointing is not pathognomonic as Bárány thought. Nystagmus is variable in direction, but is most often toward the diseased side; there is inequality of rhythm and amplitude, slow and wide on the diseased side and rapid on the sound side. Many observers have shown experimentally that total or partial ablation of the cerebellum does not cause nystagmus unless the vestibular nuclei are damaged. Tests of the vestibular function give paradoxical results with the different tests. Concomitant symptoms of the cerebellar syndrome (trembling, hypermetria, asynergia and adiadokokinesis) will fix the diagnosis.

Tumors of the fourth ventricle are accompanied in some cases by a vestibular syndrome. Vertigo, characterized by appearing or increasing with changes in position of the head, is frequent. The gait is uncertain, and the head is bent

forward. Nystagmus is often absent and, when present, varies in direction even during the examination. Disturbances of associated movements of the eyes are frequent. According to Alfandary, they are due to pressure on or destruction of the posterior longitudinal bundle. The insidious evolution of the tumor, the late appearance of the vestibular syndrome and the lack of localizing signs make the diagnosis difficult. The sign of Bruns, the flexed head and grave signs of intracranial hypertension point to the correct diagnosis.

The multiplicity of symptoms accompanying peduncular tumors may readily be understood when the anatomic relations are visualized. Most often, vestibular manifestations are absent, and, when present, are not clearcut. Vertigo is more a sensation of fog or dizziness. Nystagmus is vertical and rapid, and is associated or not with disturbance of conjugate movements of the eyes upward or downward, with interference with convergence but with integrity of the instrumental reactions. The associated deafness, syringomyelic dissociation, cerebellar symptoms, nuclear paralysis of the eye muscles and, eventually, the involvement of the motor branch of the fifth nerve or of the optic nerve will permit localization of the tumor.

Supratentorial tumors cause very slight and infrequent vestibular symptoms and mostly through intracranial hypertension. When tumors of the frontal lobe involve the frontopontocerebellar bundle, static disturbances, spontaneous deviation or lateropulsion may be present.

All intracranial tumors may directly or indirectly be manifested by vestibular disturbances of a more or less characteristic type, but none of them alone are diagnostic. Other factors, clinical, historic and radiographic, must also be considered in order to arrive at the correct diagnosis.

Syphilis frequently attacks the eighth nerve, and its neurolabyrinthine manifestations sometimes so closely resemble the late syndrome of postencephalitic parkinsonism that careful examination is necessary to differentiate them. Acquired syphilis, in both the secondary and tertiary stages, may attack the eighth pair of nerves, and its manifestations may be cochlear, vestibular or both. The cochlear symptoms are of sudden onset or are rapidly progressive, but have no other distinctive characteristic. The vestibular type is indicated by the usual symptoms, disturbed equilibrium, vertigo, nystagmus, etc. It is frequently dissociated: lesions limited to one group of canals, especially inexcitability of the horizontals and dissociation of reactions, e. g., one reaction being abolished and the others conserved. Lund and O. Beck thought that the combination of vertigo, spontaneous nystagmus and past pointing with normal vestibular excitability was never seen except in syphilis, but it is met with frequently in multiple sclerosis. In the associated form the cochlear manifestations, contrary to the conditions in epidemic encephalitis, are more marked. The concomitant signs will establish the diagnosis. In neurolabyrinthitis of the tertiary stage, manifestations of discrete syphilis occur; there are no cutaneous or visceral lesions, and the Wassermann reaction is negative or doubtful. The association with paralysis of other cranial nerves is frequent. In a large number of cases, examination of the cerebrospinal fluid showed a positive result of the Bordet-Wassermann, the Vernes and the colloidal benzoin tests. In a series of studies of labyrinthine reactions in tabetic patients, Rebattu found vestibular disturbances as frequent as the disappearance of the pupillary reaction to light. In late hereditary syphilis, neurolabyrinthitis occurs in two forms: the fulminating, almost exclusively cochlear form, in which deafness supervenes almost overnight, and the progressive form, which affects both the cochlea and the vestibular apparatus. The deafness is profound and of the perceptive type. A fact of diagnostic importance is the relative preservation of bone conduction. No other disease except otosclerosis presents this picture. The vestibular syndrome shows some peculiarities. Buys found inexcitability in the rotation test while the caloric reaction was preserved, but this finding is not constant. Ramadier studied the galvanic test and always found the same result: integrity of the nystagmic reaction, absence of the static reaction and hypersensibility of the auditory reaction. The sign of Hennebert is characteristic of late hereditary

syphilitic neurolabyrinthitis. This is a positive fistula sign. It is provoked by pneumatic compression and aspiration of the air in the auditory meatus. It differs from the usual fistula sign in that the nystagmus is rotary, horizontal or oblique, while in the usual fistula sign, the nystagmus is always horizontal. (Bárány taught that Hennebert's sign was provoked in the absence of a perforation of the membrana tympani.—Abstractor.) It is said to be present in a large proportion of the cases, and never to be present in acquired auricular syphilis or other diseases of the eighth nerve.

Late auricular manifestations of epidemic encephalitis do not present a prognosis of vital gravity. The gravity is limited to the functional impairment.

The sheet anchor of treatment is scopolamine. The favorable influence of labyrinthine stimulations on the elementary reflexes of posture and the hypertonia of parkinsonism suggests the thought that scopolamine may have a direct action on the labyrinthine reflexes. Scopolamine should be supplemented by antiseptic treatment with methenamine, sulfarsphenamine given intravenously, etc. The intercurrent vasomotor disturbances may be controlled by epinephrine, insulin, pilocarpine, physostigmine salicylate, atrophine, the nitrites and iodides.

An extensive bibliography is appended. DENNIS, Colorado Springs, Colo.

EXPERIMENTAL STUDIES ON THE CORTICIFUGAL OPTIC CONNECTIONS IN RABBITS AND APES. A. BIEMOND, Ztschr. f. d. ges. Neurol. u. Psychiat. **129**:65, 1930.

Monakow (1889) was the first to describe corticifugal optic fibers on the basis of experiments on cats, dogs and rabbits. He stated that a fiber was given off from every optic center, and that a fiber also terminated in each one. Thus, there were two parallel systems of fibers the directions of which were opposite. He found the following situation in rabbits: (1) Centripetal fibers: large ganglion cells of the retina to the lateral zone of the lateral geniculate body; from here and the pulvinar as visual fibers to the third and fifth cortical layers of the area striata, and here again connected with other cortical territories by an intermediary cell. (2) Corticifugal fibers: large pyramidal cells of the third cortical layer in the area striata to form visual fibers passing to the superior colliculus and the external geniculate body; from the superior colliculus back to the retina.

Munk (1890), in the course of studies on stimulation of the occipital cortex, found that eye movements so elicited could no longer be produced after cutting the radiating fibers of the corona radiata. He concluded, therefore, that there were radiating fibers running peripherally from the visual centers in the cortex to lower centers. Boyce (1895) demonstrated corticothalamic fibers in the cat by means of secondary degeneration studies made after lesions of the anterior third of one cerebral hemisphere. He also found fibers from the cortex to the superior colliculus coming from more posterior parts of the hemisphere. His observations are vague and uncertain. Simpson (1901) found fibers running between the cortex and the superior colliculus, most of them being homolateral, but some crossed. He found these fibers in cats, but was unable to demonstrate them in dogs or apes. Flechsig (1901) made the important observation that there was a fiber tract from the calcarine fissure to the superior colliculus. These observations were based on myelogenic studies. Dejerine described fibers not only from the cortex to the colliculus, but to the lateral geniculate body as well.

Probst (1902) experimented on cats, destroying the poles of the first, second and third occipital gyri. He found: 1. There was a definite secondary degeneration in the superior colliculus of the same side, and a few degenerated fibers going to the colliculus of the opposite side. He found the fibers from the retina occupying a more lateral position in the colliculus, while the corticifugal fibers were more central. Fibers from the retina, moreover, were chiefly crossed, while the corticifugal fibers were chiefly homolateral. 2. Fibers were followed into the lateral thalamic nucleus of the same side. 3. Most important of all, fibers were found passing to the lateral geniculate body of the same side. Beevor and Horsley

(1902) found similar connections. They were able to demonstrate them also in apes. These authors were the first to demonstrate connections between the cortex and the lateral geniculate body in apes. They were unable to demonstrate these connections from the parietal, temporal or prefrontal cortices, but could from the motor cortex. Berls (1902) made unilateral lesions of the posterior part of the brain of rabbits and made the following observations: 1. The cortico-collicular fibers are entirely homolateral in the rabbit. 2. The lateral geniculate body was degenerated in its dorsomedial aspect. 3. Degeneration was present in the lateral nucleus of the thalamus.

Bouman (1905) found, after destruction of the visual cortex, a bundle of fibers that passes through the cerebral peduncle and penetrates the ventral portion of the lateral geniculate body without ending there. The fibers from the occipital lobe end in part in the dorsal part of the lateral geniculate body, in part in the lateral and posterior nucleus of the thalamus and in part in the superior colliculus where they occupy a superficial position. These experiments confirm the findings of Probst. Niessl von Mayendorff (1911) denied that the visual fibers end in the colliculus, but asserted that most of them pass to the pulvinar. Poljak (1927) accepted a corticifugal connection with the superior colliculus, but denied any connection with the lateral geniculate body. Brouwer (1927) asserted that there was a corticifugal connection not only with the superior colliculus but also with the lateral geniculate body.

Biemond destroyed the area striata in seven apes and two rabbits. He found that twelve to eighteen days after the production of a unilateral lesion of the area striata there was secondary degeneration not only in the homolateral striata sagittalia and superior colliculus, but also in the homolateral lateral geniculate body. This is a confirmation of Probst's work on cats and dogs, and of Berl and Bouman's work on rabbits. The discovery of such a widespread Marchi degeneration twelve to eighteen days after operation shows definitely the existence of a corticifugal optic connection of the area striata with the lateral geniculate body. Minkowski believed that fibers from the cortex to the superior colliculus are corticifugal and not corticopetal.

Is there a definite localization of the degenerated fibers in the lateral geniculate body after a localized destruction of the area striata? Corticifugal degeneration in all cases of lesions of the area striata in apes, according to the researches of Biemond, are most marked in the central part of the lateral geniculate body, or to state it more accurately, in that portion wherein Brouwer and Zerman localized the macular field in their studies on the retinal projection onto the lateral geniculate body. Biemond was unable to demonstrate secondary degeneration in the lateral geniculate body after injury of large sections of cortex exclusive of the area striata.

Is it possible that in the corticifugal fiber system that connects the area striata with the geniculate body there is localization analogous to that which exists in the corticopetal system of fibers? Biemond states that not only every quadrant of the retina has its specific projection on the cortex, but that every part of the geniculate body corresponding to a specific retinal projection area can be influenced by its own cortical projection area in a corticifugal direction. The same holds true for the macula. His observations agree with those of Bouman in rabbits, except that Biemond found degeneration of the stratum medullare superficiale in the superior colliculi. He could not substantiate the observations of Probst in cats and dogs, viz., a degeneration of the medial and lateral parts of the stratum medullare superficiale in corticifugal degeneration, and a localization in the center as a result of enucleation of the eye. It is of interest that in Biemond's series of apes with lesions of the area striata, the secondary degeneration was localized constantly in the dorsal part of the brachium, in contrast to the ventral localization of the degeneration after destruction of the retinal parts.

ALPERS, Philadelphia.

TUMORS OF THE QUADRIGEMINATE PLATE. J. H. GLOBUS, Arch. Ophth. **5**:418 (March) 1931.

The gross and microscopic anatomy of the quadrigeminate plate and the course of tumors in this location are discussed. The feature of anatomic defects was considered by reason of its contiguity to the roof of the aqueduct of Sylvius and its relationship between the third and fourth ventricles. The physiologic side was then considered, in that, in the anterior quadrigeminate bodies, there are probably nuclei that serve as important centers for the extrinsic and intrinsic ocular mechanisms; and near by is the nuclear material aggregated on the ventral aspect of the aqueduct of Sylvius, including subgroups of the oculomotor nerves and the contiguous trochlear nerves.

In this discussion, the author uses the term neoplasms of the quadrigeminate plate for tumors known in the literature usually as tumors of the pineal gland, or pinealomas. He wishes to use the former term rather than the latter because the term tumor of the quadrigeminate plate not only helps to identify its exact anatomic location, but also excludes the need for accepting the view that these tumors arise from the pineal gland. The term pineal tumor, or the more recently suggested term pinealoma, on the other hand, finds its usefulness in the fact that tumors of the quadrigeminate plate take their origin from pineal rests, no matter where found, and in the course of their development resemble various phases of the developing pineal body, including the advanced histogenetic states of the mature pineal gland.

In this contribution, the author was concerned mainly with the description of illustrative instances of expanding lesions in the region of the quadrigeminate plate. As he stated, "These lesions, as a rule, compress the aqueduct of Sylvius and thus cause the production of internal hydrocephalus, which in turn provokes a series of symptoms which are characteristic of increased intracranial tension and which are more specifically identified as the cardinal signs of tumor of the brain." It has been known for some time that anatomic alterations in the anterior quadrigeminate bodies, or similar lesions, were associated with impairment of upward gaze and with skew deviations. The anatomic reasons for this are discussed as follows: As the lesion expands beyond the limits of the quadrigeminate plate, it makes inroads into the zone of the periaqueductal gray matter, either by pressure or by direct invasion. This results in anatomic distortions of the median and lateral nuclei of the third cranial nerve, leading to functional disturbances in the intrinsic and extrinsic mechanisms of the eye. These disturbances include typical Argyll Robertson pupils, or various modified or irregular forms of the so-called Argyll Robertson pupil, and at times complete internal ophthalmoplegia. In the disruption of the extrinsic mechanism there is also great irregularity in the relative involvement of the two eyes and in the degree of paralysis of the individual muscles with further expansion of the lesion, other structures in the midbrain are encroached on. The pyramidal tracts, the red nuclei, the substantia nigra and the cerebellar peduncles become compressed, dislodged or altered in one way or another, with the result that various forms of paralysis (tremors, muscle rigidity, abnormal gaits) are added to the clinical picture.

The author states that tumors of the brain in the region of the quadrigeminate plate do not present difficult problems in diagnosis. The diagnosis is based on the appearance of signs and symptoms of increased intracranial tension, disturbance of the mechanism of the intrinsic and extrinsic ocular muscles, as partial or complete external and internal ophthalmoplegia, impairment of upward gaze, skew deviations, cerebellar and pyramidal tract manifestations and signs of vegetative dysfunction. All are symptoms of pathologic processes in this region. Ventricular puncture of the posterior horns and ventriculography will assist in establishing a diagnosis of bilateral symmetrical internal hydrocephalus anterior to the aqueduct of Sylvius.

A series of seven cases is presented, with the histories and the results of medical, necropsy and microscopic examinations. All of the cases terminated fatally. The microscopic reports in all showed more or less similarity, some being much alike, others less so. In general, these tumors presented histologic features that

placed them definitely among the neoplasms commonly called pinealomas. Foreign body cells were found in some tumors and streams of small, deeply stained cells. Transitional forms of these round cells were found, and in one, microscopic examination of the tissue showed much of the structure of the pineal gland itself.

In the general comment that closes the article, the more prominent clinical features are again outlined. These are commented on in greater detail, and are as follows: (1) manifestations of increased intracranial tension: headache, vomiting and papilledema; (2) ocular disturbances: ophthalmoplegias of various types and degrees of intensity, diplopia, paralysis of upward gaze, skew deviation and other forms of dissociation of ocular movements; (3) signs of involvement of the midbrain: tremors, rigidity and retropulsion; (4) cerebellar signs: posture of the head, unsteady gait and station, intention tremors and awkward execution of skilled movements, and (5) signs of involvement of the pyramidal tract: loss of power in the extremities, exaggeration of the deep reflexes and the presence of pathologic reflexes, Babinski's sign, etc.

Among the less constant and indirect signs and symptoms are: (1) mental disturbances, dulling or depreciation of the intellect, and (2) vegetative dysfunctions, somnolence, polydipsia, polyuria, changes in the skeletal growth and disturbances in the development of secondary sexual characters.

SPAETH, Philadelphia.

CHRONIC CHOREA AND ITS RELATION TO THE STRIATUM. L. TOKAY, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **32**:209 (Oct.) 1930.

This paper is based on a review of the literature on chronic chorea and a clinico-anatomic study of two personal cases observed by the author.

Case 1 was that of a woman, aged 71, in whom chronic progressive generalized chorea developed at the age of 56. The chorea was associated with a progressive mental weakness, which, though definite, was not severe. In conformity with the reports in the literature, in this case the changes in the cells were also marked; they were not senile changes, but were definitely degenerative. The degeneration had progressed to destruction, which was most marked in the third layer of the cortex, although occasional areas of destruction were also observed in the fourth layer of the parietal lobe as well as in the deeper layers. The degeneration and destruction affected predominatingly the small ganglion cells. The caudate nucleus was considerably atrophied and flattened out, but the large as well as the small cells in it were fairly well preserved. In contrast to this, the putamen was very poor in cells; the small cells had practically disappeared and the large cells were markedly degenerated. The entire brain was relatively free from cellular lipodystrophy. The cells in the pallidum and thalamus were also affected, but not nearly as severely as those in the striatum. The degenerative process in the cerebellum was very severe; here, whole rows of Purkinje cells had disappeared and those remaining showed swollen dendrites. Extensive cellular lesions were also observed in the granular layer, but the dentate nucleus seemed to have been affected most severely. The glial reaction was strikingly within normal limits; only here and there was there evidence of pathologic glial formation. In spite of the patient's age, the arteriosclerotic changes in the vessels, in general, were not unusually severe; they consisted of a thickening of the middle coat and occasional homogenization and dilatation of the adventitia. Only in a few vessels in the putamen were calcifications observed in the middle coat with corresponding areas of disintegration of tissue; these were most advanced in the most ventral portion of the putamen. Finally, some of the walls of the vessels had abnormal ganglion cell-like formations either within them or attached to them. The ependyma was very thin, and there was considerable hydrocephalus. There were no evidences of inflammation anywhere.

Case 2 was that of a woman, aged 76, in whom chorea had developed two years before admission to the hospital and had lasted for twelve years. The choreiform movements involved chiefly the head and both upper extremities, the left more than the right. As this patient presented psychic disturbances during the later years of the illness, most authors would probably include this case in the

group of Huntington's chorea. The psychic disturbances, however, were not progressive, and resembled those of presbyophrenia; she had good days and bad days, and the nature of the mental symptoms could well be accounted for by senility. The brain did not show a striking substratum for such mental disturbances. The condition of the cells was that usually observed in senile brains; no senile plaques were found. There was evidence of a more or less chronic edema of the cortex, which may perhaps account for the peculiar mental picture. Tokay is therefore inclined to consider the case as one midway between a focal and a degenerative chorea. In this case, however, the significant histopathologic change was an involvement of both striata, which was more marked on the right side. Whereas the posterior portion of the caudate nucleus appeared relatively normal, its head and ventral portion were severely affected. The changes in the latter consisted: (1) of a more chronic destruction of the cells, especially the small cells, and (2) of a severe degeneration of the large cells and glial proliferation. In addition, on the right side, there was a severe, though less chronic, softening of almost the entire head of the caudate nucleus and adjacent portions of the putamen, and another focus of softening in the internal capsule that involved almost one fourth of the frontothalamic system. Since the choreiform movements were definitely more severe on the left, and the focal lesion was more marked on the right, the correlation between the two is obvious. The author, however, does not know what rôle the frontothalamic system played in the symptomatology of the chorea, although the fact that capsular lesions in this region do not produce involuntary movements would seem to speak against the theory that the frontothalamic system has anything to do with the production of involuntary movements. In the absence of lesions in other parts of the brain, then, the lesions in the caudate nucleus must be held responsible for the chorea. According to most authors (Vogt, Mingazzini and others), movements of the head are represented in the most oral portion of this nucleus, those of the upper extremities in the mesial portion and those of the lower extremities in the caudal portion. In the case cited, the distribution of the choreic movements can be readily correlated with that of the predominating lesion in the most oral portion of the striatum.

KESCHNER, New York.

FORCED GRASPING AND THE FRONTAL LOBE. PAUL SCHUSTER and JULIAN CASPER, Ztschr. f. d. ges. Neurol. u. Psychiat. **129**:739, 1930.

Schuster was at first inclined to think that forced grasping might be due to lesions both in the frontal lobe and in the basal ganglia. In his later work, comprising eighteen necropsy studies, he ascribes to the frontal lobe the more important rôle in the production of the symptom. Still further observations have led him to believe that the lesions in the basal ganglia are of no significance in the production of forced grasping. Schuster and Casper report three cases studied by serial section and several others studied in routine fashion.

Case 1 was that of a man, aged 72, with a light paresis of the right arm and forced grasping in this member. Necropsy revealed softening in the gyrus fornicatus, marked atrophy of the corpus callosum, softening in the medial portion of the first frontal lobe and a small area of softening between the first and second temporal lobes. Case 2 was that of a woman, aged 74, with a left hemiplegia and marked forced grasping of the left hand. Necropsy revealed atrophy of the left frontal gyri, softening of the posterior half of the first frontal lobe and the right callosal connections, a small softening in the knee of the left internal capsule and some injury of the substantia subependymalis and the occipitofrontal bundle. Case 3 was that of a man, aged 65, with paralysis of the right side and forced grasping of the right hand. Necropsy revealed a softening in the first frontal lobe on the left side, softening of the gyrus fornicatus and the left callosal connections, softening in the superior parietal gyrus directly connected with that in the first frontal lobe and an area of softening in the gyrus supramarginalis of the left side. Case 4 was that of a woman, aged 75, with paralysis of the right arm

and leg and a definite grasping tendency in the left hand. Necropsy revealed softening of the first frontal lobe and the gyrus cinguli. Case 5 was that of a man, aged 59, with a forced grasping of the right hand. Necropsy revealed an area of softening deep in the white matter of the first and second frontal lobes; other small and older foci were present in the basal ganglia between the caudate and putamen. Case 6 was that of a woman, aged 73, with a paralysis first of one side and then of the other, and with evidence of forced grasping in the left hand. Necropsy revealed an area of softening in the gyrus fornicatus and the left half of the callosum.

The three cases studied in serial section all showed, grossly, areas of softening in the white matter of the first frontal lobe and the adjacent parts of the gyrus fornicatus, as well as in the corresponding homolateral half of the anterior part of the corpus callosum. The changes in the basal ganglia were insignificant in comparison with those in the cerebrum. The basal ganglion lesions, moreover, were fresh as compared with the older areas detailed. The striatum and thalamus were practically intact. The rest of the cerebrum was practically untouched. There were no lesions in the internal capsule or pes pedunculi. Two large fiber systems in the neighborhood of the softened areas were destroyed: the cingulum and the occipitofrontal bundle. Microscopically, the gross observations were entirely corroborated. The basal ganglia were entirely intact. The degenerated areas were the first frontal lobe, the gyrus fornicatus and the anterior homolateral half of the callosum.

Schuster and Casper emphasize, therefore, the degenerations in the aforementioned areas in the production of the forced grasping reflex. They look on forced grasping as a release symptom, and emphasize the fact that injury to the central pyramidal tract prevents the occurrence of forced grasping. In other words, forced grasping can take place only in the presence of an intact pyramidal tract, very much like the state of affairs in chorea and athetosis. Schuster and Casper believe that the frontal lobe normally exerts an inhibitory effect on the action of the pyramidal tract, and that with disease of the frontal area the pyramidal tract acts unopposed in the production of forced grasping. This symptom may appear in disease of both lobes. One case is reported of bilateral forced grasping in the presence of bilateral frontal lobe disease. The phenomenon may appear in cases of frontal lobe atrophy as well as in frankly destructive lesions, and three such cases are reported.

The inhibitory tract, which prevents the occurrence of forced grasping under normal conditions, has its origin in the first frontal convolution and probably also in the gyrus fornicatus. Schuster and Casper believe that in order to produce forced grasping it is necessary to block the impulses from both frontal lobes, and this is done effectively by a lesion in the anterior part of the corpus callosum, which seems to be uniformly involved in all the cases.

ALPERS, Philadelphia.

ANASTOMOSES OF THE CEREBRAL BLOOD VESSELS. R. A. PFEIFER, J. f. Psychol. u. Neurol. **42**:1, 1931.

Pfeifer's anatomic investigations of the cerebral circulation, carried out on the brains of infants in which the vessels were filled with the patient's own blood (asphyctic-hyperemic brains), show that Cohnheim's views as to the existence of end-arteries in the brain are incorrect.

According to Pfeifer, the circulation of the brain consists of three mechanisms:

1. The derivative mechanism. This supplies the brain with blood and conveys it to its proper destination. The pia mater may be said to be the best example of this so-called derivative circulation. It is made up of arteries, arterial stems and branches, arterioli, precapillaries and a venous system. The arteries convey the blood to the brain through the most direct, and therefore shortest, channels. The carrying away of the blood from the brain is much more complicated and demands a greater number of veins than arteries, with a comparatively complicated but purposeful vascular architecture.

2. The nutritive mechanism. This mechanism accomplishes its purposes by means of special peculiarities within the vascular walls, through which there occur the interchange of gases, transudation and exudation, as well as resorption. It consists of the entire capillary network, which supplies the parenchyma of the brain with blood through the enormously increased surface of the vascular system acting as one "continuous vascular apparatus." This nutritive type of circulation also includes the capillary arteries and veins as described by Spalteholz.

3. The regulating mechanism. This mechanism equalizes the variations in pressure and controls the speed of the circulation. It consists of special devices which seem best to serve these purposes. Thus for the lowering of pressure there are frequently interposed "throttles" between the derivative and the nutritive circulatory mechanisms; for speeding up the circulation in the veins there exist "injector vessels," and for equalizing pressure between two or several remotely situated capillary areas there are vessels of greater caliber than the capillaries themselves which also possess the property to reverse the direction of the current.

The term "anastomosis" is applied by Pfeifer to an extracapillary vascular connection between two blood vessels, i. e., shorter connections between two arteries, or between two veins, or between an artery and a vein in the surrounding nutritive circulatory mechanism. Accordingly there exist arterial, venous and arteriovenous anastomoses. Owing to the great significance of the arterial and venous anastomoses as compensatory mechanisms in disturbances of the circulation, they are also designated as "collaterals." They belong exclusively to the derivative circulatory mechanism and are not infrequently vessels in which the blood circulates in both directions ("reversible currents"). This phenomenon never occurs in arteriovenous anastomoses; in these the blood current is regularly in one direction only, i. e., from artery to vein. Arteriovenous anastomoses may be regarded as "vents" for overfilled arteries and occasionally as injector vessels for veins. They belong, therefore, to the regulating circulatory mechanism. Whether or not the arteriovenous anastomoses are mostly closed, i. e., whether they exist as a sort of vasa serosa which open up only under unusual circumstances, has not as yet been definitely ascertained.

Anastomoses are found in every part of the brain, though they are perhaps most common in the frontal lobes and most numerous in the region of the arterioles and venules. Frequently they are embedded directly in the capillary network. They always serve to distribute the blood and to regulate its current; they never serve for nutritive purposes in the strict meaning of that term. Their functional significance, however, cannot be underestimated, because under the influence of new circulatory conditions their lumina regularly become wider and their walls thicker.

In arterial anastomoses there are rarely found short connections between the large trunks of the cerebral arteries in the cortex. Anastomoses are much more frequent between branches of the same vessel, as well as between a trunk and branches. From a cytoarchitectonic and angiotectonic point of view it is noteworthy that not every nerve cell has its own capillary loop, but, on the contrary, every vascular loop contains within it a collection of several nerve cells. The author's preparations also yielded undoubted evidence that numerous arterial anastomoses exist between the vessels of the cortex and those of the white matter. Thus far the tendency for veins to form plexuses has not been observed. The author, however, has no doubt of the existence of such venous plexus formations, for otherwise there could exist no collateral circulation in the brain, and the latter would suffer from the lack of a more or less constant blood supply.

KESCHNER, New York.

THE MECHANISM OF EPILEPTIC SEIZURES; SOME DATA FAVORING THE HYPOTHESIS OF A VEGETATIVE EPILEPTOGENOUS CENTER IN THE DIENCEPHALIC REGION. ALBERTO SALMON, Studium **20**:9, 1930.

Emphasizing the essentially neurovegetative nature of the introductory phenomena of the epileptic seizure (vasoconstriction, tachycardia, mydriasis, exophthalmos, goose-skin, initial leukopenia, glycosuria, etc.), the author reviews

the clinical, pathologic, pharmacologic and experimental data tending to support the hypothesis that the diencephalic (infundibular) neurovegetative apparatus plays a fundamental rôle in the predisposition to, and initiation of, the epileptic discharge. The author's main argunfents are: Demole's experiments with the injection of calcium and potassium salts into the region of the tuber cinereum have shown that the former causes muscular relaxation and sleep, while the latter causes motor agitation and epileptiform convulsions; Cyon Horsley showed that the slightest electric stimulation of the hypophysis induces convulsions; observations of Müller and Högner showed that generalized tonic convulsions may result from sudden hypertension in the third ventricle; an epileptic seizure is usually followed by deep sleep, indicative of the functional depression of the infundibulum; epileptic seizures subside under the influence of phenobarbital, somnifen, chloral, etc., drugs possessing elective pharmacodynamic action on the diencephalic sleep-regulating apparatus; epileptic attacks are a frequent symptom of tumors of the hypophyseal region; the syndromes of acromegaly, hypophyseal cachexia of Simmonds, adiposogenital dystrophy and diabetes insipidus are frequently associated with epilepsy; epilepsy is often relieved by pituitary treatment; deficiency of solution of pituitary in the cerebrospinal fluid of epileptic persons has been demonstrated by Altenburger and Stern; removal of the hypophysis is often followed by epilepsy; a lesion of the hypophysis is frequently found at autopsies of epileptic persons; paroxysmal and postparoxysmal hyperthermia in epileptic persons may be explained as the result of an irritation of the temperature-regulating center in the interbrain.

The diencephalic seat of the presumed epileptogenous center explains its sensibility to quantitative and qualitative changes in the cerebrospinal fluid. Cortical and striothalamic lesions, by reflex action, may cause overstimulation of the hypothalamic neurovegetative centers, with resulting generalized convulsions. [There is much in favor of the author's hypothesis. The observation of Penfield and the experimental and pathologic work of L. O. Morgan on the nuclei of the tuber cinereum in epilepsy (ARCH. NEUROL. & PSYCHIAT. **24**:267 [Aug.] 1930) add interesting data in support of the author's thesis. Recent studies of the acid-base equilibrium, water metabolism and blood volume in epilepsy do not contradict this concept, but rather receive a hint for their own explanation as changes subordinated to the same neural mechanism. Nevertheless, the evidence so far available in this matter does not allow more than a plausible general concept which needs, and is worthy of, much further study.]

YAKOVLEV, Palmer, Mass.

THE BROWN-SÉQUARD SYNDROME OF TRAUMATIC ORIGIN. G. GUILLAIN and R. GARCIN, Ann. de méd. **29**:361 (April) 1931.

The transmission of all the different kinds of sensation in man is not yet completely understood, and every case presenting a Brown-Séquard syndrome should be welcomed as an opportunity to correct, if necessary, the classic scheme.

Three cases are reported. In two of them a knife had penetrated the spinal canal between the sixth and seventh dorsal vertebrae, producing a hemisection of the spinal cord, and the broken blades had remained there unrecognized for periods of one and a half and seven years, respectively, without producing any spontaneous pain or any signs pointing to the presence of a foreign body. In the third case, a revolver bullet had penetrated the thoracic cavity at the right fifth intercostal space, producing a hemisection of the spinal cord at the level of the lower dorsal segments, and finally was caught in the first sacral vertebra. Common to these three cases was a short period of spinal shock with paraplegia and retention of urine, which soon subsided, to be replaced by a mild monoplegia. In the first case, ten months after the injury there were complaints of formication and sudden contractions of the muscles of the paralyzed limb, which, however, disappeared soon only to return seven months later. In the second case, an infection around the retained blade produced a sudden paraplegia after seven years. The surgical

removal of the blades in both cases was uneventful, and the meningeal scar that had formed prevented the flowing out of spinal fluid.

From a clinical and physiopathologic point of view the following facts should be recorded: In all three cases, an early sexual impotence developed and became more and more aggravated. There was a bilateral Babinski sign which only on the side of the lesion was combined with increased tendon reflexes, clonus and hypertonicity. Defense reflexes could be elicited only on the side of the lesion, while other observers, as Babinski, Jarkovski and Jumentié, reported that they could be elicited more easily in the anesthetic limb, i. e., on the side opposite to the lesion. The sensory changes did not all conform to the classic scheme presented by Dejerine. The authors found that, in contradiction to this scheme, deep sensibility in two cases, as well as the sense of position in one case, was preserved on the side of the lesion and disturbed on the opposite side. Observations extended over long periods demonstrated that the disturbances of the different sensations were diminished or had even disappeared at a time when the pyramidal tract signs were still pronounced. According to Brown-Séquard, Thomas and others, vasomotor disturbances are responsible for a rise in temperature in the paralyzed leg, which after some time is diminished, with the beginning of cyanosis of the skin. Again, in two of the cases, the rise in temperature with excessive perspiration was observed in the leg opposite to the lesion. It was interesting to note that the temperature at the surface was higher than the temperature of the deeper muscles as measured with a thermo-electric needle. In two of the three cases, sudden, not painful contractions of the paralyzed muscles were frequently observed; in violence and intensity they resembled muscular contractions following very strong electrical stimulation. Sometimes these spontaneous contractions appeared also on the nonparalyzed side.

WEIL, Chicago.

UNILATERAL PARALYTIC SYNDROME OF THE LAST SEVEN CRANIAL NERVES AND THE CERVICAL SYMPATHETIC FROM A TUMOR DESTROYING THE CRANIAL BASE. E. KREBS, P. WINTER and R. WORMS, Rev. d'oto-neuro-opht. **9**:178 (March) 1931.

The following case history concerns a patient who was the subject of a report by André-Thomas and Kudelski to the Neurological Society on March 7, 1929. At that time the paralysis was limited to the last four cranial nerves and the cervical sympathetic on the left side, and was accompanied by a tumor behind the ascending ramus of the lower jaw. In 1922, the patient, aged 32, noticed a swelling behind the ramus of the left lower maxilla. In July, 1925, paralysis of the left recurrent nerve was discovered; this was followed a short time afterward by paralysis of the left side of the tongue and palate and, a few weeks later, by difficulty in the movements of the left shoulder. Examination revealed paralysis of the left ninth, tenth, eleventh and twelfth cranial nerves and partial paralysis of the oculopupillary fibers of the left cervical sympathetic: the left palpebral slit was narrow and the pupil was dilated less than the right in obscurity, but there was no change in the complexion, no sweating and no change in the pilomotor reflex. The oculocardiac reflex was positive and equal on the two sides. The tumor extended from the angle of the jaw to the external auditory meatus and produced a swelling in the left wall of the pharynx, extending from the mouth of the tube to the level of the arytenoid. It was soft, painless and pulsating. Roentgenograms of the cranial base did not show a lesion of the bones. An exploratory operation in the neck revealed only an abnormal venous network at the bifurcation of the carotid, which was higher than normal.

Eighteen months later, an examination revealed: paralysis of the left sixth, seventh and eighth nerves in addition to the previous observations. There was no papillary edema or other sign of intracranial hypertension. A lumbar puncture was not made. Pyramidal and cerebellar symptoms and Babinski's sign were absent, the tendon reflexes were lively and equal and muscular force was normal. The tumor had increased in size, and the skin over it was not adherent. A roentgenogram revealed a perforation in the left middle cerebral fossa, extending from

about the midline outward to the outer third of the petrous bone and erosion of the floor of the sella turcica, the clinoid process and the basilar apophysis.

The origin and nature of the tumor remain to be determined. The appearance of the growth before any sign of nerve involvement suggested a point of attack low in the pharynx; considering the roentgenographic observations and the fact that the sixth, seventh and eighth nerves were involved after the last cranial nerves, it is probable that the origin was in the region of the posterior lacerated foramen. The progressive extension to the different nerves and the strict unilaterality suggest a fibrosarcoma, but the slow growth and the good general condition of the patient cast some doubt on this assumption.

DENNIS, Colorado Springs, Colo.

CHRONIC CISTERNAL ARACHNOIDITIS PRODUCING SYMPTOMS OF INVOLVEMENT OF THE OPTIC NERVES AND CHIASM. G. J. HEUER and D. T. VAIL, JR., Arch. Ophth. **5**:334 (March) 1931.

Recently, considerable writing has appeared relative to chiasmal pathology and to the various symptoms that appear, and that can be presented as a "chiasmal syndrome." As the authors state, it is found that an increasing number of pathologic conditions may involve the optic nerves and chiasm and give rise to the clinical manifestations of optic atrophy, visual disturbances and defects of the perimetric field which constitute this syndrome. The authors consider primary atrophy of the optic nerve and discuss the various etiologic factors that cause it.

In a study of forty-cases of primary atrophy of the optic nerve, 49 per cent were due to dementia paralytica, 23 per cent to pituitary or suprasellar tumor, 7 per cent to basilar fractures, 5 per cent to chronic cisternal arachnoiditis and glioma of the chiasm and 3 per cent to multiple sclerosis and methyl alcohol poisoning. In three cases, the etiologic factor was not determined. One can thus see that of this series, 40 per cent were due to mechanical causes. It seems that every large group of cases of primary atrophy of the optic nerve fall into two general classes, those caused by syphilis and a smaller division in which the cause is unknown. It is possible that among these two groups there may be a considerable number of cases of chronic cisternal arachnoiditis.

Four cases of chronic cisternal arachnoiditis are presented, each with a history and the results of clinical and ophthalmologic examinations and with studies of the visual fields, as well as the operative procedures and postoperative results. In general, frontotemporoparietal bone flaps were formed. The chiasmatic cistern was uncovered, adhesions around the optic nerve were separated as much as possible, and the walls of the cistern were resected. The dura and bone flap were replaced and sutured. During the operation, large amounts of cerebrospinal fluid were evacuated, but in no instance was a tumor found. The results of the operative treatment in these four cases were satisfactory. No postoperative complications developed, nor was there any immediate mortality. Vision improved before the patients left the hospital and continued to improve, so that at periods of three years, one year, eleven months and one and one-half months after operation, all four patients were able to read ordinary print and to resume their usual occupations. In one instance, in case 4, the satisfactory postoperative condition was most marked as compared to the pathologic preoperative state. This postoperative state was present, although perhaps less so, in the other cases. In case 3, the vision improved from total blindness before the operation to 20/20 vision in each eye after the operation. This patient, however, retained minute, central red and green scotomas. In all instances, the studies of the fields were interesting.

SPAETH, Philadelphia.

LINGUAL HEMIATROPHY OF TABETIC ORIGIN. HENRI ROGER, Rev. d'oto-neuro-opht. **9**:165 (March) 1931.

Lingual hemiatrophy from a central or peripheral lesion of the hypoglossal nerve is rare. The clinical picture is often represented only by objective signs.

and adjacent cranial nerves are usually involved also. Isolated paralysis of the hypoglossal, due to a peripheral lesion, has been reported. Lingual hemiatrophy has been observed in Pott's disease, tumor of the basilar groove and softening in the bulb, but the three most common causes of a central origin are epidemic neuraxitis, tabes and syringomyelia. Cases of neuraxitic origin are frequent. Besides the cases of pure hemiatrophy, there are cases in which the atrophy is associated with nonrhythmic movements of the tongue, which is incessantly protruded. Other cases are bilateral but with one side more atrophied than the other.

In cases associated with tabes, most authors locate the lesion at the level of the bulbar nucleus of the hypoglossal nerve. The paralysis may be combined with paralysis of other nerves or it may be isolated. Two cases are reported.

Case 1 was that of a man, aged 75, who had contracted syphilis twelve years previously. Disturbed gait and pain in the legs were first noted and for the preceding four months he had been bedridden. Two weeks before death, a state of mental confusion existed. The clinical observations were: abolition of the patellar and achilles reflexes, hypotonia of the legs, diminution of deep sensibility, myosis and preservation of the reflex to light. The tongue was markedly atrophied and curved to the left. The pharynx and palate were not paralyzed. There was generalized muscular atrophy, predominating in the lower limbs. Senile tabes is relatively frequent, although syphilis may cause lingual hemiatrophy in dementia paralytica or with a bulbopontile lesion.

Case 2 was that of a woman, aged 54, who, for ten years had had feebleness of the lower limbs, predominating on the right side, accompanied by generalized pains; recently, feebleness of the arms had appeared, followed by diplopia and incontinence of urine. On examination a complex syndrome was discovered: abolition of the tendon reflexes in the limbs, bilateral Babinski sign, quadriparesis, more marked on the right side, slight ataxia, hypotonia of the right leg, which was flexed and in contracture, diminution of deep and superficial sensibility and atrophy of the thenar eminences; bilateral paralysis of the sixth nerves, internal strabismus of the left eye, Argyll Robertson pupils and normal vision. In this case the tabes was not pure but was combined with a pyramidal syndrome on the right side and a syndrome of the posterior columns of the cord. Bertein reported a case of syphilitic lingual hemiatrophy accompanied by perichondritis of the larynx, in which the lesions were peripheral. In some cases, for a long time the lingual hemiatrophy is the only sign present and its origin remains obscure.

DENNIS, Colorado Springs, Colo.

LESIONS OF THE BRAIN IN ELECTRIC SHOCK: HISTOPATHOLOGY OF DIFFERENT TYPES OF ELECTRIC SHOCK ON MAMMALIAN BRAINS. R. MORRISON, A. WEEKS and S. COBB, J. Indust. Hyg. **12**:364 (Dec.) 1930.

Sublethal electric shocks were administered to laboratory animals by occiputal and nasal contact, and the brains were subsequently removed and studied histologically with the aim of ascertaining whether electricity produced lesions, and if so the nature of the lesions, in the nervous system. Four types of current were used and were particularly selected because of their wave shapes, so that the factors of direction of flow, polarity, impact, heat value and frequency could be considered. It was found that lesions were produced in the brain, sometimes even after a single shock, and the nature of the lesions depended, at least to some extent, on the nature of the current, similar wave forms producing more or less similar lesions.

There were some overlapping types of lesions such as hemorrhage, which could be found in all cases, and shrinkage of ganglion cells, which could be found in three classes of cases, but in general the various combinations of lesions were characteristic of the effects of different types of current.

Nearly all of the structures in the brain were involved in these pathologic processes. The ganglion cells were swollen under some circumstances and shrunken

under others. The myelin was affected chiefly in cases in which the glia proliferated and the nerve cells were swollen. In practically all cases there were congestion and hemorrhage. Edema of the brain was a common observation and, in conjunction with the swelling of oligodendroglia and the production of mucocytic or galactolipoid degeneration, presented interesting vacuolar lesions. In an attempt to explain the mechanism of the production of these lesions, the heat generated in the brain under most vigorous electric strain was measured, and it was found to be relatively insignificant as long as the blood circulation was maintained, but it increased rapidly when the circulation was stopped.

Furthermore, by means of the special technic devised by Forbes, the vessels on the surface of the brain were observed during electric shock and it was found that the vessels constricted or dilated during the passage of the current, depending on the kind of current used. The condenser discharge and induction coil currents caused the vessels to dilate and the intracranial pressure to rise; histologically, one of the most characteristic lesions from this type of current was swelling, liquefaction and vacuolization of the ganglion cells. The alternating current, on the other hand, brought about a constriction of the pial vessels, a slowing of the blood flow, and histologically a pronounced shrinkage of the ganglion cells. It may be, of course, that these lesions were caused by the direct action of electricity on the nerve cells and glia, but in view of the fact that at least some of them could have been caused by these forms of vascular response, attention is directed to the coincidence of vascular response with type of tissue change.

COBB, Boston.

FACIAL CAUSALGIA. E. HALPHEN, Rev. d'oto-neuro-opht. **9**:171 (March) 1931.

The author discusses a case of causalgia "of indeterminate etiology and disappointing therapy, but with characteristic symptomatology." A woman, aged 35, had suffered with facial algias for twelve years which no form of therapy had succeeded in relieving. The pains began following an attack of grip, which kept her in bed for six months, was accompanied by alopecia and was followed by a long convalescence. On account of intestinal symptoms the appendix had been removed. This event was followed by an obstinate cough and purulent expectoration. Operations on the maxillary antrum, the ethmoids and the sphenoidal sinus relieved these symptoms, but severe and constant headaches then supervened. Acute exacerbations occurred whenever the patient was in a close place; heat especially induced them. The attacks were accompanied by an anxious, pseudo-anginal state, and relief was usually obtained by plunging the face and head in cold water, though on two occasions, morphine was required to bring relief. The location of the pains was periorbital, facial, occipital and nuchocervical, and they were described as pounding or hammering or like a red-hot iron; in the intervals, there was the sensation of a foreign body, spider web or hair under the skin of the cheek. The crises were followed by malaise, nausea, lassitude and insomnia. The psychic side of the picture was characteristic: the patient was restless, and feared crowds, confined places and heat. After each paroxysm she was in despair, had suicidal thoughts, lost memory and was embittered and unkind to her aged mother.

A general medical and neurologic examination revealed no blemish, no loss of weight, and no impaired vision, errors of refraction or changes in the eyegrounds. Suspecting the presence of a posterior sinusitis, the middle turbinate was removed, the ethmoids were curetted and the sphenoidal opening was enlarged. After each operation improvement was noted. Applications of cocaine to the region of the sphenopalatine ganglion relieved the pain for a period of four or five days at first, but latterly for only forty-eight hours. It was necessary to use force in the applications to attain relief and each séance was followed by great malaise and a state of syncope. The gamut of therapeutic measures, injection of alcohol, infra-red rays, roentgen rays, diathermy and anodynes, including opiates, has been run, without permanent benefit. One therapeutic procedure, pericarotid sympathectomy, remains to be tried.

The pains, modified by the surrounding temperature, the relief by cold applications, the painful radiations without relation to the nerve distribution, the change in character and the psychic state of the patient point indubitably to causalgia. The author asks: Can the cause be the attack of grip or the repeated operations on the sinuses? Sympathectomy should be as helpful as it has been in cases of causalgia of the median or sciatic nerves.

DENNIS, Colorado Springs, Colo.

MINERS' NYSTAGMUS. W. E. COOKE, Brit. M. J. **1**:615 (April 11) 1931.

The author defines miner's nystagmus as an occupational disease peculiar to workers in coal mines in which the illumination is deficient. The nystagmus is fine and rapid, rotary, pendular and vertical. The condition may be present even when the eyes are at rest, or in some cases it may be difficult to elicit and transitory. The generally accepted theory of its causation has been that it is dependent on the effect of dim light on the eye. In a dim light, the retina functions by means of the rods and not the cones. Since there are no rods at the fovea centralis, the eye must move 15 degrees or more from its midpoint to permit vision in a poor light.

Additional significant characteristics are that it affects the expert and not the novice. There is loss of volitional control of some of the extrinsic eye muscles. There is often spasm of the levator palpebrae muscle. It has some points of similarity to tetany.

In considering the pathogenesis of this condition, three further points are mentioned. First, a latent nystagmus may become evident only during anesthesia or acute alcoholism. Second, a latent nystagmus may become active in the course of acute infections and septic wounds. Finally, it may become evident and persist as a result of such a simple accident as a bruise or the more severe trauma of a fractured femur. The explanation in these latter cases is probably the absorption of toxic protein fractions which, in addition to a general effect, react on the already impaired myoneural function of the eye muscles.

The author does not dispute that defective illumination at the mine face is the primary cause of miner's nystagmus, yet he argues that if this were the sole precipitating cause there should then be many more cases of this disorder. The incidence of estimated sufferers ranges from 5 to 35 per cent, while that of those ceasing work and certified as suffering from nystagmus is from 0.05 to 0.5 per cent.

The author's study was based on the examination of fifty-seven miners who had been certified to have the disease and who had therefore ceased work. Of these, sixteen were found to have high blood pressure with renal damage. Three suffered from toxic thyroiditis, one from lead poisoning, one from diabetes mellitus, one from postencephalitic parkinsonism, four from pyuria and five from chronic purulent bronchitis. Thirty-four suffered from pyorrhea alveolaris in a gross degree, and twelve had enlarged and septic tonsils. The blood in these showed a definite increase in the percentage of monocytes, an almost constant presence of basophils and a frequent appearance of plasma cells. Not one case had a normal Arneth count. The author states that in every case there was ample evidence of toxemia to account for the abnormal polymorphonuclear picture. Thus, on the basis of this study, toxic and infectious conditions are important, both from an etiologic and from a therapeutic standpoint.

FERGUSON, Niagara Falls, N. Y.

STUDIES ON THE INTRA-OCULAR PRESSURE: PART II. THE PHYSICO-CHEMICAL FACTORS CONTROLLING THE INTRA-OCULAR PRESSURE. P. M. DUKE-ELDER and W. S. DUKE-ELDER, J. Physiol. **71**:268 (March) 1931.

This paper presents the results of a study of a second group of factors that have an influence on the pressure of the eye—changes of a physicochemical nature occurring in the blood. As in the previous study of the vascular and muscular factors controlling intra-ocular pressure, the animals employed were dogs anes-

thetized with ether and chloralose. The same perfusion apparatus was used and records were taken by the compensatory mercury manometer.

One of the factors maintaining the intra-ocular pressure at its normal equilibrium is the difference between the osmotic pressure of the plasma and that of the aqueous humor (since the capillary walls are freely permeable to crystalloids, any permanent difference between the osmotic pressure of the aqueous and the blood depends on the relative colloid content of the two fluids). Normally, the blood contains a high percentage of colloids and the aqueous humor a trace. If the concentration of colloids in the blood is increased, this relative difference is augmented, and the intra-ocular pressure, the level of which is determined by the capillary pressure less this difference, therefore falls. Conversely, if the concentration of colloids in the plasma is decreased, the intra-ocular pressure rises to approach more nearly the hydrostatic level in the capillaries.

By a second group of experiments it was shown that the intra-ocular pressure falls with an increase in the osmotic concentration of the crystalloids in the blood, and rises with a decrease in their concentration.

To measure the changes in the intra-ocular pressure with changes in the reaction of the perfusing blood, a small quantity of lactic acid was added to the blood in one of the reservoirs slowly, drop by drop; in this way the change of reaction was brought about without any significant osmotic change, and the experimental record showed a distinct drop in intra-ocular pressure (the p_H having been 6). In the same way, an alkalosis of the perfusing blood was induced by the addition of sodium hydroxide (to p_H 8) resulting in a slight rise in the intra-ocular pressure. The interest of these last observations lies in the demonstration they provide that a swelling or shrinkage of the vitreous body can bring about definite alterations in the pressure of the eye.

The mechanism of these changes is discussed; they are all compatible with the theory that the aqueous humor is a dialysate of the capillary blood, and that the vitreous body is a hydrophilic gel.

ALPERS, Philadelphia.

CEREBRAL HEMORRHAGE DUE TO TRAUMA. G. KOBAYASHI, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **32**:283 (Oct.) 1930.

A man, whose age and previous history could not be determined because he was unconscious on admission to the hospital, was thrown off a bicycle by a motor car. Examination on admission a few hours after the accident revealed: total loss of consciousness, stertorous breathing, a pulse rate of 62, multiple erosions on the face, protrusion of the left eyeball, severe conjunctival hematomas and slight bleeding from the nostrils. There were no evidences of fracture of the skull. Spinal puncture revealed pure blood. He died twelve hours after the accident. Before death he had a tonic convulsion of the right upper extremity and paresis of the left lower extremity. The reflexes were not elicitable. Necropsy revealed cerebral edema with extensive hemorrhages in the scalp, in the cranial cavity over the right cerebral hemisphere and in the meninges, as well as compression of both temporal and occipital lobes with innumerable smaller hemorrhagic areas throughout the cerebral cortex.

Histologic examination of the hemorrhagic areas showed that the bleeding was due to rhexis as well as to diapedesis; this was especially noticeable in the meningeal vessels. In view of the short duration of the disease, the degenerative changes observed in the walls of the vessels were unusually striking. The hemorrhages were most extensive in the meninges and less extensive in the gray and white substance of the brain; they were very slight in the brain stem, only a few areas of bleeding being found in the most anterior portion of the striatum. Hemorrhages were also present in the cerebellum as well as in the meninges covering it. The large vessels (basilar and middle cerebral arteries) showed involvement of their walls similar to that of the smaller vessels from which the hemorrhages had occurred. The thickening of the walls of the vessels with areas of homogenization points to the existence of vascular disease that must have preceded the injury. The smaller

vessels showed definite dilatations, which had ruptured; there were direct communications between these vessels and the hemorrhagic areas, although it must be admitted that in numerous places there could be seen perivascular hemorrhages without evidences of laceration of the brain. Occasionally there were also observed hemorrhages within the adventitia of the smaller vessels. All these observations are emphasized because they tend to show that, although trauma may be followed by hemorrhages in the meninges and brain even though the vessels are intact, such hemorrhages are much more extensive and serious in persons who at the time of the trauma are suffering from a preexisting disease of the walls of the vessels.

KESCHNER, New York.

THE MECHANISM OF ACTION OF BLOOD-LETTING ON THE METABOLISM OF WATER AND SALTS. M. S. VOVSY, N. C. BAGON and I. A. ITZICKSON, Medicobiological J. (Russian) **5**:66, 1929.

It is well known that venesection with a loss of blood of from 300 to 500 cc. leads to a lowering of blood pressure, especially the venous pressure, of about 10 per cent. This leads to a release of blood from the arteries, i. e., the capillary system. There result significant changes in the labile system involving the hematolymphatics, various tissues and the excretory organs. The mechanism of the substitution of water, salts, proteins, etc., for blood is little understood. A return of blood pressure to the original level is due not to the mechanical addition of fluids but to the adaptation of the arterial bed to the decreased blood volume. The decrease in the blood volume leads to a narrowing of the intercapillary spaces and a heightening of the tension of the capillary walls.

The subjects of the experiments were patients with hypertension on whom venipunctures were done with removal of from 200 to 400 cc. of blood before breakfast. The blood was examined before the puncture, one-half, one, two and four hours afterward and again on the following morning. Estimations were made of total solids, serum protein, chlorides, hemoglobin, red cells and blood pressure. In the ordinary, uncomplicated cases of hypertension one gets a general picture of dilution of the blood, as evidenced by a decrease of the elements studied and an increase in the chlorides. The increase in chlorides cannot be accounted for by the laws of osmosis. It is probably due to a sudden release of water by the tissues, which also contain large deposits of salts. Other factors are the amounts of diffusible salts in the blood and tissues and the nondiffusible protein ions. The condition of the endothelial walls, which act as a membrane, is also important. In cases of malignant hypertension the changes in the blood are variable; this depends on the condition of the capillary bed, which is pathologically modified.

Injections of distilled water and of hypertonic and hypotonic salt solutions lead to changes in the blood somewhat analogous to those caused by blood-letting, but less constant and less uniform. They cannot be compared with blood-letting.

KASANIN, Boston.

DISSEMINATED SCLEROSIS IN NORTH WALES. R. S. ALLISON, Brain **53**:391 (Jan.) 1931.

Allison, with the help of the Medical Research Council of Great Britain, attempts to prove or disprove certain concepts and conclusions on disseminated sclerosis that have crept into the literature in regard to contributing factors of etiology, namely, location of residence, occupation, etc., and the incidence in proportion to general population. From time to time, papers have been published stating that the disease is more frequent in rural communities, and in particular affects those engaged in the occupations of farming and wood working.

The author chose five counties in the north of Wales as a district embracing a sufficient population (492,000) and enough diversification of terrain and industries to make such a survey comprehensible. On the whole, the results were negative. The only common factor was the discovery that many patients were drinking water

from wells liable to pollution. All the principal occupations were represented among the sixty-five cases found, and in no two cases was there any common factor, such as living in the same house, or small community. Domestics and farmers suffered from the disease in about the same proportion as their incidence in the general population. Naturally, dark-complexioned types predominated, as this is a local feature. Tall and thin persons were more frequently sufferers than short and stout people. The proportion of cases was 1 in 8,600, and they were scattered through the province along the lines of density of population. The sixty-five cases included thirty-nine typical examples, ten early cases, and sixteen patients who had died of the disease. These latter were counted, but naturally they raised the incidence from 1 to 10,000 to the figure previously quoted.

The author himself believes that the cases are too few from which to draw any conclusions, but thinks that his effort may stimulate work along the same lines, which will remove many long cherished, but erroneous, ideas as to contributing etiology of chronic diseases from current medical thought.

ROBINSON, Kansas City.

PHENOMENA OF PROPULSION, RETROPULSION AND LATEROPULSION IN PATIENTS AFFECTED WITH PARKINSON'S DISEASE. NOICA, J. de neurol. et de psychiat. **31**:153 (March) 1931.

In the normal man certain influences act automatically in order to maintain the upright position. The coordination of muscle function necessary for this is most likely mediated through the cerebellum. In parkinsonism, the contractions of muscles excited by reflex pathways are slow in appearing and disappearing. To this slowness is attributed the phenomena of propulsion, retropulsion and lateropulsion. The author presents a case with a typical history of encephalitis followed by the usual parkinsonian signs. In addition, the patient was unable to stand in one position for more than an instant. If he tried to stand longer, he would take two or three short steps backward, and then two or three short steps forward. A normal person placed in the same position showed the ability to remain in it indefinitely, but there was a constant contraction and relaxation of the muscles of the extremities. The parkinsonian patient did not show this alternate contraction and relaxation of the muscles of the extremities. When the well person was asked to stand on tiptoes, he maintained the center of gravity in the proper position by bending the body slightly forward and contracting the abdominal muscles. If the parkinsonian patient attempted to stand on tiptoes, he would take two or three steps in order to prevent himself from falling. The author notes also that if the normal man is struck on the chest, there is a contraction of the leg muscles and of the muscles of the abdominal wall. If the blow is hard enough to overthrow him, these muscles relax very rapidly. In the parkinsonian patient, a light body blow produces no reaction. A heavier blow is followed by a contraction of the foot extensors, which is slowly followed by the contraction of the anterior abdominal muscles. The conclusion, then, is that abnormalities of gait manifested by the parkinsonian patient are the result of slowness in the contraction and relaxation of the musculature, which makes it impossible for the patient to maintain the proper center of gravity.

WAGGONER, Ann Arbor, Mich.

ON THE NATURE OF LITERAL ALEXIA. A CONTRIBUTION TO THE THEORY OF APHASIA. I. WOLPERT, Monatschr. f. Psychiat. u. Neurol. **75**:207 (April) 1930.

This article is a contribution to the view that agnosia, aphasia and apraxia do not occur as isolated phenomena. A detailed clinical study of a patient with literal alexia revealed the fact that in all his performances he had difficulty in differentiating the individual members of a group from one another. Thus, he was usually unable to name letters of the alphabet presented visually to him, although he always knew that they belonged to a particular group. Similarly, his

appreciation of individual details of test pictures was faulty, yet he was able to grasp the general impression conveyed by them. The same type of disturbance was brought out in the auditory field by testing the patient with complicated musical motifs. In addition, there were some amnestic aphasic symptoms which apparently owed their origin to a particular type of memory defect. This was characterized by a weakness of differentiation of the individual concrete details of more general and abstract concepts. All the symptoms exhibited by the patient were regarded as expressions of this disorder of memory, which therefore was considered the fundamental factor in the case. In all probability the symptom complex of literal alexia always arises on the basis of such a disorder. The author concludes that while alexia may be the most prominent feature of the clinical picture in certain cases, it is invariably part of a wider disturbance affecting all psychic acts. The localization of the lesion is largely accountable for the fact that one sphere of activity may suffer more than others. Even within the same sphere, however, the involvement is not necessarily uniform. Here functional factors, such as individual knowledge, character and personal experience, play an important rôle.

ROTHSCHILD, Foxborough, Mass.

THE NERVE PATHWAYS IN THE VOMITING OF PERITONITIS. F. E. WALTON, R. M. MOORE and E. A. GRAHAM, Arch. Surg. **22**:829 (May) 1931.

Vomiting in peritonitis might be due to a toxin, a nerve impulse or a hormone. Walton, Moore and Graham think that the promptness of emesis following the introduction of irritants into the peritoneum excludes the toxic or hormonic sources of stimulation. If a nervous impulse is involved, three pathways may be considered —the vagus nerve, the spinal nerves and the sympathetic nerves. The authors worked with four sets of cats, each having been given intraperitoneal inoculations of the colon bacillus; in one set a second thoracic transection of the cord had been performed; in another group sympathectomy had been done, while the third set had been subjected to vagotomy. The remaining cats were accepted as controls. In all of the animals a fatal peritonitis occurred, with vomiting as a constant feature. It was evident therefore that no one of these pathways was the exclusive carrier of this impulse. Six new cats were then subjected to both vagotomy and sympathectomy; a fatal peritonitis developed following the introduction of the colon bacillus, but in no case was there any vomiting. Before receiving the inoculation the animals were given lobeline, which brought about vomiting, demonstrating the intactness of the motor mechanism. From this it seems reasonable to assume that the afferent pathway for vomiting in cases of peritonitis uses with equal ease either a vagal or a sympathetic tract, and that the phrenic and other spinal nerves are not involved, since vomiting occurs even when they have been destroyed but does not occur when they alone are intact. If anatomists are correct in the belief that the parietal peritoneum is supplied by cerebrospinal somatic afferent fibers, it would follow that it is irritation of the visceral peritoneum that gives origin to vomiting in peritonitis.

DAVIDSON, Newark, N. J.

DYSTOPIAS OF THE CORPUS PONTO-BULBARE. ALEXEJ TSCHERNYSCHEFF and I. GRIGOROWSKY, J. f. Psychol. u. Neurol. **41**:367 (Jan.) 1931.

In 1907, Essik described under the designation of "corpus pontobulbare" a gray formation lying ventromesially to the ventral nucleus of the acoustic nerve. Masuda, who studied this structure carefully, concluded that structurally, as well as through its connections, it belonged to the nuclear formations in the pons. Marburg, on the other hand, regarded it as an embryonal medullary nucleus. The authors of this paper describe in detail the histologic changes in the pons and medulla which they observed accidentally in the course of a routine necropsy in a case of pulmonary tuberculosis. In the region of the right pontocerebellar angle there was seen at the level of the nucleus praepositus nervi hypoglossi a formation within the lateral parolivary and subtrigeminal fossae; this formation

contained a network of delicate fibers extending into the right corpus pontobulbare, and laterally to it there was a massive bundle of fibers in the form of a sling which contained a series of small islets of ganglion cells. As one ascends in the direction of the cerebrum, this formation gradually disappears, and the bundle of fibers with its enclosed ganglion cells sends out prominent prolongations between the roots of the vestibular and facial nerves and into the restiform body, curves around the roots of the vestibular nerve, diminishing in size as it ascends, and enters the middle portion of the pons, where mesially to the extracerebral root of the trigeminus and ventrally to the corpus pontobulbare it gradually disappears. As one ascends orad, the cellular elements of this bundle also disappear gradually. The right corpus pontobulbare is much larger in circumference and volume than the left. No other anomalies were found in the brain, and the observations are reported in order to put on record an additional case of dystopia in this region.

KESCHNER, New York.

ACUTE POISONING WITH PHYSOSTIGMINE. ENRICO EMILIO FRANCO, Arch. di Antropol. crim. **50**:850, 1930.

This article is a monographic study of the toxicology, pharmacodynamics, symptomatology and pathology of acute physostigmine (eserine) poisoning, with a report of two personal cases and an extensive review of the literature. Some of the author's conclusions are: There is no specific pathologic picture of acute physostigmine poisoning; the features most often encountered at autopsy are congestion, noncoagulated blood of dark color, glandular hypersecretion (salivation), hemorrhages, signs of overstimulation of the gastro-intestinal tract (profuse diarrhea) and pulmonary edema. The condition of the pupils has no diagnostic value. Death following acute poisoning is caused by asphyxia. Chemical search for the poison should be made in the blood, urine, saliva and bile. If negative results are obtained, biologic tests might be of help, such as myosis of the cat's eye caused by application of tissues or fluids suspected of containing the alkaloid. Myosis is produced with quantities of physostigmine as small as from 0.005 to 0.01 mg. (Führer). If this test is not conclusive, physostigmine may be detected by a method based on the synergic action of its combination with acetylcholin (hydrochloride), which causes contraction of the muscle of the leech; this test is sensitive to the presence of 0.0001 mg. Physostigmine is a myotic agent only if instilled directly into the conjunctival sac; if the alkaloid is introduced in other ways, the reaction of the pupil is not constant and has no diagnostic value. One must always keep in mind the vagotropic and amphotropic action of physostigmine on the neurovegetative system of man. It acts in a different manner in normal, in vagotonic and in sympathicotonic subjects.

YAKOVLEV, Palmer, Mass.

PAPILLARY EDEMA DURING PREGNANCY, CURED BY LUMBAR PUNCTURE. J. BOLLACK and N. SALGO, Rev. d'oto-neuro-opht. **9**:161 (March) 1931.

A primipara, aged 25, began to suffer with violent headaches and vomiting at the eighth month of pregnancy, which up to that time had been normal. Three years previously, the patient had had a slight transitory albuminuria, accompanied by headaches.

Examination of the eyes revealed normal vision and fields and a bilateral papillary edema. A blood examination showed a slight increase in urea and an elevation of Ambard's constant. There was no albuminuria. The arterial tension was 10 systolic and 14 diastolic and the Bordet-Wassermann reaction was negative. The tension of the cerebrospinal fluid, measured in the recumbent position, was 42 at first and 18 later; the fluid contained a small quantity of albumin, and the cell count was within normal limits. Following the spinal puncture the symptoms disappeared, and the papillary edema was greatly lessened. At term a living child was born, and the patient has remained well since, except for a double phlebitis following labor.

The presence of normal visual acuity ruled out an infectious or toxic neuritis due to the pregnancy. The slight increase of the blood urea and the raising of Ambard's constant supported the hypothesis of a papillary form of neuroretinitis from pregnancy. In support of the hypothesis of hypertension were the headaches, vomiting, the appearance of the eyegrounds and the improvement after spinal puncture was done. Eclampsia has been treated by lumbar puncture with variable results; papillary edema and intracranial hypertension in the course of chronic nephritis have been relieved by the same procedure.

DENNIS, Colorado Springs, Colo.

INVESTIGATIONS AND OBSERVATIONS OF BRAIN WOUNDS IN NEW-BORN ANIMALS. F. VIZIOLI, Riv. di neurol. **3**:605 (Dec.) 1930.

Vizioli has investigated the reaction of brain tissue in new born animals with the intention of studying in particular the phagocytic function of the microglial elements. His interest is particularly concentrated on the possible transformation of the adventitial elements of the blood vessels, of the endothelium and of the blood elements into compound granular corpuscles. From studies reported in the literature it seems established that in adult animals the compound granular corpuscles are derived, in the great majority, from the elements of the microglia. Adventitial elements participate to a lesser degree in the process; the blood elements rarely transform into compound granular corpuscles.

Because the first microglial elements appear in the last periods of embryonal life and multiply rapidly in the first days of extra-uterine life, and because the gray matter shows few microglial elements at birth, Vizioli has investigated the reaction of the brain tissue in new-born animals. His conclusions are that there is a definite difference between the reaction of the tissue of the adult and that of the new-born animal, the difference being more marked in the gray matter where the mass formation of compound granular corpuscles originating from microglial elements is lacking. In the new-born animal, from eighteen to twenty hours after a brain injury, large globoid elements appear which seem to be of hematic origin, probably large lymphocytes, and these elements constitute the majority of the phagocytic elements in the new-born tissue. According to Vizioli, some of these globoid hematic elements undergo a morphologic transformation that recalls the morphology of microglia cells. He therefore advances the hypothesis that microglial elements can originate from blood elements.

FERRARO, New York.

THE IMPORTANCE OF DISTURBANCES OF LIVER FUNCTION IN ALCOHOLIC DELIRIUM AND A CAUSAL METHOD OF TREATMENT. M. DE CRINIS, Monatschr. f. Psychiat. u. Neurol. **76**:1 (June) 1930.

The author regards delirium tremens as a toxic condition that owes its origin to impairment of the detoxicating function of the liver by alcohol. Proceeding on this basis, patients with delirium tremens were treated by a method designed to increase the functional activity of the liver. The substance used for this purpose was decholin, a cholic acid derivative, the formula of which is given as $C_{23}H_{35}O_3$ COOH. It was administered intravenously, 10 cc. of a 20 per cent solution being used. The number of patients treated was seventeen. After one injection, all but two of the patients exhibited marked improvement, the physical as well as the mental symptoms disappearing within a few hours. The symptoms recurred in five cases, but cleared up completely following a second dose of the drug. The two patients who proved refractory to the first injection showed rapid and permanent improvement when a second one was given twenty-four hours later. The author concludes that decholin is of definite value in the treatment of delirium tremens.

In view of the supposed connection between disorders of liver function and melancholic conditions, decholin was administered to patients exhibiting the

symptom-complex of melancholia. In some instances remarkable improvement occurred, but in others the drug apparently had no effect. The author is not prepared to form definite conclusions concerning the usefulness of this method of treatment for melancholia until further observations have been made.

ROTHSCHILD, Foxborough, Mass.

HETEROPLASTIC EXPERIMENTS ON THE LIMB AND SHOULDER GIRDLE OF AMBLYSTOMA. JOSEPH L. SCHWIND, J. Exper. Zool. **59**:265 (April 5) 1931.

A limb of an Amblystoma punctatum transplanted to an Amblystoma tigrinum larva differentiates more rapidly and becomes functional sooner than does the normal limb of the host, and eventually takes on the pigmentation and markings of the host. A scapula and suprascapula transplanted to the other species do not keep their specificity of form. The presence of tissue from the donor species in one portion of the girdle has no effect on the growth of the portion of the girdle formed of host tissue. The entire girdle rudiment of the embryo lies anterior to a line formed by the projection of the boundary between the fourth and fifth somites. No histologic differences could be found between the cartilage of the two species in girdles formed of both host and donor tissues. A tigrinum limb transplanted to a punctatum larva usually causes a hyperplasia of the spinal ganglia supplying it, while the ganglia of a tigrinum larva, which supply a transplanted punctatum limb, usually show a hypoplasia. Heteroplastic limbs have no effect on the number of motor neurons in the spinal cord.

The distribution of donor and host digits in single limbs formed of tissue of both species showed that the material determined for the formation of digits is localized along an anteroposterior line, the material for the first lying most anteriorly. The future radial border of the hand lies more ventrally and anteriorly than the future ulnar border. If a portion of the limb anlage is removed and replaced by flank tissue, and a normal limb develops, the missing portion of the limb anlage is regenerated from the remaining portion and is not induced from the grafted tissue.

WYMAN, Boston.

SYMMETRICAL CONFLUENT LESIONS IN THE FRONTAL LOBES IN THE WILSON-PSEUDOSCLEROSIS SYMPTOM-COMPLEX. MAX BIELSCHOWSKY and J. HALLERVORDEN, J. f. Psychol. u. Neurol. **42**:177, 1931.

This paper is based on a clinicopathologic study of two cases of undoubted pseudosclerosis. They are reported in detail by the authors on account of an unusual pathologic condition in the form of a symmetrical fusion of the lesions in the frontal lobes. The cortex showed in both cases involvement of the various laminae. In some of the affected areas there was extensive proliferation of the mesenchymatous elements—more proliferation than was necessary to repair the loss and destruction of parenchymatous nerve tissue. Extensive mesenchymatous proliferation was found even in areas in which the nerve parenchyma was relatively well preserved. It is noteworthy that the mesenchymatous proliferation in the brain bore a close resemblance to the structural changes usually observed in the so-called "Wilson liver." The overproduction of connective tissue in the cortex was in marked contrast to the poor reaction of this tissue in the lesions found in the white matter. Both cases are also noteworthy for the relatively slight involvement of the putamina in the necrobiotic process, as well as for the enormous increase of glia even in those areas of the white matter in which the myelin fibers were not markedly affected. There was also an enormous increase in the number of Alzheimer cells throughout the entire central nervous system in both cases. The authors believe that the two cases represent a peculiar modification in the phenotype of this disease, which they include among the heredodegenerations.

KESCHNER, New York.

TRAUMATIC LESION OF BRACHIAL PLEXUS WITH SYMPTOMS SIMULATING CERVICAL RIB. LEANDRO TOCANTINS, J. Nerv. & Ment. Dis. **73**:258 (March) 1931.

Lesions of the brachial plexus set up a diverse and baffling clinical picture, and the disturbance of balance in the interplay of surrounding structures may account for the perpetuation of these lesions. The case of a man, aged 40, who suffered from pain in the left side of the neck, the upper border of the clavicle and the ulnar border of the forearm, of two years' duration, is described in detail. This pain followed a severe twisting and pulling of the left shoulder while holding some loops of hose attached to a reamer. Roentgen examination of the shoulder region showed it to be normal. Swelling and paresthesia, pain and hyperesthesia of the left arm developed later. Drugs, diathermy and massage gave no relief, and all laboratory tests gave negative results. Palpation over the midpoint of the supraclavicular triangle showed tenderness in the left side, while lifting the chin as high as possible with the head thrown back produced pain on that side. The muscles about the shoulder and forearm were tender, and all the muscle groups in that region showed some weakness. The author made a diagnosis of compression and irritation of the lower cord of the brachial plexus. A splint was eventually devised that supported the weight of the arm from below rather than from the shoulder, and after a period of fourteen weeks, with galvanic treatment and graduated exercises, marked improvement was shown. Nine months after the onset of this treatment the patient resumed his work of repairing railroad cars.

HART, Greenwich, Conn.

THE CHILD OF VERY SUPERIOR INTELLIGENCE AS A SPECIAL PROBLEM IN SOCIAL ADJUSTMENT. LETA S. HOLLINGWORTH, Ment. Hyg. **15**:3 (Jan.) 1931.

The gifted child is more of a problem to himself and to his family than to society. There is a gap between his emotional stability and his intellectual status, and if he is placed in a grade in school to which his intelligence entitles him he is apt to be emotionally immature compared to his classmates; if placed in the grade corresponding to his age, he will find the work too easy and fall into idle daydreaming. If he makes proper scholastic progress, he is obliged to associate with his duller seniors, and, being the youngest in his class, he is soon bullied and tormented by his older classmates. Gifted children are disinterested in the ordinary play of their contemporaries, and occupying the play time of these children presents a special problem. In the classroom they may become troublesome because they are able to express themselves and are unduly anxious to do so. It is unlikely that a really superior child will have parents both of whom exceed him in intellectual quotient, and this reversal of the usual relationship presents delicate problems in parent-child adjustment. The domestic management of these children is especially difficult, for they are quick to appreciate the types of behavior that bring them satisfaction. These gifted children are destined to be the captains of the future, and their training is of significance to society.

DAVIDSON, Newark, N. J.

HOW WE REACH AN UNDERSTANDING OF SPEECH AND LATER OF READING AND WRITING. NOICA, J. de neurol. et de psychiat. **31**:162 (March) 1931.

The author presents the case of a girl, aged 6, who speaks well and is able to read and write. He calls attention to the fact, however, that in reading she uses a high voice and if reading an unfamiliar word she separates it first into its simple elements. This is also true of writing. Her letters are large and distinctly made. He takes these findings as proof that in learning to read, one must first read the letters before one can understand and read the complex whole, the word. In learning to write, it is necessary first to learn the components of the letters and then to assemble them into words. He presents also as proof

of these deductions the case of patients with sensory aphasia, who, although able to hear, are unable to understand spoken words, and who are able to see but unable to understand written words. However, during the period of recovery, they may be able to understand if the written or spoken word is separated into its component parts. In the case of pantomime, he points out that the action cannot be quickly and completely carried out, but that it must first be separated into its component parts before the sensory aphasic person can comprehend and imitate. The author concludes that these faculties of reading and writing are developed by imitation and by separating words and phrases into their component parts in order to understand the whole.

WAGGONER, Ann Arbor, Mich.

PSYCHOTHERAPY IN OBSTETRICS AND GYNECOLOGY. WILLIAM F. MENGERT, Ment. Hyg. **15**:299 (April) 1931.

Sex is a ground common to psychiatry on the one hand and to obstetrics and gynecology on the other. This is reflected in the old idea of the pelvic nature of the neuroses, as suggested by the etymology of the word "hysteria." In modern times it has led to many unnecessary operations to relieve neurotic symptoms. Psychiatric intelligence is necessary in managing maternity cases, and Mengert touches on the psychoses of pregnancy, as well as on the neurotic manifestations of that state, such as the perversions of appetite. The husband, too, needs education in the psychology of pregnancy. Some of the neuroses of this state represent a rebellion against its discomforts, and in Mengert's opinion a large number of cases of morning sickness are purely functional; he has sometimes thought that even cases of pernicious vomiting are often neurotic. Among the gynecologic conditions demanding a psychologic approach may be mentioned frigidity, masturbation, dyspareunia, dysmenorrhea and the menopause. Many cases of dysmenorrhea represent pains of a neurotic nature. Cases of this sort deserve thoughtful treatment and not casual condemnation as "just another neuro."

DAVIDSON, Newark, N. J.

THE EFFECT OF LABYRINTHINE AND CORTICAL STIMULATION ON THE POSITION OF THE EYES FOLLOWING SECTION OF THE POSTERIOR LONGITUDINAL BUNDLE. E. A. SPIEGEL and L. TOKAY, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **32**:138 (Oct.) 1930.

In young dogs, following experimentally produced lesions of the posterior longitudinal bundle, it was found that the intactness of that structure is more important in the occurrence of conjugate ocular movements after cortical than after labyrinthine stimulation. Destruction of the posterior longitudinal bundle is more difficult to compensate for in the occurrence of conjugate ocular movements following cortical irritation than following labyrinthine irritation. It would seem also that the secondary pathway represented by the tracts running through the substantia reticularis is of greater significance for conjugate ocular movements following labyrinthine stimulation than for those following cortical stimulation.

KESCHNER, New York.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, April 7, 1931

S. PHILIP GOODHART, M.D., *President,* in the Chair

EPILEPTIC ATTACKS SIXTEEN YEARS AFTER TRAUMA OF THE HEAD: OPERATION. DR. NATHAN SAVITSKY (by invitation).

History.—F. S., a man, aged 19, was admitted to the Montefiore Hospital on Dec. 10, 1929, complaining of convulsive seizures for one and a half years. The first convulsion occurred at night; the second, six months after the first and two more a few weeks later. The fifth and sixth convulsions occurred in one day, seven weeks before admission. All the attacks were of the grand mal type. After the third attack there were auditory auras of roaring noises in both ears. The patient now recalls that in addition, before each attack, he felt nauseated and peculiar. There were also periods during which he was "blank" and forgetful.

His birth and early development were normal, except for a fall at the age of 18 months, when he sustained a fracture of the skull. At that time there was bleeding from both ears. Since then he has had a defect of the bone in the left parietal region. There is no history of convulsive movements after the injury or during the interval of sixteen years up to the onset of the present illness. We have no exact information regarding the duration of unconsciousness at the time of the accident. There is no family history of nervous or mental disease for two generations. No significant deviations in behavior were noted in the patient. He was considered to be of average intelligence. He completed grammar school at about 14. He worked regularly when well and showed no instability in his adjustments. He had influenza in 1927, and at that time he was told that he had a rheumatic heart. An infected arm was lanced fifteen years before examination, and tonsillectomy was performed one and a half years before. His habits had always been good; he said that he did not use tobacco, alcohol or other drugs.

Examination.—Physical examination showed a defect of the bone, about 3 cm. wide, in the left parietal region; there was evidence of mitral stenosis and aortic insufficiency, probably of rheumatic nature, without signs of cardiac decompensation; the blood pressure was 120 systolic and 68 diastolic.

Neurologic examination gave negative results, except that a positive Hoffmann's sign on the right side was noted by one observer. This was not confirmed by other physicians who examined the patient. The fundi were normal.

Psychiatric study revealed nothing of significance. The level of intelligence was low normal. Behavior and insight were excellent. The affective reactions were adequate, and there were no trends or hallucinatory experiences.

Roentgen examination of the heart showed the characteristic changes of a moderately advanced case of rheumatic disease of the heart. A roentgenogram of the skull revealed an irregular quadrilateral flap of bone missing in the left parietal region.

An encephalogram showed moderate dilatation of the entire ventricular system, which was most marked in the region of the posterior horns. The anterior-posterior films showed a distinct pulling of the entire ventricular system to the

left, in the direction of the defect of the bone. The third ventricle was also slightly displaced to the left and appeared dilated. Considerable air was present in the subarachnoid spaces, especially in the region of the defect of the bone and about the pituitary gland.

All laboratory studies, including the Wassermann tests of the blood and spinal fluid, gave negative results.

Course.—The patient left the hospital against advice soon after the first admission, but was readmitted on Jan. 13, 1930. He had had a nocturnal convulsion two weeks before. One day before readmission, while thinking of the advice given to him regarding the necessity of an operation, he had a convulsion. During this intervening time he experienced severe, nonradiating pain in the right eye on two occasions.

Operation.—On Jan. 18, 1930, Dr. Davidoff operated. He reported: "On separating the adherent scalp from the edge of the bone defect, thickened membrane, representing dura, was encountered, filling the opening in the base. The scalp was lifted away so that the bony edge was palpable all around. An accumulation of fluid was present beneath it. A puncture hole was made in the center of this area, and a clear colorless fluid was removed. . . . The bony margins of the defect were then freed from all sides until the normal dura could be seen beyond the abnormal thickened dura previously mentioned. . . . After the margins were freed the junction between the normal and thickened dura was incised at the inferior end of the longitudinal defect. The peculiar, brownish gray, degenerated cystic cerebral substance was systematically scooped out by means of blunt dissection and the sucker. This process was continued toward the vertex until practically all of this tissue which was adherent to the thickened and abnormal dura was entirely removed."

Postoperative Course.—This period was uneventful. There have been no attacks since the operation fourteen months ago. The patient occasionally takes phenobarbital, ½ grain (0.03 Gm.) in the morning. Immediately after the operation he complained of numbness in the right upper limb. Astereognosis and loss of two-point discrimination were noted. There was no loss of motor power. There was some generalized hyperreflexia, which had been noted preoperatively by a few observers.

The patient is now working as a shipping clerk. The signs and symptoms of defect of the parietal lobe persist. On rare occasions he complains of paresthesia in the right side of the face. There is some hemihypesthesia on the right for all modalities of sensation. This hemihypesthesia has become more definite since discharge from the hospital. He feels much better, brighter and happier.

Comment.—The case is presented mainly because of the unusually long interval (sixteen years) between the initial trauma and the onset of the epileptic attacks. There was nothing pointing to cerebral involvement during this interval. There was also distinct absence of all other factors that might give rise to the convulsive state.

Of 1,345 recorded cases of epileptic seizures following severe injury of the head, eleven were noted with an interval of from ten to fifteen years between the initial trauma and the onset of epilepsy, and six with an intervening period of more than fifteen years. Tilmann (*Arch. f. klin. Chir.* **92**:496, 1910) reported two cases with an interval of twenty-six years; Sargent (*Brain* **44**:312, 1921) one of twenty years; Cohn and Goldstein (*Deutsche Ztschr. f. Nervenh.* **108**:161, 1929) one of twenty years; Mann (*Klin. Wchnschr.* **9**:218 [Feb. 1] 1930) one of twenty years; Robertson (*Canad. M. A. J.* **16**:541, 1926) one of sixteen years. All of the patients except Mann's were operated on.

My patient's convulsive seizures were always generalized in spite of the focal anatomic changes. The rarity of jacksonian seizures in cases with long free intervals is well known. The histopathologic, clinical and surgical aspects of this problem have recently been thoroughly discussed by Foerster and Penfield.

DISCUSSION

DR. LEO M. DAVIDOFF: The clinical picture is certainly not common, but we have seen as many as five or six such cases at the Neurological Institute; they all seemed to conform to the picture presented by this patient, namely, that of a person who in adolescence or childhood sustained a severe injury of the head, and after a long interval convulsive seizures developed. In all the patients there were defects of the skull, and at operation there was found a cystic degeneration of the brain, porencephalia, underlying the bone defect. Several of them have been operated on at the Neurological Institute. This man has not had a convulsive seizure for fourteen months and represents the kind of case that Foerster, in Germany, and Penfield have recently reported. The surgical problem is often serious in that the defect occasionally occurs over the motor area; then the patient has to make up his mind whether he is going to submit to the seizures or suffer from hemiplegia. Fortunately, in this boy the defect was definitely behind the motor area, and although it is unpleasant to have a motor sensory defect, he was willing to submit to that. Fortunately, he is rid of his seizures.

DR. GEORGE V. N. DEARBORN: What is the least injury that would lead to this delayed result? Can you tell how small an injury to the head of a child will eventuate in this way? If a boy falls heavily onto his forehead, without any fracture, is there danger of convulsive seizures developing later?

DR. S. P. GOODHART: Predisposition must be considered.

DR. DAVIDOFF: In the cases that I have seen there has always been a severe injury.

DR. GOODHART: Fracture?

DR. DAVIDOFF: That is difficult to state. Fifteen or twenty years ago fewer roentgen examinations were made, and the diagnosis was not certain. Almost invariably the patient has fallen from a crib or has been hit with a baseball, and a serious cranial trauma with loss of consciousness has followed.

DR. MICHAEL OSNATO: Sargent, when he reviewed an enormous number of craniocerebral injuries in the British Army during the World War, gave statistics that are pertinent to this discussion. Of about 24,000 men who received severe craniocerebral injuries with a gross defect, the convulsive state developed in only 4.5 per cent. There must be, obviously, some factor or factors other than trauma. Incidentally, while this case shows good surgical results, the time is still too short to prove a direct relationship between the convulsive seizures and the injury. One knows that spontaneously, for reasons that are almost entirely unknown, these persons may be free from seizures for indefinite periods, so that my attitude would be receptive, but extremely conservative.

DR. NATHAN SAVITSKY: I shall add merely that in all the cases I included in my study, 1,345, there was a severe injury to the head. The criterion that I was guided by was loss of consciousness, when such information was given in the report. As Dr. Davidoff pointed out, in the older literature reports of roentgen examinations were not available, but all these patients gave a history of loss of consciousness after a severe trauma of the head. In other cases in which minimal injuries give rise to attacks, the question of idiopathic epilepsy developing independently in the injured person must be considered. That brings up a different problem. Epileptic seizures following injuries to the extremities and severe psychic trauma are reported, but I have included only cases resulting from severe injuries to the head.

A CASE OF A DERMOID OVERLYING THE CEREBELLAR VERMIS, WITH A REVIEW OF THE LITERATURE ON INTRACRANIAL DERMOIDS. DR. SAMUEL BROCK and DR. DOROTHY KLENKE (by invitation).

Stimulated by our experience with the following case, we have surveyed and summarized the cases of intracranial dermoids in the literature, commenting on some of their histologic and embryonic features.

History of Case.—W. F., a garage worker, aged 27, was referred to the New York Neurological Institute on April 12, 1930, by Dr. E. D. Friedman, with a

diagnosis of "tumor of the fourth ventricle." He complained of headaches, roaring noises in the ears, nausea, dizzy spells and double vision. The illness started in September, 1929 (seven months before admission), with headaches. However, he had noted flashes of colored light and a peculiar odor (uncinate fits?) on different occasions for about two years. The important positive neurologic observations were: bilateral papilledema, a slight and variable right external rectus weakness, nystagmus on extreme gaze to either side and questionable weakness of the lower part of the left side of the face. While under observation he had several attacks characterized by headache, nausea, dizziness, nystagmus and weakness and trembling of the extremities. In these attacks there were almost always a palsy of the right branch of the sixth nerve and fixation of the head, the chin being directed to the left. The cerebrospinal fluid pressure was increased. Roentgen examination of the skull showed small areas of calcification in the midline of the posterior fossa, in the region of the fourth ventricle. Roentgenograms made after ventricular injection of air showed dilatation of the ventricles and of the aqueduct of Sylvius as far as the area of calcification.

A suboccipital craniotomy was done in two stages. At the second operation (June 17, 1930), Dr. Elsberg removed a soft cystic neoplasm overlying the vermis and separating the cerebellar lobes. It contained much mucoid material, many long hairs and several calcareous plaques. A cavity, 8 by 6 by 4 cm., remained. The patient was discharged as cured on June 30, 1930, and has had no symptoms since.

Comment.—Following other authors, we believe that otitic cholesteatomas should be classified as cholesteatosis, and that intracranial cholesteatomas should be called epidermoids.

A review of the 39 cases of intracranial dermoids so far reported in the literature was made, each case being classified and summarized. Twenty patients were male; 11 were under 10 years of age; 33 were single and six were multiple dermoids; they occurred everywhere in the brain, but 13 were in the midline of the posterior fossa; 29 were definitely cystic and 25 were pial.

In Dr. Cushing's series of 936 verified tumors of the brain there were 3 dermoids, 11 epidermoids and 4 teratomas. In the Neurological Institute's series of 450 verified tumors of the brain there were 2 dermoids, 4 epidermoids and no teratomas.

This article appeared in full in *The Bulletin of the Neurological Institute of New York* **1**:328 (June) 1931.

DISCUSSION

Dr. Foster Kennedy: The case that Dr. Klenke described presented a good deal of difficulty before operation, while the diagnosis was being considered. The patient showed a fairly clear picture of uncinate irritation, in contrast to which there was the calcification below the tentorium. This calcification was verified as being a massive extending lesion by the ventriculogram, which demonstrated the dilated ventricles, so that it was possible in this case to have important clinical diagnostic features overruled by diagnostic features developed mechanically, which I am always sorry to see, lest it increase our dependence on mechanical methods of diagnosis. It is only right, however, to give the devil his due, and to say that it was by roentgen examination and by the ventriculogram and by the overthrowing of apparently valuable diagnostic clinical leads that we arrived at the correct diagnosis.

Dr. Klenke spoke of calcareous shadows as being suggestive of dermoid and epidermoid growths, which of course is true. It must be remembered that shadows of a crescentic character, not unlike those seen here, are often found as the result of angiomas, and less often as the result of calcification in tuberculomas.

I put a question to the patient, because it occurred to me that perhaps Dr. Klenke would not object to my using her case to point a moral that I see emerging from this situation in a slightly different manner. I asked the patient when the symptoms of headache and dizziness, that he had had for so many months, disappeared, and he said that that occurred two weeks after the operation; just now he said that he had not had any recurrence of those symptoms. Not wanting

to shift attention from a consideration of this subject, I may say that some of us have been examining with considerable intensity, in Bellevue Hospital, the after-results of injuries of the head: cases coming under the influence of the Compensation Act and those not coming under the Compensation Act. It has been the experience of us all that injury of the head, with perhaps some deformity of the ventricular system, is properly associated with what we call a postconcussion syndrome, comprising pain and dizziness, and these symptoms are dependent on the deformity of the ventricular system, lasting for from two to three years. Here is a man with an enormous lesion—true, a midline lesion in the brain—which has lasted for a considerable number of months and which has tremendously dilated his entire ventricular system; yet that man was capable of recovery from all his subjective symptoms within two weeks of the operation. The moral, I take it, of recovery from serious deformity of the brain such as was present in this case may be applied to less serious deformities of the brain occurring after an injury to the skull.

DR. ISRAEL STRAUSS: Will Dr. Kennedy elucidate his comparison between symptoms of the postconcussion syndrome with disturbances in the ventricular system and the relief of headache, dizziness, and so on, following the removal of the tumor in the case presented?

DR. KENNEDY. I do not know that I can elucidate it. The point I would make clear is that here is a man with a seriously deformed ventricular system who has received entire relief from the symptoms within two weeks after an operation that must have produced a good deal of bony disturbance. I am speaking of cases in which mild injuries of the head are followed by subjective symptoms for a period of a year or more. My belief is that the subjective symptoms that we call the postconcussion syndrome are often largely the result of states of suggestion and fear, and that this patient is a man in whom suggestion is not operative, but in whom the organic situation is due to a severe injury, capable of being entirely cleared up in a very short time.

DR. STRAUSS: I thought Dr. Kennedy wished to insinuate that the postconcussion syndrome is a neurosis. Of course he left that to our imagination. My question was put so that he would say it. I also noted that he said that in the course of his work at Bellevue Hospital they had noticed, through encephalograms, that there was distortion of the ventricles in some posttraumatic cases. It seems to me that the conditions that we find in a tumor of this kind and the conditions that Dr. Kennedy has alluded to are not quite the same. In the first place, we are dealing with a neoplasm causing obstruction to the flow of cerebrospinal fluid, exerted slowly and gradually over long periods of time, and by the removal of that tumor the condition that we call intracranial pressure is relieved. We do not know in these cases how many of the symptoms complained of are due to intracranial pressure entirely, and how many are due to the tumor in this localization, because Dr. Kennedy admitted that his neurologic diagnosis could have referred to any region other than the subtentorial one. When we are dealing with the postconcussion syndrome, in which we find a disturbance of the ventricular system, and find that one ventricle is larger than the other—I am speaking only of those cases in which we can demonstrate by encephalography some change in the ventricle—we are dealing with something that has not influenced the ventricle *per se*; not being due to an interference with the flow of the spinal fluid, it must be caused by some pathologic process that has occurred within the substance of the brain and has caused the deformity of the ventricle by diminution of the brain substance, which makes one ventricle larger than the other, by a diminution of the brain substance that has drawn the ventricle outward or by a hemorrhage that has taken place on the surface of the brain, causing an interference with the absorptive power on one side. In fact, one can visualize a number of processes that may take place in a postconcussion syndrome with displacement of one ventricle or, sometimes, of both. In other words, I think that Dr. Kennedy is wrong if he draws a comparison between a case such as this and a case of the type that I have described. I am speaking only of cases of postconcussion syndromes in

which, as Dr. Kennedy says, there is as a rule a change in one ventricle. I do not think, therefore, that Dr. Kennedy is correct in saying that such a case, with evidence of organic change in the brain as revealed by change in the ventricle, can be looked on entirely as one of psychic trauma or suggestion. It is not infrequent to find cases that contradict this theory. I happen to have a patient at the hospital today, a man aged 44, who has a tremendous internal hydrocephalus, and who until a year ago made no complaints with reference to his head. He was a pressman; a year ago he had an accident in which his hand alone was injured, and he now has serious organic cerebral disturbances. We did an encephalography, removed 300 cc. of spinal fluid and injected air, but despite the removal of 300 cc., he still has a level of fluid that looks as though he had 300 cc. more. Nevertheless, until this trauma to his hand, the man showed no evidence of such a degree of internal hydrocephalus. I do not mean that the trauma caused the internal hydrocephalus. I merely mean that in a case of this kind such a degree of internal hydrocephalus, which goes back to childhood, has produced no symptoms; the brain has accommodated itself to it. Likewise in cases of tumor, the symptoms, which are due to an increased intracranial pressure of slow development and long duration, are relieved when the foreign body is removed; but in a case of concussion, in which one can see a distortion of the ventricles or of one ventricle, I believe that the distortion indicates to a pathologist that some pathologic process has taken place within the brain substance, and in such a case I do not think that one is justified in attributing the symptoms complained of to the cause that Dr. Kennedy has suggested.

LOCAL ANAPHYLACTIC INFLAMMATION (ARTHUS PHENOMENON) IN THE BRAIN OF THE RABBIT. DR. LEO M. DAVIDOFF, DR. BEATRICE CARRIER SEEGAL and DR. DAVID SEEGAL.

A number of neurologic conditions that are seen clinically could be accounted for on a basis of local anaphylaxis of the nervous system. However, no case has yet been so proved histologically. The successful demonstration of the Arthus phenomenon in other organs has led us to hope that the same could be accomplished in the brain. Three groups of rabbits, with adequate controls, were chosen. The essence of the experiment consisted, with modifications in each group, of injecting a foreign protein into some area in the brain and after an interval reinjecting the same protein into the same area.

The majority of the experimental animals showed both clinical and histologic evidence of local anaphylaxis in the area into which injections were made. In the controls the results were negative. In the animals showing a positive response there were evidences of cerebral disease. Sometimes convulsive seizures occurred immediately after the injection. More frequently the animals appeared normal for from one-half to one and a half hours and then began to breathe rapidly, hunch up as if in great discomfort and sometimes twitch locally or have a generalized seizure. Sometimes they held the head and eyes rotated to the side contralateral to the injection, or there were actual rotary movements toward that side. Often there was paralysis of the contralateral half of the body. A given animal may show only a few of these symptoms and to a mild degree, but in the severe cases they are progressive and usually end in death within twenty-four hours.

Grossly, the lesion seen in the brains of the experimental animals was striking. The side of the brain containing it was congested and enlarged, and the midline structures were displaced toward the opposite side. On transverse section, the entire center of the hemisphere was softened and hemorrhagic, and the narrow margin of approximately normal tissue was edematous.

The histologic picture of the Arthus reaction in the brain resembles closely that described in the skin and subcutaneous tissues by Arthus and Breton, Gerlach, Doerr and others, allowing for the differences in the fundamental structures of these tissues. It consists chiefly of edema, extensive hemorrhage and marked leukocytic extravasation, chiefly of the neutrophilic polymorphonuclear cells.

DISCUSSION

DR. ARMANDO FERRARO: Dr. Davidoff's paper represents a serious attempt to put on an experimental basis a problem the importance of which is becoming more and more manifest. Whereas the study of anaphylaxis in internal medicine has reached some substantial results, its application in neurology and psychiatry is still in its infancy.

A few attempts, however, have been made that tend to bring the study of allergy and anaphylaxis in particular onto experimental ground. I may mention in this connection the work of O. Rossi in investigating the action of autoneurotoxins. In studying the allergic phenomena produced by the use of iso-antigens, he expressed the hypothesis that it is possible to produce an autoneurotoxic serum just as it is possible to produce autohemolysins. Such a hypothesis would explain lesions of the nervous system secondary to the production of toxic antibodies resulting from the primary lesion of the nervous system.

Such a conception has been utilized by Marburg in his explanation of the pathogenesis of the lesions following trauma of the spinal cord, a conception to which I subscribed in my own report on medullary concussion.

Another step, much more on theoretical bases, has been taken by Buscaino in his attempt to put epilepsy on an anaphylactic basis. Buscaino believes, in fact, that in the so-called idiopathic type of epilepsy the fundamental anomaly is a condition of dysthyroidism, a dysfunction of the thyroid, the result of which is the liberation of abnormal proteins of thyroid origin, which sensitize the body and therefore generate a convulsive seizure whenever new protein material becomes liberated and put into circulation. The epileptic seizure, therefore, represents the equivalent of an anaphylactic shock, and consequently Buscaino advises the use of anti-anaphylactic treatment. Such a conception is extended by him to the so-called symptomatic type of epilepsy also, which represents the summing up of an organic lesion of the brain itself, generally cortical, plus a secondary autointoxication which may develop into anaphylactic reaction.

The lesions of the endocrine glands and more particularly of the thyroid need not be morphologically evident, but the dysfunction may be represented by merely qualitative changes of a physicochemical nature.

Dr. Davidoff's paper recalls also to my mind the possibility of applying an anaphylactic theory to the explanation of some recurrent nervous conditions, as he himself mentioned at the beginning of his paper. I remember particularly a case which Dr. Keschner illustrated at one of the meetings of our Society of a recurrent type of so-called myelitis, which caused considerable discussion, and I remember that Dr. Davidoff and Dr. Hyslop pointed out the possibility that such recurrent attacks of involvement of the spinal cord might be based on allergic phenomena. I sympathize with such a hypothesis and would go so far as to advance the hypothesis that in mental disease one may be able to witness phenomena that have an allergic basis. Being a convinced organicist and believing in the toxic and infectious origin of mental diseases, it seems natural to me to think in terms of biology. Therefore I do not see why, in cases of autointoxication, one cannot witness phenomena comparable to anaphylactic shock, which would specifically affect the cortex of the brain as a whole and be responsible for sudden attacks of mental confusion, manic outbursts, or other allied mental reactions.

The study of allergic phenomena in connection with the nervous system may also open an important field for therapeutic measures. In this connection I would mention the recent work of Billard on so-called phylaxis. Phylaxis is, in the conception of Billard, a protective mechanism which the organism, and more especially the nervous system, opposes to the action of poisons or toxins. Such a condition of phylaxis can be artificially enhanced. For instance, sparteine seems to protect against diphtheritic and tetanic toxins. The mineral content of mineral water seems, on the other hand, to protect the organism against the noxious effects of sparteine itself. Some neurotoxins might, therefore, create a protection against the action of other neurotoxins.

It is not difficult to understand the possibility that further studies might indicate the various sensitizing agents responsible for anaphylactic reactions and the possi-

bility of counteracting the action of such agents by the use of special drugs or substances. All these investigations require sound experimental bases, and therefore every attempt, as that of Dr. Davidoff and the Drs. Seegal, to put on such a basis this important problem must be highly appreciated and congratulated.

DR. H. A. RILEY: After the preliminary sensitization of the brain, did Dr. Davidoff make any attempt to produce the allergic phenomenon by intravenous injection or any other method of introducing the material rather than by again injecting it directly into the brain?

DR. ISRAEL WECHSLER: The clinical significance of this subject has been brought home to me on two recent occasions. Dr. Davidoff made allusion to migraine, and I shall report the case of a woman who had suffered from hemicrania for years. One day she came to me saying that she had been vomiting for days, and that she had severe headache. At the time, the picture was not typical of migraine. I watched her for several weeks and found no neurologic signs. One day bilateral choked disks, with hemorrhages, ataxia, and evidence of facial paresis developed. The suspicion of a neoplasm arose, of course, and, together with Dr. Elsberg and Dr. Davidoff, I examined her. We decided that an encephalography should be made. The patient refused this, went home from the hospital, and gradually recovered. The papilledema receded; the hemorrhages and ataxia disappeared, and she is now perfectly well. I have since wondered whether we were not dealing with a case of edema on the basis of migraine and also on the basis of anaphylaxis.

I have seen another case, that of a boy who was sensitized for scarlet fever, by an injection of streptococcus serum, following which hemiplegia with aphasia promptly developed. He also had a severe anaphylactic reaction. He later recovered completely.

These two cases point to some of the clinical applications of the experimental facts that Dr. Davidoff has presented.

DR. FOSTER KENNEDY: Would it be out of place for me to suggest that this has been a matter of interest to a number of us at Bellevue Hospital for a dozen years; about that long ago we published a series of cases of angioneurotic edema with localized cerebral signs. Also we were able to produce a series of cases with local cerebral symptoms and syndromes following serum sickness. There is not the least doubt in my mind that urticaria manifested in the skin can form localized lesions in the brain.

DR. CHARLES DAVISON: A number of investigators engaged in the study of the problem of allergy are inclined to view the reaction of the skin as neutral in origin. I wonder what histopathologic changes were found by Dr. Davidoff and the Drs. Seegal in the hypothalamic nuclei. The histopathologic alterations shown to us resembled those found in trauma and edema of the central nervous system. It is highly probable that this mechanism of anaphylaxis is encountered much more frequently than one thinks, although I must confess that I have never seen pathologic changes exactly similar to those presented tonight. It would not surprise me to find changes such as those found by Dr. Davidoff if cases of epilepsy and of transient or periodic myelitis came to autopsy immediately following an attack.

DR. RICHARD M. BRICKNER: How extensive was the eosinophilic reaction? Were there any, or many, rabbits in which a considerable interval elapsed between the first and second injections?

DR. LEO M. DAVIDOFF: In answer to Dr. Riley, these experiments are entirely preliminary. We wanted to assure ourselves that the Arthus phenomenon can be produced in the brain, and we used whatever method we could to obtain it. Now that we feel sure that the picture can be produced both clinically and histologically, work is being continued on dogs by Dr. Kopeloff and myself. We are placing the antigen in the dog's brain, and after a considerable interval are giving a single intravenous injection. Some dogs have already shown definite convulsive seizures on the contralateral side following the injection. This work has not been included in the paper presented.

The cases cited by Dr. Wechsler and Dr. Kennedy are, as they have said, those of conditions that have been seen for a long time and recognized; it is the

existence of such cases that has spurred us to attempt to produce the phenomenon experimentally and to study it histologically in a manner that has not been done in human beings. Dr. Davison has mentioned that no such histologic picture in a human case has ever been demonstrated.

In regard to Dr. Brickner's question about eosinophilia, I may say that the impression of an eosinophilic reaction in anaphylaxis is one that is perhaps erroneously conceived, at least as far as the local anaphylactic reaction is concerned. In generalized anaphylaxis there is an accumulation of eosinophils, especially in the lung, but in the local anaphylactic reaction, the greater part of the leukocytes are of the neutrophilic variety.

Regarding intervals, we have used no one period. The reason for the use of a multiple antigen has been to prolong the period of sensitivity. For example, one may inject half a dozen antigens in a mixture. In the later shocking experiments, then, it is possible to use any one of these antigens, and after sensitivity to one of them has been worn out, one may begin with the next antigen, etc. We have some animals, particularly in the ocular experiments, that showed evidence of shock nearly one year after the original injection into the eye.

THE NEUROTIC CHARACTER AND THE PERVERT: A CLINICAL STUDY. DR. GREGORY ZILBOORG (by invitation).

There are many cases which the clinician is unable to diagnose in accordance with the current psychiatric nosology. The patients present few, if any, psychologic symptoms in the clinical sense; they usually show more or less definite defects of behavior, and consequently they fail to function in an adult way or on a proper level of psychosocial adjustment. To this group of persons belong the "queer fellows," the maladjusted, the adventurers, the chronic wanderers, the perverts, and other abnormal types. For want of a better designation they are frequently classified in a group called "constitutional psychopathic inferiors" or "psychopathic personalities." These labels connote a constitutional, hereditary defect and naturally, although silently, discourage many a therapeutic endeavor. In the course of the last ten years or so the clinical concept of the "neurotic character," or more fully "neurotic character without symptoms," was introduced (Reich, Alexander). Generally speaking, a neurotic character is a person whose behavior constantly brings him into conflict with conventions of civilized life and even with the law, but who seldom, if ever, presents any clinical symptoms of neurosis or psychoneurosis. Neurotic characters may show a number of gradations from mere "queerness" to frank criminality. If the deviation is found chiefly in the sphere of sexual functions, one is dealing with a pervert whose perversion may transgress the boundaries of purely individual predilections, and the person will thus fall under the rubric of criminal, as guilty of exhibitionism, extreme forms of sadism, compulsive seduction with assault, etc. Clinical studies of such persons lead one to believe that the neurotic character is amenable to treatment, and that psychoanalysis lege artis usually produces a cure. The inner problems are similar to and at times even identical with those of a clinical neurosis. The difference between the neurotic character and the patient with a neurosis lies primarily, not in the inner structure and nature of the psychologic conflict, but in the mode of expression of that conflict. The person with a neurosis expresses his conflicts by means of symptoms (autoplastically), while the neurotic character achieves the same aim by means of behavior, by "acting out" (alloplastically). There are a number of neurotic characters whose difficulties of behavior profoundly disturb their peace of mind. These are the best psychotherapeutic risks.

A case of a youth, aged 19, was chosen as an illustration. Objectively he appeared to be a normal, healthy person. The clinician would have sought in vain to find any physical "stigmata" or psychologic defects. His chief trouble was a singular type of fetishism. He stole fur pieces, fur coats, feminine underthings and masturbated on them; he carried a razor blade and, when in crowded places, stealthily and skilfully cut the tails off women's fur pieces. Combined with this drive was an exhibitionism; he masturbated in theaters, in railroad stations and other public places, and was apprehended many times. He was caught by the

police for the first time when he was 12. At the age of 19, he was tried, released on probation and admitted to a hospital for mental diseases. A rather deep analysis was successfully carried through. The patient remembered having been seduced at 2½ or 3 years of age by a Negro maid who had a fur piece. The deeper structure of the infantile neurosis was worked out. It was discovered in the course of the analysis that from the age of 6 or 7 years until puberty the patient suffered from a frank compulsive neurosis, which was never recognized, and which gradually disappeared in favor of an extreme intensification of his perversions. The main thesis of the paper is that perverts like this are neurotic characters who are curable by means of psychoanalysis; that the underlying factors conditioning the neurotic, perverted behavior are usually severe neuroses of early development which pass unnoticed; that a deeper analysis of such persons is possible only if the first stage of analysis (from five to eight months) is performed in a hospital for mental diseases (not in a jail). As soon as a proper working transference is established, a prohibition is instituted against the patient's giving in to his impulses, and from then on he becomes an ambulatory patient who like any other person is exposed to the normal stimuli and temptations of life. It is to be emphasized definitely that under the influence of the analytic situation (transference) the patient actually gives up the most flagrant part of his behavior—a result impossible to obtain under other circumstances. The patient then finds himself in the midst of many temptations, but the gratification of his infantile (neurotic, perverted) wishes is totally frustrated by the analytic procedure. As a result he becomes socially safe and psychologically tense; his conflicts are stimulated to the utmost degree; their infantile substratum is brought into the open, and the analysis can thus be completed under most favorable circumstances. Once the infantile neurosis is brought to light, the analysis proceeds along the classical line of procedure in such cases.

DISCUSSION

Dr. Bernard Glueck: No matter how you may be constitutionally disposed toward psychoanalysis, or how difficult it may be for us to transport ourselves from the realm of organic medicine of the papers to which we listened earlier in the evening to this realm of psychologic medicine, we all must agree that the essay has succeeded in giving a comprehensive and clearcut view both of the clinical situation and of the theoretical background by means of which we understand the problem that Dr. Zilboorg has presented to us.

In the first place, I should like to say a word or two about the great prevalence of similar problems. The fact that this boy went to Bloomingdale, or the fact that some other patients of the same type escape being managed by the law and have the opportunity of being treated where they should be, simply emphasizes the rarity of this sort of occurrence. Most patients of this kind are dealt with in the traditional legal manner, and of course are not affected in any constructive way. They contribute a great deal to the large percentage of cases of crime and misconduct that are to be found in penal institutions. Why are these methods of the legal and even of the traditional psychiatric approach so impotent in achieving any constructive results? To my mind, it is due to the fact that we attempt to deal with a patient on the plane that he presents to us. A patient of this type, as Dr. Zilboorg has indicated, is using an alloplastic or behavioristic method of dealing with his conflict, and we respond in the traditional manner by trying to deal with his behavioristic manifestations, ignoring the subjective basis of the manifestations. What was done in the case reported was first to transform the particular type of difficulty into a kind that could be dealt with through the psychoanalytic instrument. The procedure indicates also the specific nature of this instrument, and how definitely causal a method psychoanalytic therapy is. It is important therefore to recognize that before one can do anything with a problem of this sort, one has to convert it into a problem that might be manageable psychoanalytically. In spite of the extensive experimentation in the applications of psychoanalysis to all sorts of problems, it is true that its greatest promise lies in the field of the transference neuroses.

Another point I wish to emphasize is that the traditional manner of dealing with disorders of conduct is to ask the patient to give up something that has become very precious to him, without any compensation that would, so to speak, balance the situation emotionally. It should be remembered that in the process of growing up the necessary privations are accepted by the child only in return for certain compensatory security-giving experiences. This is a very important feature in the entire problem of child guidance and social practice. Miss Anna Freud, in her latest book, has called attention to a generalization that I think is significant, namely, the difference between the process of rearing and the process of education. As she pointed out, in the process of rearing we give to the child, whereas in the process of education we demand of the child. The one, the process of rearing, is in the service of instinct. The other, the process of education, is in the service of culture. The essayist has clearly pointed out that it was only after an adequate kind of transference had been established that he considered it safe to ask the patient to abandon some of his neurotic and antisocial tendencies. The child never gives up anything in the service of socialization except in return for something that is very precious to him for other reasons. That is why we are so frequently disappointed when we use the method of urging a patient to change his conduct, of preaching to him how nice it would be and how good it would be if he did change his conduct. That is not the way people who have committed themselves to a certain way of dealing with their problems relinquish these methods. They do it in return for a certain emotional gratification which has to do primarily with enhancing their sense of security for dealing with their own instinctive difficulties, and that is what has been achieved in this case by way of the transference.

Another point that I wish to emphasize refers to the general field of the psychoneuroses, namely, that these patients fundamentally suffer from a difficulty or an inability to be sufficiently true to their biologic destinies, the man finding it difficult or impossible to be sufficiently masculine, and the woman sufficiently feminine.

I need not enter here into a detailed consideration of the reasons for these difficulties except to point out that, as in the case reported, a faulty working out of the mechanism of identification plays an important rôle as part of a flight from instinct.

As regards the specificity of the fetish, you probably have drawn the conclusion from the paper that it is entirely accidental. The last patient of this sort with whom I worked used rubber clothing instead of furs, but otherwise acted in the way Dr. Zilboorg described. He stole, destroyed and masturbated, always in connection with rubber clothing. The thing went back to an incident at the age of 4 when he was sexually assaulted by the family chauffeur who wore a rubber coat. This boy had his greatest difficulty during rainy days when there were so many boys running around with rubber coats on. On these days he had to confine himself to his room; he did not dare to go out.

As to the importance of the psychoanalytic procedure in hospitals, I think that this case indicates that one does run across cases in which one really could not apply this type of treatment in an ambulatory way, at any rate not during the entire period of treatment, and there are undoubtedly many cases that can only be handled psychoanalytically in institutions. It was this opinion that led me to open my own institution. But I am not yet ready to say definitely to just what extent a strictly psychoanalytic therapy can be carried out under an institutional regimen. Of the 130 or more patients that we have had at the hospital since its opening, perhaps one-fourth were especially suited to analytic treatment; two-fourths more had been treated in all sorts of ways, and this method was used more or less as a last hope. It is this section of our material that emphasizes a phase of psychoanalytic therapy that perhaps is not recognized in private practice, namely, a certain degree of danger in the instrument itself for patients with a limited capacity to absorb and integrate the material that the analysis brings to the surface.

DR. LAWRENCE S. KUBIE: Dr. Zilboorg's paper demonstrates with unusual clarity the difference between the analytic method and even the most painstaking

and conscientious efforts to assemble an accurate history by nonanalytic means. Dr. Zilboorg's patient was an only child of intelligent parents who had been closely observant of the situation for years; yet all that they could tell, and all that the patient himself could tell at first, was that for five or six years he had been practicing a perversion. Under analysis a story developed that reached backward to his third or fourth year. Beginning with the episode in the laundry, a whole series of important events unrolled: his sleeping in his parents' room, his mother covering him with her fur coat, the onset of masturbation, the disappointment at the age of 10 years, the neurosis at 12 years, etc. A wealth of significant details is brought to light which reminds one of the difference between gross and microscopic pathology. In analysis one is in reality looking through a microscope.

This brings me to my second point, one that has no exact relationship to the case under discussion, but which I mention because it may make the method of analysis seem a little less alien to a group of neurologists. I have in mind the fact that the fundamental method of psychoanalysis, that is, the method of free association, has a close relationship to the work of Pavlov. The essence of Pavlov's work is the fact that two impressions that impinge on the nervous system with a definite time relationship establish within the nervous system a functional (and presumably a spatial) relationship. The essence of the method of free association rests on the assumption that two ideas that arise in the nervous system in a definite time relationship must also have some functional relationship, one to the other. In short, the analyst maintains that if two impulses establish interconnections merely because they enter the brain at the same time, then two ideas that emerge from the brain together must also have some interconnections. This simple principle is the microscope through which the analyst looks.

Finally, to return to Dr. Zilboorg's case, it is well perhaps to underscore something that he has already emphasized, namely, that there is nothing essentially peculiar or unusual about this case, and that if one studies patients who have not actually developed perversions one will find traces of impulses of a similar nature.

DR. ISRAEL WECHSLER: I was greatly impressed by the excellence of the paper and the lucid way of presentation, but I am rather disappointed that Dr. Zilboorg did not speak more fully of the neurotic character. What he did was to read a paper on compulsion neurosis. Compulsion neurosis, in my opinion, is a disease that is not entirely curable. Despite the facts that psychoanalysis is the only form of therapy that has any success with compulsion neuroses, that it is the only method that gives adequate psychologic insight into the condition and that it does effectively remove many symptoms, I have yet to see a complete cure, although I know analysts assert that they have cured patients. To me the compulsive neurotic character represents a constitutional condition. I do not know whether and how much heredity plays a part, but I do know that the compulsive neurotic patient bears a close resemblance, both psychologically and clinically, to the schizophrenic patient, and while one can effect a certain degree of recovery by means of psychoanalysis, fundamental neurotic make-up is involved, which no amount of microscopic analysis (by the way, a happy phrase) can cure. I hope some day to present before this society a paper on the subject, but I may take a few moments to speak of some observations that I made. I have seen a number of persons with compulsive neurosis who have definite constitutional make-ups. Dr. Zilboorg rather rapidly slurred over the fact that his patient had feminine pubic hair. That may be of some significance. I have seen quite a number of women with compulsion neurosis who have a definite masculine habitus. Their hands are not of the tapering, soft-cushioned feminine type, but they have the large, spade hands of men. Some of these women have a little hair on their breasts and nipples and occasionally there is one with flat feet, which is rather uncommon in women. Such women also lack the supraclavicular pads of fat. Most of the patients with compulsion neurosis, contrary to hysterical patients, who are of the emotional type, are rather of the intellectual groups. Theirs is a logical (masculine), orderly type of mind, and the neurosis consists of overintellectualization. On the surface the problem is, or seems to be, an intellectual one. Perhaps there is some significance in the fact that when man "deteriorates" he

becomes feminine, and when woman deteriorates she becomes masculine. At the menopause some women develop masculine traits—a little hair on the face, a gruffer voice, etc. An aging man gets a piping voice; perhaps his breasts develop a little.

The French have used the word "degeneration" in connection with psychasthenia (compulsion neurosis). That is not a suitable word, because it has a moral connotation, but there is some substratum of truth. The French are excellent observers, even though they have been rather hesitant in accepting the modern dynamic trend of psychology. If we eliminate from the word degeneration its moral connotation, it is not an unsuitable term, and carries with it a useful and illuminating concept.

Without knowing exactly what constitution is, or precisely what neurotic character means, I should say that the pendulum has swung too far in the direction of environment, and away from constitution and heredity. Since psychosexual or other constitution is something that is inherited, the only thing we can do is to deal with the environment; therefore by all means let us direct our efforts to the analysis of the environmental influence, going back as far as early childhood; but saying that that is all there is to the story is to my mind a great mistake.

I hoped that the reader of the paper would say something about perversion. The difference between perversion and neurosis lies in this: in both instances there is regression to infantile levels, but in perversion there is little or no repression, and certainly no inner conflict. The neurotic person has his inner conflict; the pervert has accepted the regression and has solved his inner problem. Incidentally, Dr. Zilboorg has done a great piece of therapeutic work by converting the alloplastic into the autoplastic symptoms. Another point is that true perverts do not know that they are sick, do not admit that they are sick, and do not go to physicians. Most perverts do not go voluntarily to a neurologist. It is usually when they come into conflict with their social environment or with the law that neurologists see them. In connection with compulsion, and in reference to so-called degeneration, it is a remarkable phenomenon that perversions increase with age, often coming to the surface in the male after the age of 45 or 50, that is, when the heterosexual impulses weaken. It is a fact that penal institutions are full of men whose first crime was committed after the age of 50, and that that crime was in the sphere of sex.

To sum up these few words, I wish to stress that there is such a thing as an unalterable constitution, that compulsion neurosis bears the mark of a deep constitutional character, that it is akin to schizophrenia, and that as a type it belongs to the neurotic character group.

DR. ZILBOORG: I am grateful to Dr. Wechsler for his remarks, which are very stimulating. He says he believes in the constitutional nature of compulsive neuroses and schizophrenias; he appears to have very strong beliefs, yet he admits that he does not know what the specific constitutional factors are that are operative in these so strikingly individual afflictions. I do not know either. We both find ourselves, therefore, on the same plane of ignorance. I do not see any reason why we should stress so glibly the importance of this unknown constitution in mental diseases. Is it not true that in an epidemic of typhoid fever, cholera, plague or pneumonia, not everybody falls a victim to the raging disease? Those whose constitutions are stronger, escape unscathed. Medicine disregards constitution. This may sound a too strong and even unwarranted statement; yet is not the whole history of medicine the history of treating sick people despite their constitutions? As a psychotherapist I shy off from constitution, because it is a source of therapeutic fatalism and of medical nihilism.

As to a compulsive neurosis being an organic disease, that is another belief; in other words, a poor foundation for a scientific system. Dr. Wechsler said that I slurred over too hastily the fact that my patient showed a slight tendency to feminine distribution of pubic hair; in this physical characteristic he would see the stimulus in favor of an organic point of view. The trouble with such a point of view is that it looks like a neat bone of contention in the heat of an age-long argument. This should remind us of the fact that one of the greatest weaknesses

of psychiatry is the usual absence of control cases. It is true that many psychotic or neurotic men have a feminine distribution of hair, but do we know how many non-neurotic and non-psychotic persons have an abnormal distribution of hair? I had a patient who suffered from a depression and who married on recovery. She had the typical masculine distribution of body hair. She has recently given birth to a third baby, and continues to remain perfectly well. All this does not mean that I deny the importance of constitutional factors in the causation of pathologic mental conditions. I want merely to state that only after all biographic, that is, ontogenetic factors are accounted for have we a right to talk about constitution; otherwise we run the danger of making of constitution a sort of waste basket for our ignorance.

As to perversions, I should like to take issue with Dr. Wechsler at some other time. At present I wish merely to reiterate that perversions are sexual gratifications on an infantile, that is, pregenital level. The practice of perversions may or may not be accompanied by a conscious or unconscious psychologic conflict. Perverts who have failed to settle the inner conflicts that are associated with their sexual deviations are curable by psychoanalysis; those who have settled their conflicts and have accepted their perversions are probably incurable. That is the reason why some homosexuals can, and others cannot, be cured.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, April 16, 1931

SIDNEY D. WILGUS, M.D., *President, in the Chair*

THE QUANTITATIVE MEASUREMENT OF PUPILLARY AND LIGHT REACTIONS.

DR. LEO L. MAYER.

In 1915, Hess devised an instrument for the quantitative measurement of pupillary reflexes. The cases of numerous patients examined have been reported by both Hess and his pupil Groethuysen. In this country, Barkan and Adler have furthered the interest in Hess' instrument. Recently, Sander has perfected a simple but efficient model.

It consists essentially of a glass slide divided into an upper and a lower segment. The upper segment is uniformly darkened so that only 2.3 per cent of the light from a small bulb is allowed to enter the eye. The lower segment, however, is a graduated wedge allowing from 2.3 to 55 per cent of the light to pass through. An arbitrary scale on the top of the slide is graduated from 1 to 21. Number 1 allows 55 per cent of the light to pass through it, and varying percentages of light pass through until number 22 is reached, this last being the same as the upper segment. By means of a push spring the glass slide is raised so that the homogeneous part above gives place to a portion of the graded part below. It has been shown that normal reactions of the pupils, both direct and consensual, and also normal response for light perception fall in the range between number 16 and 21.

The method of examination is as follows: The patient is seated before the instrument with his head steadied by a chin rest and side braces. The round glow of the small lamp shining through a slit and the glass slide is focused on the eye. Beginning with number 1, decreasing amounts of light are momentarily released until they no longer elicit a reaction. This point is considered that of motor discriminative acuity. Certain precautions are necessary. A binocular loupe or similar magnifying arrangement should be used to watch for the slightest movement of the pupil. Also one must be sure that the patient is fixing a distant object so that the accommodation reflex or convergence reaction is not mistaken for the light

reflex. The consensual reflex is elicited in a like manner, the opposing eye being illuminated moderately by means of a flashlight.

It is believed that with these measurements, together with a knowledge of the visual fields, the condition of the optic nerve and other neurologic conditions, an inference as to the localization of a lesion may be made.

In order to complete a discussion of this subject, mention should be made of other methods of measuring the pupillary reflex. Engel, of Munich, has devised an instrument that regulates the strength of a lighted bulb in amperes so that varying candle powers of light are exposed to the pupil. Lehrfield, of Philadelphia, has a similar apparatus, but it is limited to only 3 degrees of illumination. The great advantages of the Sander instrument are in its simplicity and cost.

THE KLIPPEL-FEIL SYNDROME. DR. PETER BASSOE.

Roentgenograms of the neck showing the characteristics of this condition were demonstrated. The patient, a woman, aged 32, has practically no neck and was born in that condition. The mobility of the neck is greatly reduced, and the hair line on the back of the neck is at the last cervical spine. The head is large and tilted to the right and forward. The roentgenograms show the cervical vertebrae to be fused into a solid rod. The different segments can be made out, and it appears that the normal number of cervical vertebrae is present. The case fulfils all requirements for the "syndrome" established in 1912 by Klippel and Feil: (1) limitation of movements of the head; (2) low margin of head hair and (3) absence of neck, the head resting on the shoulders.

EXPERIMENTS ON THE USE OF THE SENSE OF TOUCH IN RELATION TO LANGUAGE. DR. ROBERT H. GAULT.

One hundred and twenty-four records of experiments on deaf subjects in the laboratory have demonstrated that when appropriately trained deaf persons are enabled to see the face of a speaker, and at the same time to feel the speaker's words through the teletactor, they interpret speech more accurately and completely than they are able to do as unaided lip-readers. The median superiority of results in dual stimulation over and above the results for lip-reading are 20 per cent. That is, for every 100 words interpreted by lip-reading alone, 120 was the median number interpreted by lip-touch reading.

For both scientific and practical purposes it is important to know what are the particular sources of the advantage of double stimulation. So far, our laboratory results have shown the following: (1) Of 120 pairs of consonantal qualities, the members of 35 can be discriminated better by the sense of touch alone than by the eye of the lip-reader alone. (2) Of 103 groups of homophenous words selected at random, the members of 95 can be discriminated by the sense of touch alone to at least 80 per cent of perfection. By the method of lip-reading alone discrimination of the same items can be made only on a chance basis. All that the subjects know in experiments on this and the preceding topic is that they are working now on this pair or group of stimuli and now on that. (3) In bisyllabic compounds the accented syllable can be localized much more accurately by the sense of touch alone than by the eye alone. This is true even of "A" grade lip-readers. Scores for lip-reading center around 65 per cent. Those for touch alone are centered about 85 per cent. (4) The emphasized word in the sentence is localized more accurately by the sense of touch alone than by the sense of vision. Scores for vision are in the vicinity of 70 per cent and those for touch in the vicinity of 80 per cent. (5) As means for discriminating between very short intervals of time, the sense of touch alone lags but little behind the sense of hearing alone. (6) The sense of touch slightly surpasses the sense of vision in the discrimination of the very short intervals of time that were employed in the experiments comparing touch and hearing. (7) The sense of touch is very crude as an instrument for discriminating pitches. Frequencies must differ from 5 to 10 per cent in the scale in order that they may be discriminated at all.

DISTURBANCES OF SPEECH AND PRAXIA IN ORGANIC LESIONS OF THE BRAIN. DRS. H. DOUGLAS SINGER and A. A. LOW.

Reviewing the records of the Speech Clinic of the Research and Educational Hospitals of the University of Illinois, Drs. Singer and Low found that diagnostic errors are very common in the speech defects incidental to the infantile cerebral palsies. Children in whose cases feeblemindedness or faulty speech habits had been diagnosed at a competent child guidance clinic were found on reexamination to present aphasias, alexias, apraxias or various combinations of these syndromes, consequent on a birth palsy or on a postinfectious encephalitis contracted in early life. This state of affairs was brought out with great force when a systematic survey was made of the children of the Jesse Spalding School for the Handicapped Children of Chicago. Many children who were found to suffer from some form of aphasia or a partial agnosia had been classed as feebleminded and treated as such. But when the children were, on the basis of their psychometric rating, placed in their respective subnormal classes, it was observed that they could not maintain even the reduced scholastic schedule provided. On the other hand, it was the general impression of the teachers that many of the "feebleminded" children exhibited, in their general appearance and in their behavior outside the classroom, a mental alertness that was in striking contrast with the diagnosis. It was the general conviction of the teachers, based on years of observation, that the routine psychometric grouping was inadequate for the purposes of class training.

An arrangement was made with the school authorities to have the children tested at the Speech Clinic of the Research Hospitals. One of the first children tested was a boy, aged 11, who had been at the school for two years. When admitted he was unable to say even a single word. After two years of training, the teachers had been able to teach him two words, namely, "yes" and "no." In view of the obvious futility of all speech training, the question arose as to what other training to substitute. When the boy was subjected to special tests, it developed that he was suffering from a partial word-deafness which rendered him unable to understand colors, numbers, numerical notions and right and left conceptions. To words connoting spatial relations, like "above" and "below," etc., he was partially word-deaf. Nouns, adjectives and verbs he understood well. The class of words to which he was completely or partially word-deaf were promptly understood when they were written on a slip of paper. In this case, the teachers were instructed to teach the boy by the visual route only.

Most of the patients with cerebral palsies tend to develop athetoid choreic movements. Aside from the grossly visible athetoid movements of fingers, cheeks and forehead, there is almost regularly present a fine quality of athetoid movements of the lips and tongue whenever these structures are innervated for the purpose of articulation. In order to eliminate these associated movements, a method had to be evolved for teaching the children how to effect a principal movement and to suppress all superfluous associated movements that had gradually grown around the principal movement. Thus, in order to pronounce the sound "b," the lips must be tightly pressed together and lightly protruded in the midline. While this is being done, the angles of the mouth must be kept in a fixed and relatively motionless position. But many children, when initiating the sound "b" innervate precisely the angles of the mouth and, instead of the desired principal movement of the center of the lips an associated movement of the angles of the mouth is started. This associated movement either vitiates the purity of the sound or obliterates it altogether. Another handicap to successful articulation is the partial apraxia of the lips and tongue which is frequently encountered among spastic children. In order to overcome the athetoid movements and the apraxic defect, a series of graded lip and tongue exercises were evolved, both against resistance and without resistance.

DR. PAUL SCHROEDER: We have known about Dr. Low's work for some time and have felt that there was a possibility of getting at speech difficulties. At

the behavior clinic we get some patients with speech difficulties, but as a rule they are associated with behavior difficulties. In that group there are instances of cerebral palsy.

In regard to the statement that the question of the child's intelligence cannot be left entirely to the psychologist, we wish to support him and state that we do not as yet know from the members of our psychologic staff to what extent the intelligence quotient is influenced by education or lack of it. We find many borderline persons in this group, and the fact that they do not progress is the basis for exclusion from school. We believe that greater leeway should be given such a child and that further tests regarding intelligence should be made than are ordinarily included in the psychologic tests.

DR. MARY E. POGUE: Several years ago, I was asked to make a survey of the rooms for subnormal children in the Chicago public schools. There are probably 5,000 in this special division, including the ones who are still in the usual graded rooms and who are waiting to be transferred.

Our laws are such that children are obliged to remain there until the age of 16. This is a good law, but there is a question how well it works for the subnormal child. Public schools are for the greatest good to the greatest number. If these full grown boys and girls are forced to remain in the subnormal division up to the age of 16, surely we ought to have something more to offer them.

I asked the various teachers with whom I came in contact in this division what happened to these children when the school doors closed behind them, and the answers I received, almost without exception, were that fully one half of them went to work. There is no follow-up, and it is not known what the subnormal children find to do in the community. I know of no place in the United States where there is such a follow-up. Surely, if one knew what these children find for themselves, one could better fit them to take their place in the community.

DR. RALPH C. HAMILL: I have seen two children recently whom I suppose might come in this class, though neither had had infantile cerebral palsy. One patient, a boy, aged 11, read only at the level of the first grade. The case proved to be only a fear situation. This was cleared up, and within a week he was reading at the level of the sixth grade.

When a baby brother was brought home from the hospital, another patient, a girl, aged 3½, promptly began to talk baby talk. She recovered from this and began wetting the bed; this was remedied, and she began talking baby talk again. Obviously she did not wish to talk well. I think that this phase must be kept in mind, because children are so suggestible. In the examination procedure it is easy to find a fault and attract the child's attention to it and have the child then persist in that fault as though it had an organic defect, although such a defect is not present at all. When it comes to the finest form of examination, such as curved letters and straight letters, I confess that I cannot think that there is some element in the brain that has to do with curved letters as against straight letters.

DR. SIDNEY D. WILGUS: One of the school principals in Rockford has a large group of such children, and he recently made a social survey of a group of children who had graduated, with interesting results. I think that few of them had encountered social difficulties, some were earning good salaries, and most of them seemed to be doing very well. I think that a coordination of all of the studies made would be very valuable.

DR. A. A. LOW: With reference to Dr. Schroeder's remarks, I emphasized that the psychologist is more than willing to do his share in testing spastic children; it is the neurologist who has stood aside. Dr. Hamill, if I understood him correctly, meant to suggest that some of the speech symptoms found in such children might be of a functional nature. While this is true, it is comparatively easy to make the differential diagnosis and to establish which of the symptoms are functional and which organic.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

April 14, 1931

An Initial Visit. Dr. Philip R. Lehrman, New York.

In his paper "Bemerkungen über einen Fall von Zwangsneurose" printed in 1909 and translated in English as "Notes on a Case of Obsessional Neurosis," Freud wrote the following footnote: "Dr. Alfred Adler, who was formerly an analyst, once drew attention in a privately delivered paper to the peculiar importance which attaches to the very first communications made by patients." Freud then discussed the patient's opening words which laid stress on the influence exercised over him by men, that is, on the part played in his life by homosexual object-choice; but immediately afterward, the opening words touched on a second motif which was to become of great importance later, namely, the conflict between man and woman and the opposition of their interests.

The instance that I shall report is that of a first interview at the home of a patient whom I had no occasion to see again. I have chosen this example in preference to the initial visits of my regular patients under analysis, for obvious reasons.

In February, 1931, a young woman telephoned to ask if I would call to see her sister. With marked anxiety in her voice, she told me of her sister's invalidism and detailed many of the physical symptoms, but would not tell who she was, where she lived, or who had referred her unless I promised to make the visit. I could not make the promise until I knew how far I would have to travel. The same woman repeated the same request on two successive days, adding more symptoms each time and telling me, as if by way of warning, that many great specialists had failed in her sister's case; she was still reluctant, however, to tell the whereabouts of the patient. Finally she told, again as if by way of warning, that their home was located in a far section of another borough; I then said that I would make the call at 7 p. m. She gave her name and address, but called a few hours later to plead that I make the call earlier because the suspense of waiting for me was causing her sister much suffering.

When I arrived at the originally appointed hour, a woman in the early thirties answered the door bell and escorted me to the parlor by way of the kitchen, where a young man sat at a table. Though facing me, he kept his eyes on a book and made no sign of greeting me. The young woman introduced herself as the sister who had called me, and informed me that she was a few years older than the patient, who was the youngest in a family consisting of one brother and four sisters. The parents were dead, the father having died fifteen years ago and the mother last year. Since the mother's death, the youngest sister had had a complete collapse, had been in bed most of the time, and for the past few months had become so much worse that it was necessary for my informant to resign her position in order to nurse the patient. The latter had to be catered to every minute of the day because she suffered much physically; as a result of this preoccupation with the patient, the sister-nurse lost much weight, and the home was neglected. The shabbiness and untidiness attested to this neglect, and the broken furniture and bare floors were evidence of prevailing poverty. She indicated that her sister was in the adjoining bedroom, but when I made a gesture to enter she insisted that I listen to her first, as the ill sister's poor memory was not equal to recalling all the facts. In her hand she held a few sheets with stenographic notes and began reciting the profuse physical symptomatology of an illness that spared no organ. The minutest detail of each physical symptom had to be described, and there were many repetitions of her own sad plight and sacrifices since her sister's illness. As if to cover up some other guilt, she confessed that she had not been quite truthful when she told me that she was the next youngest in the family to the patient, who was 27, for her brother, whom I had noticed on my arrival, was 29, two years younger than the informant, who was 31 and not merely two years older than the patient as she had first told me.

I now edged my way into the sick chamber and in the semidarkness saw a woman, well fed and reclining in bed. Though her hair was disheveled and evidently not so well cared for as one might expect since she had such a constant attendant, she was by far the prettier of the two sisters. She was smiling, and no sooner did I engage her in conversation than the sister interposed herself between me and the patient and interrupted to tell me of a peculiarity that she had neglected to mention, namely, that the patient must eat the moment she felt hungry, and that unless food was given her immediately she had a weak spell that caused intense suffering. The sister, she impatiently continued, was now showing all the signs of this peculiar hunger; then, as if by a magic gesture, she brought a chair to the bed on which were several plates containing a well prepared dinner. Furthermore, she feared that her sister might not be able to eat in my presence, and that the inevitable weak spell would occur. The patient, however, did not seem to comply with what appeared to be her sister's wish, and proceeded to eat with apparent good manners. The sister then addressed her directly and, as it were, commanded her to agree that she could not eat unless she were left alone. Once more I was in the adjoining room listening to the sister's recital of physical symptoms and signs. She warned me that the sister ate very slowly, and that I must be prepared for a long wait.

It became evident to me that this sister was attempting to monopolize the entire time that I had allowed for the call, and that by devious means she would frustrate my examination of the patient. I gathered that she had used the same tactics with many physicians whom she had called. It became clear that her dilatory manner and the warnings on the telephone were means with which she attempted to discourage my visit, but since I was there, she tried to keep me away from the patient. To this end she exploited her sister's polyphagia as a last resort, for she had had ample time to serve her sister's dinner before my arrival. She betrayed herself by the following remark: "Doctors may think I don't let my sister get well"; when I questioned her, she readily admitted that no one had ever made such a statement. It was distinctly her own inward awareness of her own ambivalent attitude. I determined to outwit her, and at her next uncertainty as to some detail of a symptom, I suggested that her sister might enlighten us about it, and I promptly entered the patient's room. Once there, though the sister was close on my heels, I politely but firmly demanded that I be left alone with the patient. She stepped out reluctantly, and I shut the door and obtained the patient's story. She was cooperative and agreeable, and as frank as possible for a first visit.

Briefly the case was one of hypochrondriacal depression following the mother's death one year previously. The illness was a continuation of her mourning state. A few months prior to the mother's death, a physician who called regularly on the mother, who was suffering from diabetes, discovered that the mother had a cataract. No sooner was this diagnosis announced than my patient became immobile, as if petrified, and had a weak spell. She said, "I saw death, nothing but death." She resigned her position as secretary to a prominent attorney in order to nurse her mother better during the terminal illness. The mother died, and when my patient returned from the funeral she had a bowel movement that weakened her so much that she had to go to bed; there she had remained since. The bowel movements, with the same effects, had occurred three or four times daily, and the weak spells could be averted only if she ate something. In the past few months the weak spells had occurred also when there was no bowel movement, and the sister had had to quit work in order to be ready with food whenever a weak spell threatened. During these attacks she had had all the sensations of dying, and as a result she moved about slowly if at all. At the beginning of the illness she made several attempts to dress herself, but that took many hours.

She talked complacently about her illness and about the various members of the family; when she mentioned the oldest sister, however, her countenance changed; her smile disappeared, and she became visibly angry. The oldest sister, who was 40, had become a widow fifteen years before and had returned to live in the parental home. She had an infant son, and the patient, who was then 12, assumed full charge of the infant. She said, "I was better than any mother to

him." The father's death occurred at about this time and she "found something to live for" in bringing up this infant. The oldest sister was unappreciative of this attention, which relieved her of any responsibility toward her son, and became actively hostile to my patient; rather, the patient felt this hostility, though there was no clearcut evidence of it and she could not relate anything specific. She felt this hostility no matter what task she was engaged in at home; while practicing at the piano, she would overhear her sister pass some remark, not about her or her playing, but about something in general. This would upset her as much as if the remark had been directed at her, and she would not be able to continue playing. Here the patient showed all signs of once more living through that episode and said emotionally: "She got the best of me. It is she who got the best of me. I believe she was jealous of me." These irritations made her ill at that time. She had a feeling of choking, burning sensations on top of the head, and palpitation and sensations of hot and cold all over the body. Also, the hips somehow got out of shape, and this distortion baffled many physicians. However, she finally recovered. In her present state some of the former anxiety symptoms reappeared.

A cursory physical and neurologic examination revealed nothing pathologic.

From the impressions that I have reported here as faithfully as my talents permit, I shall discuss the case psychoanalytically. Most obvious is the nurse-sister's ambivalency toward the patient. This manifested itself in sacrifice, which she regarded as a help to the sister, and in the subtle manner with which she defeated any attempt to help. Over the telephone she had given evidence of this duplicity. She called for help, but at the same time delayed giving the whereabouts of the patient. At home she attempted to monopolize the time that belonged to the physician and patient. As in this she was partly successful, her unconscious guilt became intensified, and she was compelled to confess the crime in order to ease her conscience. Instead, she confessed that she had lied about her age. In the lie, however, she displaced the brother (who accepted this elimination by his manifest indifference) and the youngest sister instead of the brother became her rival. In the nursery it is a common observation how the young child behaves toward the new-born. By all manner and means he attempts to distract the parental attention from the new-born rival. In this home there was once more a situation, the prototype of which had existed long before: The youngest sister, helpless in bed, regressed to an infantile oral level, demanding constant attention for her polyphagia, which was gratified by this sister-nurse. The sister-nurse-mother rôle served to keep in repression the original hostility toward the younger rival. The hostility betrayed itself, though, in the remark: "Doctors may think I don't let my sister get well," which was a confessed projection of inward guilt. The sister-nurse, ridden with guilt, now expiated by sacrificing herself as a nurse; but in this rôle she maintained the younger sister in a state of helplessness and removed her as a rival on an adult basis.

The patient unconsciously seemed to be aware of this hostility, but spoke of it as belonging to the oldest sister, when she said: "She got the best of me; she is jealous of me." She had had an intimate acquaintance with such hostility, for she herself had experienced it when after the father's death her oldest sister, the widow, brought the infant to her home. At that time, during puberty, she reacted to it in a characteristic fashion. The love made vacant by the father's death was transferred to the infant nephew, and the hate for the new rival was projected to the oldest sister whom she displaced as mother. But even then something went amiss in her solution of the Oedipus conflict: Illness of an anxiety state occurred.

In the present illness, which obviously was a reaction to the mother's death, the hypochondriacal depression followed the mechanism described by Freud in his paper "Mourning and Melancholia" (1917). There was the special characteristic of melancholia, a regression from object cathexes to the still narcissistic phase of oral libido. But whereas in the nontransference neurosis of melancholia there is a refusal of food, in this patient's polyphagia the object was devoured and expelled anally. The actual oral-anal sequence was reversed, though, in the patient's symptoms. The more one considers the level to which the patient's ego had regressed and the narcissistic identification in the object-cathexis which

still persisted, the more one is inclined to consider the gravity of the illness. The patient's erotic cathexis of her lost mother as an object underwent a twofold fate. Part of it regressed to identification, but the other part, under the influence of the conflict of ambivalence, was reduced to the stage of sadism. By means of this sadism she developed weak spells, which on the one hand enacted the mother's death and on the other served for self-punishment. But the sadism was utilized for another purpose: to vent her hate against the nurse-sister, whom she had enslaved by demands for constant attention and whose sense of guilt she had exploited for this manner of punishment. Thus the illness involved both sisters, and the question arose whom to treat first.

In this mutual neurosis one sister complemented the other as in a Shakespearean drama (Ludwig Jekel); the character was split up into two personages, each of whom then appeared not altogether comprehensible until once more conjoined with the other. This mutual neurosis was a reaction to a mutual guilt. The patient expiated in her dying spells, and the sister expiated in her nursing. The physician (as the brother) was excluded, as a man only intensified the unresolved Oedipus complex. For the death of the mother both sisters felt guilty, and in this relationship toward each other both had found means for restitution and expiation, as in "The Brothers Karamassoff" all the brothers share the guilt of the patricide, though the actual deed was committed by a fourth and illegitimate son.

In conclusion, I may point out that the initial interview is replete with material that is of importance to the physician. The direction of the illness, its epinosic and paranosic gain, often becomes transparent, while the deeper structure of the neurosis is subtly indicated and can be utilized for prognosis.

Besides what the patient unconsciously shows, the person who is his steady companion is usually involved in the neurosis. This person is the target for the neurosis, or he is the surrogate for those at whom the neurosis is directed. But his rôle is not only passive; he has an investment in the patient's illness and will frustrate any attempt at liberating his hold. However, this system is not impenetrable, for it betrays itself by the elaborate cloak of "best intentions" which the psychoanalytic method has learned to uncover. This is the first resistance to any analysis, and every patient exploits it. In the first visit it is therefore necessary to maintain a strict analytic technic, and the less the patient is questioned for data for the record file the more he will reveal of his real problem. Also, one is thus able to test the strength and nature of the patient's resistances, and the capacity of his ego to make another adjustment. One must bear in mind that the patient comes not for a cure in the popular sense of the term, but for gratification of those components of his instinctual trends which is denied him by his environment, as well as by part of his own psychic organization. The illness is not only satisfactory to part of the patient's mental organization, but one must reckon that it is a way out also for the patient's parents, siblings, spouse or sweetheart, and at times, even for the family physician.

COMPLEMENTARY NEUROSIS IN A MARRIED COUPLE. DR. CLARENCE P. OBERNDORF, New York.

Although a neurosis in either member of a married couple inevitably becomes a source of unhappiness to both, often both members may have entered marriage while suffering from neuroses. Occasionally these may complement each other, welding a series of individual abnormal reactions into a compact abnormal mass; but, on the other hand, the symptoms manifested in the neurosis of one may so clash with those of the other that life becomes intolerable. I shall report a case of the latter class.

Mr. and Mrs. B. had been advised by their lawyer to obtain a divorce. Their family physician suggested a psychiatric consultation primarily because of recurrent physical symptoms in both husband and wife for which he could find no organic basis.

To interpret the marital impasse it is necessary to retrace historically the situations accountable for it in each patient. Mr. B., the third child in a family of four, had been raised in orthodox traditions. From childhood, he had been extremely devoted to his mother and overconscientious. The latter characteristic

was associated with a masturbation conflict. The patient's social contacts with both men and women had been extremely limited. His indulgence in heterosexuality prior to marriage had been infrequent and as a rule not satisfactory. Previous to his engagement he had had no love affairs.

Mrs. B. was the second child of a family that lived in poverty during her early childhood. Her mother, an ambitious, hard working woman, constantly berated her husband for his indifferent commercial success. Her older sister was a smart, tricky, sharp, quick child. As a very young child, Mrs. B. had been dubbed a "dumbbell," but she thought that her mother's idea of her stupidity was due to Mrs. B.'s fear, as a child, of expressing herself because of the reprimands with which her mother immediately greeted her opinions.

A trauma at the age of 6, when she was masturbated by an uncle, added to her preexistent self-consciousness and feeling of guilt. Moreover, a vaginal discharge developed for which she was taken to a physician who scratched the lip of the vagina with the end of the slide in making a smear. From that time on, the patient's mind apparently was closed to any vaginal impressions of sex, and the rectum became fixed in her mind as the sexual and forbidden organ. She developed into a good little girl and continued to act as such; her voice retained its childishness at the age of 33, when she began treatment. As though enveloped in a haze, she passed through school, became a teacher, married and bore children, as she says, "without knowing what it was all about."

Mrs. B.'s younger brother, an unusually bright boy, was always praised by the mother and before long Mrs. B. fixed on him as an ideal. This ideal had developed into a firmly fixed masculine identification. Her desire to dominate her husband, her frigidity and her criticisms made life intolerable.

Mr. B. was unconsciously extremely subservient, and overcompensated this trait by a pompous reserve. Just before entering marriage he was rudely disillusioned concerning the love which he believed his mother felt for him. He hoped to secure from his wife in marriage that type of maternal affection which he craved. To that end he unconsciously assumed a docile, feminine attitude which he thought might propitiate his wife. With each member unconsciously assuming an inverted rôle, while consciously attempting to sustain the normal one, their marital life from the beginning was a constant brawl. Their differences extended to every detail of the household, but especially to the rearing of the children.

Their analyses were undertaken concurrently at first. The husband improved more rapidly than the wife, who continued under treatment for over three years. A marked alteration in their sexual relations, reflected in a better social relationship and the disappearance of many neurotic conversion symptoms in each patient, followed analysis.

THE PRESENT STATUS OF PSYCHOANALYSIS AS A PSYCHOLOGIC AND THERAPEUTIC SYSTEM. DR. FRANZ ALEXANDER, Chicago.

Psychoanalysis started as a therapeutic attempt of Freud and Breuer to cure cases of hysteria by psychotherapeutic measures. In the course of thirty years a consistent theory of the personality developed. The explanation of this development is given in the unique coincidence of the aims of research and therapy in this field. Even at the time when Freud still used the method of cathartic hypnosis, the reconstruction of the history was the crucial part of the therapy. More and more the aim of therapy became that of making unconscious mental content conscious, which is synonymous with the reconstruction of certain situations in which repressions took place. Psychoneurotic symptoms evinced themselves as manifestations of such mental content, which the conscious part of the personality refused to accept. The relief of psychic tension, however, is possible only through "passage" through consciousness. Therefore, the aim of therapy was to make repressed tendencies conscious.

The goal-conscious technic of relief from repressions must be based on knowledge of the psychic mechanism of repression. After this insight had been established, the whole development of psychoanalysis was directed toward solving the psychologic problem of repressions. This solution was due to the invention of the method of free association, which is also the basis of dream analysis. Dream

analysis has proved to be the way of obtaining the deepest insight into the interplay of repressing and repressed forces.

Repression is due to a kind of unconscious selective and controlling function acquired by the personality during development. The selective principle of repression follows the code of education conveyed to the individual. The inner representative of this code is the super-ego, an especially socially adjusted part of the personality. The function of the super-ego is automatic and preserves the atmosphere of the playroom. Neurotic symptoms are results of overstressed repressions. The aim of the psychoanalytic technic is to replace the automatic control of the super-ego with the conscious judgments of the adult ego.

This technic is realized in psychoanalytic therapy. The method of free association brings unconscious mental content into consciousness. This process is supported by the emotional attitude of the patient toward the analyst. The analyst undertakes the controlling function of the super-ego, that is, the rôle of the parents toward the child, since the super-ego is an introjected image of the parents. Through the analysis of the emotional reactions of the patient toward the analyst (transference manifestations) it is possible not only to reconstruct the conflicting situations of childhood but also to help the patient to a reorientation toward the same conflicts.

The quantitative principle of psychoanalysis is: 1. The manifestations of transference are repetitions of the original conflicts, but repetitions in smaller psychic quantities. 2. Whereas the original infantile conflicts met the weak infantile ego, in the manifestations of transference the same conflicts meet an adult ego which has greater chances to solve them.

In the indications for psychoanalytic therapy one has to consider these circumstances. Suitable cases for psychoanalytic therapy are only those in which one can assume a well developed ego which will be able to face the unconscious repressed forces. For cases that do not fulfil these requirements another technic must be found which contains a kind of ego-education as a preparatory treatment for the proper analysis. The significance of the psychoanalytic technic lies in the fact that it is based on psychologic knowledge of the processes underlying the therapy, which distinguishes psychoanalysis from all present forms of psychotherapy.

DISCUSSION

DR. J. RAMSAY HUNT: As I listened to Dr. Alexander, the first professor of psychoanalysis in this country or I believe in any country, I could not but think of the extraordinary development that has taken place in this field since those early studies of Freud in 1892. It will be remembered how Freud returned to Vienna to practice neurology after graduate study in the Charcot clinic, where the psychogenic conception of hysteria had its origin. Here began his association with Breuer, whose early investigations of hysteria marked the beginning of the great movement that is now known as psychoanalysis. Freud has continued slowly and methodically, without interruption, his study of mental function, based on empiric observations, the formulations of which today constitute the foundations of psychoanalysis. These formulations have had, and are still having, a profound influence on psychiatry, sociology, academic psychology and, indeed, on the thinking of everyday life. It is an amazing contribution for one man to have made, and in my judgment the most important that has been made in our time to the field of psychologic science.

I shall emphasize only two points that I have in mind. One concerns the present status of psychoanalysis as a psychologic system. Psychoanalysis has gradually expanded into a large psychologic system with complex formulations and a new nomenclature.

This is what usually takes place in psychology and forms the basis of a new school. Such formulations, however, are based on personal interpretations, are often more subjective than objective and are not always susceptible of final proof. This is certainly true of many of the interpretations of psychoanalysis, especially in the sphere of the dream and the symbol. Whether these formulations of psycho-

analysis will stand, no one can say now; certainly, not all of them, for many are merely new terms for old recognized expressions of mental functioning.

Freud himself has said that psychoanalysis will not have arrived as a science until it is accepted by academic circles in Europe. He realizes that recognition from other sources will have to determine the future position of psychoanalysis as a psychologic system. When that time arrives, however, no one can doubt but that a large body of important facts will be taken over and incorporated in any psychology of the future.

My other point is in regard to the present state of therapeutics in psychoanalysis. I am not sure that it has advanced as much as had been hoped. It has been spread too thin, and what Freud—who early sensed this danger—called wild analysis is rampant in both lay and medical circles. I believe that in this country the mistake has been made of using psychoanalysis—or what is euphemistically called psychoanalysis—in too many different kinds of cases. Psychoanalytic therapy is in somewhat the same state as polyglandular treatment in the endocrine field. Every patient that comes to some psychoanalysts appears to be regarded as "grist for the mill," and these patients are subjected to psychoanalysis, whether the condition is psychic or physical. Even mental deficiency and the organic epilepsies are subjected by some to its healing powers. I doubt whether this should be called psychoanalysis. It is rather a study of a case by one who is interested or proficient in psychoanalysis. I believe that the time has come to be definite in understanding what psychoanalysis is. It is a difficult and highly technical procedure, requiring a great deal of time and skill, and its application should be limited to a carefully selected group of cases. I think that the leaders in the field should make this clear and not let the idea prevail that almost any patient can be treated by psycoanalytic methods by almost any one who has been analyzed and has a smattering of psychologic knowledge. The human mind is too important, and I believe that psychoanalysis is too important a method, to be reduced to such a level of activity.

Dr. Smith Ely Jelliffe: In phrases somewhat similar to Dr. Hunt's introductory remarks I wish also to say that I am not a psychoanalyst. What do I mean thereby? I mean that if, for instance, I have to do some minor repairing of the water pipes in the house, I am not a "plumber," although I believe that a good plumber is the only person who can do the job properly. If I should have a patient with malaria I should certainly give him some quinine, but because I gave him quinine I would not necessarily be a "quininologist." For certain disturbances there is only one thing that really amounts to a tinker's execration. In that sense I am a thoroughgoing "psychoanalyst." I am firmly convinced that the outline that has been given here is a thoroughly scientific procedure so far as the formulations have advanced. All formulations, however, are in the process of being made and only a fool thinks that he knows everything at the present time.

With the application of the psychoanalytic principles it seems to me that one gets an extraordinary insight into individual difficulties. I shall therefore present a couple of thumb-nail sketches, illustrative of some of the principles that Dr. Alexander has elaborated.

A brakeman from Portland, Oregon, came into my office once. He told me that every month he had a severe depression, so severe that he wanted to commit suicide. It lasted for four or five days, and he was prompted to throw himself off the train on which he was a brakeman. This was very interesting. I said, "Well, when did it begin?" Mind you, this was early, the first hour, and Dr. Lehrman has told us something about the importance of the first hour. "Three weeks after my mother died" was the first statement he made. His father had been thrown off a car and killed by a railway train, the way the patient wanted to commit suicide. For ten years he had had an attack every month. In a few minutes I learned that the attack occurred not every month, but every twenty-eight days. This, with minor details, occupied practically the first hour. I said, "Bring me some dreams." The next day he told me some dreams. Mind you, he was a brakeman on a railroad—not one of these highly intelligent college professors who are the hardest to treat, but a very simple person. We talked about the dreams. We learned that every twenty-eight days when his mother menstru-

ated she had an attack of depression lasting four or five days. When he lost his mother he kept her by having similar attacks of depression. I saw him twice. Five years later he wrote and told me that he had not had any further trouble since his talk with me. This may have been a miracle and it may not. It shows that simple people who do not have many obfuscations may require only simple explanations. It was only necessary for him to see the way by which he sought to hold on to his mother, and he said to himself "cui bono?"

A girl, 24 years of age, charming and talented, was brought to me by a fellow practitioner in this city. She had a terrific pain in the back. She had had shoes to lift up one leg, special corsets, etc. All sorts of things had been done for her. I talked to her and asked, "When does it bother you most?" "When I play the violin," she said. "When did you first notice it?" "When I was playing the violin." "What were you playing?" "Let me see. I don't know." "Just tell me what comes first to your mind." "Wagner, I believe." "What else?" "Siegfried." "What else?" "A quarrel between Hagan and Siegfried." "Yes, and what happened to Siegfried?" "He got stabbed in the back." "Who is stabbing you in the back" "I don't know." "Think." Dr. Alexander has spoken of some of the conflicts that might be in consciousness in the ego system. It did not take us more than the hour to find out that a favorite sister was trying to stab her in the back. This sister was trying to steal her sweetheart, and had nearly succeeded. We talked it over. I asked her if she was going to allow her sister to steal her sweetheart and not make any effort to prevent her? She said, "I want the man. I had him first. I am going to have him!" She got him, and she got well promptly.

The "Short History of Julia" is an interesting story by Isa Glenn. Julia was a nice southern girl with a "nice" super-ego. She had been told by her mother always to give her little sister what she wanted. She gave up her lover to her younger sister. At 40 years of age, she again fell in love. The daughter of the little sister ran away with her new beau. Julia went on being a charming, attractive maiden aunt just because she let not only her little sister but also a little niece run away with her beau.

I have found it useful at times, when people say they do not see anything scientific about psychoanalysis, to ask them if they have ever seen a rainbow? What causes a rainbow? Some primitive people do not know. Some persons have no knowledge of the fact that light can be broken up, i. e., analyzed, into its spectral parts. It is not enough, however, to know that light can be broken up into its primary colors. Just step into an astronomic laboratory. The scientist says that there is hydrogen in the atmosphere of a certain star millions of miles away. How does he know that there is? He says that the spectroscope has analyzed the light from that star. He can see such and such Frauenhöfer lines; he can tell whether there is iron, calcium, etc., in the star. One goes away bewildered and wonders how the spectroscope can do so much. Similarly, psychoanalysis is an instrumental device for the analysis of the make-up of the personality, as the spectroscope is a technical method for the anlysis of the spectrum of ordinary white light. The human personality is highly complex and difficult of analysis.

These two sketches, however, have their counterpoints. One sees many patients who come day after day, week after week, month after month and year after year, not only to me and others practicing psychoanalysis, but even to Freud. I remember not long ago I was in Vienna and entered into conversation with the captain of a certain hotel restaurant. Freud's name came up, and this man wanted to know something about him. I asked him why? He said that a certain man who had been there for four years was a patient of Dr. Freud. What was the matter with him? "Well, when he first came here he used 400 towels a day and now he uses only 25." This was a typical washing phobia—four years spent on a patient with a washing phobia by the master himself! I once had a patient who had been treated by physicians in this city; for fourteen years they had passed sounds, and for eleven years more they had massaged his prostrate. He had had twenty-five years of this kind of treatment by reputable genito-urinary specialists for a neurosis. If I could not do more for a neurosis, no matter how severe it

was, in twenty-five years I would give up and begin to do plumbing. He is but one, of I hate to state how many, I have seen in the same predicament.

I have told this story before, but it interests me and I am going to tell it again because it illustrates what credit the analyst gets for having cured or at least helped a neurotic patient. Persons with a neurosis are peculiar, and I might quote what the Quaker once said about other people.

While in Paris in 1906, I had a telephone message that some one wanted to see me. I went and found a man sick with an asthmatic attack. One of the interesting things about psychoanalysis has been the precision that has been brought about as to the dynamic nature of a difficulty. That is what is called nosology or diagnosis, although psychoanalysis is not primarily interested in nosology; it is interested in dynamics. Nevertheless, nosology comes into the survey. So it did not take fifteen minutes to ascertain that the gentleman had a typical anxiety neurosis, which showed itself as an asthmatic attack following sexual frustration. His attacks would come on within seventy-two hours after coitus interruptus. I talked it over with him and his wife. I spent four hours on two successive days explaining the whole business. They listened. I did not see them again. Ten years later, in a hotel in Santa Barbara, Calif., some one bowed to me as I walked out of the dining room. Out in the lobby the patient came up to me, shook hands and said, "You don't remember me," I said, "Wait a minute—Paris—asthma." He said that was right, and we had a little chat. I later asked him how the asthma was? He said that in Paris he had found the "finest pink medicine," and that ever since then he had not had asthma. Those are the thanks that one usually gets for results of therapy in psychoanalysis.

Dr. A. A. Brill: Dr. Alexander gave a full résumé of everything that has happened in psychoanalytic development. As I listened to him, I thought of 1908 when I followed the same course before this section, when Dr. Pritchard was the chairman; at that time we did not have the ego and the id, and a number of other formulations that have been developed by Professor Freud since. I was particularly impressed by what Dr. Alexander told of his own contribution to the development of the ego, namely, the bribing of the super-ego. I shall take a few moments to tell you how this bribing of the super-ego may show itself. A patient was obsessed by murderous thoughts toward her mother, to which she reacted with all sorts of obsessive reactions—washing, etc. She had been coming to me for about a year. While the Snyder-Gray murder case was tried in New York, she attended the trial every day. She lived through every detail of the crime. Each day she reported everything to me. When the murderers were condemned to die, she was much affected. On the day when they were executed she was much depressed and cried. The next day she told me that she was perfectly well. All her symptoms had disappeared. She refused to see me; she telephoned that she needed no treatment. I had had enough experience to know that this cure would not last, and that she would come back. Here was a clear example of the mechanism of bribing the super-ego. By living through and identifying herself with the criminals she bribed her super-ego, and for a while could free herself from all her symptoms.

Dr. Alexander: If one wishes to formulate or characterize the position of psychoanalysis in the realm of psychotherapy—and this especially concerns the remarks of Dr. Hunt—one can best express it by emphasizing the fact that the psychoanalytic cure is based on knowledge of the underlying psychologic processes, whereas all other psychotherapeutic methods, whether successful or not, rely on vague empiric observations that certain things help the patient.

Quinine was used for malaria before one knew of plasmodia. The Indians employed quinine for malaria and cured it. Nevertheless, in organic medicine a process of therapy is considered scientific only if it is based on knowledge of the underlying physicochemical processes. Similarly, psychoanalysis can be considered the only scientifically founded psychologic therapy among the psychotherapeutic methods, because it is a goal-conscious procedure based on knowledge of the psychologic processes underlying the cure.

Book Reviews

DIE PROBLEMATIK DER SPRACHHEILSCHULE IN IHRER GESCHICHTLICHEN ENTWICKLUNG. By KARL HANSEN. Price, 3.60 marks. Pp. 100. Halle: Carl Marhold, 1929.

The author considers his discussion under six main heads: (1) cultural and historical conditions back of the public work in correction of speech in Germany, (2) basic presuppositions for the program for public speech correction, (3) courses for the correction of stuttering, (4) classes and schools, in a strict sense, for correction of speech, (5) extension of work in correction of speech and (6) the nature of correction in foreign countries.

Courses and classes in correction of speech owe their existence to general social and cultural conditions. Work in correction of speech is only a branch of other types of corrective work, such as that for the blind, the deaf and dumb, the feebleminded and the crippled. It dates from the first half of the nineteenth century as a part of the political life of the times. Its basic principle was the development of a sympathetic attitude toward the person with a speech defect who presented an abnormality that was remediable. Early in the beginning of an interest in this field the religious schools carried on the bulk of the work. Private gifts, although amounting to a great deal, were insufficient to care adequately for the speech-handicapped children. Organized state support was the real solution to the problem. In 1919, the German government issued an article to the effect that youth is to be protected against exploitation and neglect and that the state and community must promote means to assume the responsibility for such protection.

Although Gutzmann, in 1874, gave a great impetus to work in speech correction, interest was relatively slack until recently. The complete realization of what both the person with a speech defect and society suffer ushered in a greater development of both intensive and extensive corrective measures. The author presents facts to show the nature and degree of the handicap of a person with a speech defect in school, society, business and life. A person with a speech disorder must not be considered merely as defective in speech but as defective in his whole mental and emotional organization. His trouble must be viewed as arising from a whole system of disturbances. In general, environmental stresses and strains acting on a faulty constitution furnish the basis for the development of disorders of speech.

Granted that there is a problem here and that the state is willing to do something about it, are there sound corrective procedures to bring to its solution? The author feels that there are such procedures. It is possible to give normal speech to a large percentage of persons with speech defects. The Gutzmanns (Albert and Herman) were leaders in developing pedagogic methods for the understanding and management of cases of speech disorders. For stutterers, breathing, voice and rhythmic exercises and the practice of joining vowels and consonants were introduced. To 1900, practically all of the corrective work was carried out according to Gutzmann's methods. In realizing that all of the persons with defects handled were not being helped, and that some who had improved subsequently relapsed, an analysis was made of the whole speech corrective program. It was found first that the general environmental conditions (parent-child and parent-teacher cooperation, regularity in attendance, weather, etc.) were important. In the second place, although the methods used were largely physiologic, the psychologic factors were not inconsiderable. The spirit in which the exercises were given might be the most important single factor. A purely mechanical administration of the corrective drills appeared to be stultifying. The personal equation was felt to be a large factor in the success of the method. In the third place, the speech defect was frequently complicated by other defects, and unless the latter were properly evaluated and managed, uncertain results often obtained. The child must be treated as a whole.

The question of who should be responsible ultimately for the entire program is a tangled one. All factors considered, it seems best that physicians and teachers should work together.

Gradually, a variety of pedagogic procedures crept into not only the schools in different parts of the country but also the schools in any given community. Conflicting theories arose in regard to the nature and management of persons with speech defects, until today Germany has a great mixture of therapeutic procedures. However, the predominant idea in all of them is to treat the child and not the disorder. He must be considered as a biologic unit. A warning note has been sounded against hypnosis and psychoanalysis. The management of stuttering according to Nadoleczny may be of interest. He considers the method under the following heads: (1) voiceless articulation, (2) singing, (3) rhythmic speaking, (4) slow, monotonous, monodynamic, monotemporal speech, (5) repetitive speech, (6) after deep inspiration, the utterance of nonsense syllables as they may occur to the stutterer; (7) scanning or a staccato form of utterance, (8) full voice rising with the melody — dynamic, rhythmical cadence and (9) "legato" speaking. The author quotes M. A. Richardson in regard to the treatment of stutterers. The latter emphasized exercises that are intended to be merely vehicles for suggestion. The aim is to give the child self confidence by removing the phobia connected with speaking. Every lesson begins with a deliberate releasing of tension and a striving after complete ease and quietness. Autosuggestion, breathing exercises, rhythmic movements and mimic gestures are utilized.

Teachers use the regular school hours in correlating work in speech correction with school work. Reading, singing and writing are good subjects in which to join together these two types of work. The child may be required to associate writing and speaking. Persons with speech defects should, if possible, be given sound health. Swimming, gymnastics, dancing and open-air living are employed to produce health. Independence in thought and action should be cultivated. The joy of living and the desire for free and unhampered emotional expression ought to be acquired. Although many children may be handled profitably in a group, there is need for individual instruction. When handled in numbers, children should be grouped according to age, kind and severity of defect, level of mental ability and achievement in school. It is felt that children who stutter offer a real danger to normal-speaking children when the two groups are thrown together. The latter are apt to acquire certain undesirable mannerisms, if not real stuttering, from the former. Certain children who are inclined toward stuttering suffer most from associating with stutterers. When children are handled in the strictly speech corrective schools, as many as possible of the regular school courses are taught so that the children will not become retarded scholastically to any serious extent. Parents can assist greatly in carrying out the retraining programs at home. In most of the public schools the work in speech correction is done by the regular teachers in the classrooms.

Reliable criteria for determining degrees of improvement in speaking are important. The phonograph, the pneumograph, the breathing mask, the laryngograph, nasal olives, the labiograph, the ergograph, the photographic camera, the stroboscope and the roentgen rays have been used, particularly in certain laboratory centers. A cure should consist of esthetically satisfactory and phonetically correct speech in relation to the environment in which the child lives. When the stutterer is free consistently to express himself without mental and physical blocks, he may be considered cured. The author places as much importance on the personality of the teacher as he does on her training and technical skill. The teacher should have a good background in general and vocal anatomy, physiology, neuropathology, psychology, speech pathology, phonetics, development of language of children and pedagogy. The physician, who should be a psychiatrist, should act as the director, the leader, while the teacher should act in the capacity of carrying out the program proper without, however, sacrificing her own specialized training or initiative.

The author's closing thought is that the organized nation is responsible for the provision of means for the mental and moral development of its members.

THE TREATMENT OF BEHAVIOR DISORDERS FOLLOWING ENCEPHALITIS. By EARL D. BOND and KENNETH E. APPEL. Price, $1.75. Pp. 163. New York: The Commonwealth Fund, Division of Publications, 1931.

To the neurologist a book that emphasizes treatment comes as something of a novelty. This book describes in a practical manner the way in which children with postencephalitic behavior disorders are managed in the department for mental and nervous diseases of the Pennsylvania Hospital. The school, which was opened in 1924, limited its membership to patients under the age of 12 with normal intelligence who had had encephalitis but did not have paralysis agitans. The survey covers a study of sixty-two badly behaved children; fourteen had no history of encephalitis; the other forty-eight were definitely postencephalitic.

In the first chapter, the authors give a description of the disease, which is simple enough for nonmedical readers and accurate enough for the neurologist. The concept of the behavior disorder as a continuation of the acute encephalitis is established. The second chapter is devoted to the histories of the children, but the reader is not wearied with individual life stories; a few illustrative biographies are given. In the third chapter, the organization of the school is described, emphasis being laid on the need for adequate housing, proper personnel and an intelligently planned schedule. The nurses were trained to tolerate with equanimity behavior that would precipitate a fit of ill temper in the ordinary worker. An occupational therapeutist, a teacher, a night nurse, a matron and a part time psychiatrist completed the staff. Overactivity on the part of the children was neutralized by adherence to a very busy but interestingly varied schedule. In school, recitation periods were short, and children were allowed to move their chairs when they felt restless. In the shop, there was little trouble with discipline, the children being well occupied with their work.

Chapter IV is entitled "The Struggle for a Point of View." The child was encouraged to think of the hospital-school as a place to which people came to be cured. This point of view was not carried so far that the child could fall back on illness as an excuse for bad behavior. They were told that they had been sick, but that now they were no longer ill. Temper tantrums were usually ignored, an attitude that often led the child to abandon this method of attracting attention. The authors mention repeatedly that the Pennsylvania Hospital is 175 years old, suggesting that the children were awed by the antiquity of the institution. The fifth chapter is concerned with "The Development of Rapport." The methods for achieving this relationship include an attitude of informality (the officials often taking part in the children's games), occasional outings, frank sex instruction, extensive reading aloud and the creation of a friendly approach, a tactful manner and a hopeful atmosphere. The technic of influencing behavior is discussed in the sixth chapter. Giving praise and reward, distraction during excitement, punishment by withholding things wanted, attention to physical defects, adherence to schedule, willingness to explain, humor and dramatization are some of the methods used.

The results are analyzed in the seventh chapter. Of the forty-eight postencephalitic children, forty-six improved while they were at the school. In almost every case a normal sleep cycle was restored. Twenty-six were discharged; of these, six became worse after leaving, thirteen made doubtful progress, and seven did well. Many of those whose course after discharge was poor had been replaced in unfavorable environments.

The manual is practical, but its utility is somewhat impaired by the haphazard arrangement of the methods of treatment. For instance, the question of rewards for good behavior is introduced in chapter III under the general heading of "organization," and is resumed in chapter VI. Indifference to tantrums, which is a method of influencing behavior, is discussed not under the chapter head so named but in the section on point of view, whereas the actual technic for the development of this point of view is presented in the chapter following. The discussion of the schedule and the question of its regularity and individualization are started in chapter III and finished in chapter VI. It is unfortunate that the authors did not arrange the therapeutic methods in more orderly fashion.

Bond and Appel have made a significant contribution to neurology, for they have demonstrated that the outlook for these unfortunate children is not necessarily hopeless. Many of them can be made useful members of society; in their own phrase, "The thing *can* be done."

THE DIAGNOSIS AND TREATMENT OF BRAIN TUMORS. By ERNEST SACHS, A.B., M.D. Price, $10. Pp. 381. St. Louis: C. V. Mosby Company, 1931.

The author is right in stating in his preface that none of the standard books on neurology deals with the subject of tumors of the brain as completely as the subject deserves. This book is therefore timely.

The book is divided into nine chapters. The first deals with surgical anatomy and physiology. This chapter is unusual in that it discusses the relation of the intracranial contents to the surface topography, a valuable and much needed detail. No attempt is made to give the finer anatomy and physiology. Chapter 2 gives the methods of examination. This chapter also conforms to the usual facts found in neurologic textbooks, the exception being a discussion of the surgical aspects of such conditions as concussion of the brain and a discussion of roentgenograms and the injection of air, which are treated in detail. The third chapter discusses the surgical pathology of tumors of the brain. The tumors are divided into four groups and conform to the current views of Bailey and Cushing and Penfield. Chapter 4 discusses the general symptoms and signs of increased intracranial pressure. This chapter, as well as the following one, which discusses focal signs and symptoms, gives an adequate and comprehensive discussion of the symptomatology of cerebral lesions. In the next chapter, tumors of the cerebellum, pons and medulla are adequately presented. Chapter 7 discusses diseases of the pituitary gland. Chapter 8 is valuable in that the differential diagnosis between tumors of the brain and other conditions is given. The last chapter, consisting of 53 pages, discusses operative technic and postoperative treatment.

The book differs from most books on surgery in that only 53 of 381 pages are devoted to operative technic and the balance to diagnosis. This, after all, is the keynote of good neurologic surgery, for the accurate diagnosis of a tumor of the brain is necessary before operative intervention should even be considered.

The reviewer, who has followed surgery of the brain since its modern aspect, that is, since the time of Cushing, has certain definite convictions and agrees with the author, who states that "any man who goes into neurological surgery today should first have had a thorough training in neurology; only in this way can he develop his own critical judgment, and not be merely the hands that do the work for the neurologist." It is, of course, true that in the beginning the neurologic surgeon was merely the hands that did the work for the neurologist. Obviously resenting this position, the neurologic surgeon has stepped to the other extreme and now in some instances scorns neurologic advice. Fortunately, however, the swing today is in a more healthful direction, and in some of the neurologic centers the tendency is for the neurologist and the neurosurgeon to combine for the good of the patient, which is as it should be. This could never have been accomplished were it not for the fact that the neurologic surgeon feels that he has at last attained his place in the sun.

Incidentally, neurologists have lost a great deal in allowing the neurosurgeon to take from them the direction of the treatment of their patients. In many respects it has worked a hardship on the patient, for even the neurosurgeon will concede that in only a small percentage of cases is he able accurately to localize tumors even with all the extraneous methods in vogue today. Moreover, surgical results are not so brilliant.

So far as this book is concerned, it is a safe and sane presentation of the subject for the student and general practitioner. Nothing else could have been expected from a surgeon who has always and consistently been an exponent of scientific methods.

LEHRBUCH DER ALLGEMEINEN PHYSIOLOGIE. By E. GELLHORN, PH.D., M.D., a. ö. Professor of Physiology, Halle, and Associate Professor of Physiology, University of Oregon. With the collaboration of L. ASCHER, Berne, W. VON BUDDENBROCK, Kiel, C. OPPENHEIMER, Berlin, and J. SPEK, Heidelberg. Price, 47 marks. Pp. 741, with 126 illustrations. Leipzig: Georg Thieme, 1931.

When Bayliss wrote his monumental "Principles of General Physiology" about fifteen years ago, it was rather generally felt that he was perhaps the last author who would both be able and feel inclined to cover single-handed the entire field of general physiology. In the present volume, which has to do with a somewhat comparable field, the editor has wisely secured the collaboration of four other specialists, each well known for his work in his own branch of the subject, and has in this way succeeded in covering a larger number of topics in a more thorough and authoritative manner than would otherwise have been possible. The section of the book devoted to the physicochemical properties of the cell is contributed by the editor of the volume, E. Gellhorn; those on the physiologic chemistry, and the energetics of cell processes, by C. Oppenheimer; that on cellular morphology and the general physiology of development, by J. Spek; that on excitation processes, by L. Ascher, and that on tropisms, by W. von Buddenbrock. It is evident from this brief summary of its contents that the book omits very little commonly included under the term "general physiology." It is particularly valuable in bringing together in one place a large amount of interesting material that has hitherto been widely scattered. Though the general reader may not feel the omission seriously, the special student will be somewhat handicapped in his use of certain parts of the book by the absence of sufficiently detailed references to the original literature.

LEITFADEN DER PSYCHISCHEN HYGIENE. Edited by DR. ERWIN STRANSKY. Price, 17 marks. Pp. 312. Berlin: Urban and Schwarzenberg, 1931.

Not without a recognition of the influence of the movement in America, the present outline gives a valuable picture of the reactions and activities of representative European workers. Stransky, one of the early initiators of hygienic interests, and Kauders outline the essence and the program and history; Stransky, the relations to psychopathology and psychiatry; Kogerer, the relations to the neuroses and psychotherapy, and Brezina, the relations to somatic hygiene. Heller discusses education, Stransky the sexual life, Kauders the sports, Polland eugenics and sociology, Stransky the civilization of today and K. Grosz the criminology. The organization of mental hygiene is described by Kogerer (the provisions of care in the German-speaking countries), Noé-Nordberg (the care of patients with alcoholism), Rothenberg (the movement in America) and Schiff (the activities in France). The articles are distinguished by a considerable degree of critical judgment and freedom from a blind acceptance of dogmatic propaganda. There is a definite preponderance of medical experience over futuristic claims, with a fuller review of the interweaving with somatic helps and social demands than is met with in the somewhat stereotyped practice and theory of mental hygiene groups on this side of the Atlantic and in England with their frequently one-sided attention only to child guidance. The American reader is struck by the difficulty of the rendering of "mental" hygiene by "psychische" hygiene, and the much more strongly parallelistic than behavioristic slant of the terminology. There is, however, no doubt about an important interpenetration of the practical points of view and much less hesitancy to face the adult problems as well as those of the child. The movement seems to be in the hands of soundly and broadly trained and experienced physicians.

VOM JENSEITS DER SEELE: DIE SCHEINWISSENSCHAFTEN IN KRITISCHER BETRACHTUNG. By MAX DESSOIR. Sechste neu bearbeitete Auflage. Price, 16 marks. Pp. 562. Stuttgart: Ferdinand Enke, 1931.

Max Dessoir gives the most comprehensive review of the personages and claims in the occult sciences. With a general discussion of magic, he treats as parapsychology dreams and hypnosis, telepathy and clairvoyance, and mental automa-

tism; under paraphysics, the most famous mediums and their performances; under occult science, cabalistics, Christian science, the anthroposophic philosophy and movements, and finally under magic, idealism, the principles of the underlying conceptions and logic. Throughout he gives the reports of the outstanding performers and observers and the facts as well as the critical discussions. It is not a specially alluring picture of the studied and spontaneous archaism, and hardly of a type that would cheer the critically minded concerning thinking humanity. The believer is not treated in an offensive way, but is hardly likely to find encouragement when in a doubting mood. At the same time, the book is exceedingly informing concerning the many ways in which magic can hold modern attention under the name of science. In contrast to Coover's Stanford Studies with its big volume of experimental records, Dessoir's book is an essentially historical account of all the noteworthy cases and records, although in briefer form than in the account in his two volumes of "Der Okkultismus in Urkunden." He emphasizes in this whole field the prevalence of multiple possibilities of interpretation in very definite but not decisive directions.

HANDWÖRTERBUCH DER PSYCHISCHEN HYGIENE UND DER PSYCHIATRISCHEN FÜRSORGE. By O. BUMKE, G. KOLB, H. ROEMER and E. KAHN. Price, 25 marks. Pp. 400. Berlin: W. de Gruyter & Company, 1931.

The publication of this handbook of mental hygiene shows the interest with which the German-speaking countries turn to the field of mental health. Over seventy articles, from one to twenty-nine pages each, are offered. An outline of pathopsychology by K. Schneider gives a survey of abnormal variants of a normal psychology (twenty-nine pages). A discussion of the philosophies deals with the transformation of world views up to naturalism and the various psychopathologies, including sex and the neuroses. The history and scope of mental hygiene are given by Roemer (seventeen pages). Culture, civilization and art receive fifteen pages; criminal biology, thirteen. Heredity is treated by Lange; the sex life, by Maier. Special attention is given the institutional and also the various forms of open treatment of the mentally sick (sixty pages). Kahn offers a summary of his work on the psychopathic personalities, Wlassak a concise but informing account of the alcohol problems. The hygiene of work is well treated. Throughout, in contrast to the American trend, attention is devoted to adult rather than to child study, and the psychoanalytic methods are but briefly reviewed. The book forms a welcome supplement to the prevailing interests in American trends.

PSYCHOLOGIE DER VORPUBERTÄT. By DR. H. VORWAHL. Price, 6.50 marks. Pp. 160. Berlin: Ferdinand Dümmler, 1929.

This is indeed a good introduction to the actual life and particular problems and reactions during the years immediately preceding puberty. The author offers the results of the literature, of questionnaire returns and of autobiographies and biographies. He discusses the personal relations (the parents, the brothers and sisters, especially the sisters, and the friendships); the play, escapades, gang life, the class and social situation, and the question of secrecy and self-consciousness; the relations to values (the mental horizon, literature, religion, morality, the ranking of values, selection of career and sexuality). The book is not a mere abstract discussion, but is full of concrete material as seen by the understanding educator and student of young life. The conscientious correlation and bringing together of material also from the pertinent German literature make the book not only of descriptive but of genuinely critical value and an interesting supplement to the study of life-periods and to American studies, which are not so specifically devoted to such limited but important phases.