Points of consideration in diagnosis of brain tumors

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POINTS OF CONSIDERATION IN DIAGNOSIS OF BRAIN TUMORS

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I. INTRODUCTION

The progress of the surgery of intracranial tumors has been associated intimately with the advancement of asepsis and surgical technique in general; methods of more accurate diagnosis and a correlation of the pathology of tumors encountered with the clinical course of the patient. It is a long way from the early trepanations of Jaboulay to the present surgical technique of an osteoplastic craniotomy. The meticulous details of an intracranial operation are characterized by strict hemostasis, the use of cotton pledgets moistened in saline solution for sponges; the collection of blood unavoidably lost during the operation so that it may be used as a transfusion if necessary; the use of silver clips to ligate bleeding cortical vessels; and finally, among many other technical details, the employment of an electrosurgical unit for transsection of the cerebral cortex, and a removal of large vascular growths.

Closely associated with these more or less technical matters, and in fact by their nature a challenge to the mechanical side of neurological surgery, have been the contributions to art of diagnosis, localization, and histopathology of intracranial growths.
Physiological experiments have added to our knowledge of the function of the various parts of the brain and to the mechanics of the cerebrospinal fluid pathway. The ophthalmoscope and perimeter, the diagnostic instruments of a branch of medicine distinct from neurology and surgery, also have made it possible to localize intracranial tumors more accurately and earlier in their course.

The contributions of the science of roentgenology to neurological surgery have been innumerable. The correct interpretation of the direct evidences in the skull of various intracranial neoplasms is not only possible but the corroboration of the probable pathology to be encountered at operation, is now a common occurrence. When one adds to this the visualization by ventriculography and encephalography of the deformities produced by tumors, the dependence which neurological surgery places upon roentgenology may be realized.

Finally, all of these forward steps in matters surgical and diagnostic would be of little avail were it not for the progress which is being made in the correlation of the pathology of the lesion and the clinical history and course of the patient. Today a diagnosis of
an intracranial tumor in a given location is not enough. The surgeon is able more often than not to be cognizant of the probable pathological nature of the lesion which he is to attack.
II. Histogenesis of the Brain as Interpetated by Bailey and Cushing (1).

The histogenesis of the brain furnishes the indispensable background for an understanding of its tumors.

"The anlage of the central nervous system is differentiated early in embryonic life from the ectoderm along the axial line. This long strip of ectoderm becomes thickened to form the medullary plate and its middle portion is depressed to form the medullary groove. The elevated edges of the groove come together and fuse, converting it into the medullary tube, the anterior portion of which becomes enlarged and subdivided by constrictions into the three primary vesicles of the brain.

At first the medullary plate is composed of a single layer of columnar epithelial cells which may be called the medullary epithelium. An active proliferation of these cells occurs, and simple primitive arrangement is in some portions lost. By the continued division and differentiation of the cells the enormously complicated structure of the brain finally comes into existence.

The earliest sign of differentiation is the appearance within the medullary epithelium of round ves-
cular cells in mitosis. They are known as germinal cells and from them neuroblasts are differentiated. These germinal cells continue to multiply and they elongate the remaining epithelial cells and separate them from each other in their outer portions, thus transforming them into primitive spongioblasts. Some of the germinal cells differentiate at once, but others continue to divide giving rise to new generations of undifferentiated cells known as indifferent cells, a term which implies that one is unable to predict what they will become in their future development. We prefer to speak of these indifferent cells as medulloblasts.

**NEUROBLAST**

The neuroblast at first is a globular cell with a nucleus and the cytoplasm collected toward one pole, their processes are put out into opposite directions but soon one is withdrawn and the cell assumes a piriform shape with a single long process coming from the smaller end and the cell is known as a **unipolar** neuroblast.

In its further development the neuroblast puts out multiple processes in various directions and becomes known as a **multipolar** neuroblast. These processes increase in length and complexity until the final transformation into an adult **neurone** is marked by the deposition
of myelin around the second half of intra-uterine life.

**SPONGIOBLAST**

The primitive spongioblasts meanwhile are not inactive. They may be divided into two types, (I) Those in which the nucleus with the bulk of the cytoplasm lies near the ventricle, the future **ependymal** cells; and (II) those in which the nucleus with most of the cytoplasm lies remote from the ventricle, the precursors of **neuroglia** cells. The outer extremities of both types continue off in long tails to the external limiting membrane. These cells remain in this primitive stage in the region of the roof and floor plates of the medullary tube. Elsewhere, especially in the region of the cerebral hemispheres, a further and complicated transformation of the primitive spongioblasts occur. They divide by amitotic division, giving rise to **bipolar** spongioblasts.

Schaper first called attention to the fact that a single origin from the medullary epithelium alone was insufficient to account for the great numbers of spongioblasts in the developing central nervous system, even though it was known that the latter continued to divide amitotically. He therefore proposed the formal hypothesis that the germinal cells did not neces-
sarily differentiate into neuroblasts, but might continue to divide on an undifferentiated plane of development, and eventually become either spongioblasts or neuroblasts.

**MEDULLOBLASTS**

We have no means of identifying these indifferent cells or medulloblasts except by negative characteristics, but Schaper's hypothesis, which is generally accepted, is necessary to a comprehension of the normal histogenesis of the brain, of malformations of the brain and for an understanding of brain tumors.

The unipolar spongioblasts undergo a further transformation into astroblasts which are distinguished by a broad process attached to the wall of a blood vessel, where it becomes enlarged into what is known as the "sucker foot," and by short stubby processes which extend in many directions from the opposite pole of the cell. Neuroglia-fibrils begin to develop in the cytoplasm of the astroblasts during this stage, which is about the fourth month of intra-uterine life. Not in all the astroblasts do fibrils develop, and therein arises the distinction between the fibrillary astrocytes of the marginal and sub-cortical regions, and the protoplasmic astrocytes of the cortex. These two types to-
gether comprise the **neuroglia**.

There has been as yet no thorough study of the development of the **Oligodendroglia**, but fragmentary observations by Hortega indicate that these cells originate from indifferent cells which wander among the fibres of the long nervous pathways and there differentiate into oligodendroglia, and also occasionally into fibrillary neurological cells. They are therefore of ectodermal origin and akin to the protoplasmic and fibrillary astrocytes.

**THE MICROGLIA**

There are no studies of the development of the **microglia** in the human being, but Hortega's observations on the lower animals indicate that they are of mesodermal origin and spread from pia matter and the choroidal telas into the central nervous system rather late in its development. The microglial cells, though scattered throughout the brain substance, predominate in the gray matter.

In the normal brain these four adult elements which have thus far been discussed (the neuroglial, microglial, oligodendroglial, and nervous cells) may be distinguished with a certain degree of accuracy merely by their nuclei, but a study of their processes in the
manner described is essential for precise differentiation. In addition, one must consider three types of cells which have undergone a special development—the pineal, choroidal, and ependymal cells.

**PINEAL CELLS**

In one restricted area of the roof-plate, the cells of the medullary epithelium proliferate to form the pineal parenchyma, which in addition to neuroglial cells contains also the parenchymatous cells of the pineal body.

**CHOROIDAL CELLS**

In the region of the choroidal tela the primitive epithelium transforms itself readily into the cuboidal epithelium which covers the choroidal tufts.

**EPENDYMAL CELLS**

As stated, the cell-bodies of some of the primitive spongioblasts remain attached along the ventricular wall. They lose their cilia and the blephoroplasten collect in a group in the cytoplasm, in which state they might be called ependymal spongioblasts. But should they lose their peripheral processes they are reduced to the cuboidal cells lining the cerebral ventricles and central canal of the spinal cord, known as the ependyma."

The foregoing brief account of the histogenesis of the
brain may be represented in the accompanying diagram formulated by Harvey Cushing. (1).
III. Classification of Intracranial Tumors

I. First Group—Fibroblastic tumors (Meningioma, psammoma, dural endothelioma, meningeal fibroblastoma.)

These tumors comprise about 45% of all brain tumors. Since they are always well encapsulated and never invade brain tissue, they are among the most favorable tumors with which we have to deal. Their removal frequently offers unusual technical difficulties because of the great size they may attain as well as the marked increased vascularity of the over-lying bone, the dura and, in some cases, also the scalp. The blood supply of the tumors comes usually from the dura, though at times from vessels in the pia which may be huge and very friable.

From a pathological standpoint, however, they are extremely favorable as they never destroy nervous tissue, merely displace and compress the brain or spinal cord. They are usually firmly attached to the dura, hence have been called dural endothelioma, but it has been shown that they originate from the arachnoid and from those tufts along the large venous sinuses which form the pachionian granulations. This explains the fact pointed out by Cushing (2) that the vast majority of these tumors
are attached near the larger sinuses where the pacchionian bodies are most numerous. At times the bone is completely destroyed by pressure atrophy, at other times there is a hypertrophy of bone over the site of the tumor. There may be actual invasion of the bone by tumor cells, these areas of invaded bone may be tender and give valuable clues to the location of a tumor, or they may also give a characteristic appearance in the X-ray, indicating that the bone is laid down perpendicularly.

Grossly these tumors are usually smooth, round and nodular like a potato, but may have small nodules connected by an isthmus with the main part of the tumor. Microscopically, the cells may be arranged in columns separated by bands which arise from the dura, thus giving the appearance of alveoli. In rapidly growing tumor these bands are less prominent and the entire tumor is composed of a mass of nuclei surrounded by considerable cytoplasm which gives the impression of endothelial cells. In slow-growing tumors, whorls are found which are composed of concentrically placed cells and when these undergo degeneration, pachyman bodies are found at the center. Davis says, (3), "these latter tumors show a definite shadow in the X-ray, because they contain the whorls of cells in which calcium is deposited."
Perineural Fibroblastomas---In this group belong the tumors arising from the cranial and spinal nerves. The most common site for these is the cerebellopontine angle where the so-called acoustic neuromas or eighth nerve tumors occur. Occasionally tumors also develop from other cranial nerves. There has been considerable discussion about the nature of these tumors. As the name implies, some have thought that because the tumors were so closely connected with the nerves they were true neuromas but careful histological studies by Cushing (4), Councilman (5), and Skinner (6), have shown that all the elements composing these tumors are of fibroblastic origin, and that none of the cells are developed from neuroglia or neurones.

Grossly, the tumors have a very characteristic appearance. They are yellow or brownish yellow, smooth, glistening and they not infrequently have small cysts on their surface. They are adherent to the petrous surface of the temporal bone at the porous acusticus. Microscopically, the tumors present a very typical appearance. They are composed of streams of parallel fibers which form eddies or whorls in some places.

The confusion about the pathology of these tumors has been due, in part to the fact that occasionally there
occur in the cerebellopontine angle, connected with the eighth nerve, neurofibromata which are part of a general process—von Recklinghauser's disease. These tumors, in contradistinction to perineural fibroblastomas, contain nerve fibers which run through the tumor mass. Microscopically, the two types look much alike; the presence of nerve fibers in the tumor, and the presence of nodules elsewhere in the body, help to distinguish the two processes.

3. Second Group—The Gliomas

About 45% of all brain tumors belong to this group. Neurological surgeons have realized for some years that there are wide differences in gliomas regarding gross appearance, histology, operability and prognosis.

What we have been in the habit of calling gliomatous cysts offer an excellent prognosis, and the patients, after operation, have remained well for years. Some gliomas are well encapsulated, though solid, and are almost as readily enucleable as a monigeal fibroblastoma. Others are diffuse, infiltrating with ill-defined margins, very difficult to remove and, if they are to be removed, require extensive resections—partial or complete lobectomies. Still others have occasionally been inhibited in their growth by deep X-ray
therapy. These facts have called forth an explanation.

It is only since gliomas were studied by applying the methods which were first used by Del Rio Hortega on normal brain tissue, that an explanation has been forthcoming. This is the differentiation of various glial elements by the silver and gold staining methods. The application of these studies to the study of tumors has been carried out, to a great extent, by Bailey and Cushing, (1), Bailey, (7), Pendfield, (8), and Greenfield, (9).

As a result of these studies, it has been possible to divide the gliomas in various distinctive types based on their histological characteristics. They may be cystic, encapsulated, affected by X-ray therapy, or may be diffuse and infiltrating. By recognizing these types at the operating table, better treatment can be instituted and a more intelligent prognosis given. The recognition at the operating table of a medulloblastoma, which is the one type of glioma that responds remarkably to X-ray, is in itself a most important contribution.

Based on the various types of cells, which develop from the medullary epithelium, Bailey and Cushing, (1), have been able to identify tumors in which these
cells predominate and have differentiated fifteen tumor types. Penfield, (8), in his discussion of tumors, describes only ten of these types and even some of these are exceedingly rare.

The ten groups that Penfield has described are as follows:

"Astrocytoma  Spongioblastoma unipolare
Ependyma    Oligodendroglioma
Astroblastoma Medulloblastoma
Pinealoma    Spongioblastoma multiforme
Midulloeplithelioma Papilloma"

(I) Astrocytoma

About one-half of all gliomas fall into this group. "According to Bailey and Cushing, (1), they are said to constitute even more than 50%." This is the most favorable type of glioma, since it is slow growing cystic, well encapsulated and contains in its wall a projecting nubbin which is the growing projection of the tumor. The cyst contains a bright yellow, which usually contains gelatinous material. This is probably a secretion from tumor cells. The wall of the cyst is made up of flattened out fibroblastic neuroglia. The character of the tumor is determined by a study of the nubbin. The predominating cells are astrocytes. The nubbin is
usually bright red, velvety in appearance and quite vascular, though there may not be more than one large vessel running into it.

"The wall of the cyst may contain calcification which occasionally can be seen on an X-ray picture, but we have had no instance of calcification in a nubbin." (3).

These tumors may occur in any portion of the brain but the cyst usually presents near the surface. Sachs says, (10), "If this nubbin is removed a cure will be effected. As long as the nubbin remains, even though the cyst is emptied and all or most of the wall is removed, the cyst reforms. When the nubbin is removed, even if some of the cyst wall remains, the process is stopped--cured."

(2) Ependymoma

These tumors are much rarer than the astrocytomas but are also slow growing and fairly well encapsulated tumors. At times they are nodular and suggest a meningeal fibroblastoma but they are embedded in the brain tissue under the pia arachnoid and consequently can be grossly differentiated. In Bailey and Cushing's, (1), series, the majority of these tumors occurred in the cerebellar region--nine out of twelve--but in a series
of eight cases studied by Drs. Fincher and Coon, (11), they found:

"1.-Five of the eight occurred in cerebral hemispheres.

2.-Ependyomas in the cerebral hemispheres, being encapsulated tumors, offer a favorable prognosis.

3.-The only tumors in children showing calcification in the X-ray picture were ependymomas.

4.-Cystic fluid that does not coagulate may be valuable diagnostic sign at the operating table.

5.-The demonstration of ependymal spongioblasts with the silver carbonate stain is the most valuable histological aid in diagnosing these tumors.

6.-The tumors contain true rosette, small cavities lined by columnar."

(3) Astroblastoma

These tumors are rare. In Bailey and Cushing's, (1), series there were but thirteen astroblastomas in their two hundred fifty-four gliomas.

This tumor is less differentiated than an astrocytoma. The predominating cell is an astroblast, which is the transition cell between the spongioblast and astrocyte. The tumors are not well encapsulated but grow fairly slowly. In one case of Cushing's the symptoms
had begun fifteen years previously, but in all the other cases the tumor had existed a much shorter period. The predominating cell resembles a nerve cell but is smaller and stains well with gold sublimate.

(4) **Spongioblastoma Unipolare**

These also are rare tumors. Bailey and Cushing, (1), found only nine examples in their series. The predominating cell is the unipolar spongioblast. The tumor in all of these cases had been present for four years. It was partly cystic and in a number of cases could be completely.

(5) **Oligodendrogliaoma**

This group, though small, has a favorable prognosis if the tumor is recognized before it has become too large. These tumors are well encapsulated, firm, pinkish in color, and often contain calcified particles. On account of their slow growth, they may not produce any other symptoms except general convulsions for a long time. Histologically they present a very characteristic picture—a mass of cells with a dark spherical nucleus in the center of a clear cytoplasm which stains poorly.

(6) **Medulloblastoma**

This is an unusually interesting group of tumors
as it seems to be the only group which is definitely influenced by deep X-ray therapy. These tumors are much more common in young children but occasionally do occur in adults. In children they are usually found in the posterior fossa and lie in the median line, growing from the roof of the fourth ventricle. They have a characteristic gray appearance and are clearly demarcated from the surrounding brain tissue; hence in removing them a line of cleavage may be found.

These tumors do not metastasize through the circulation but form deposits which are spread by the cerebrospinal fluid through the subarachnoid space.

This tumor grows rapidly and contains numerous mitotic figures. Both spongioblasts and neuroblasts are found throughout the tumor, which would seem to indicate that the tumor has developed from a bipotential cell—a very young embryonic cell, a medulloblast—hence Bailey and Cushing, (1), have called these tumors medulloblastomas.

(7) Pineal Tumors

Tumors arising in the region of the pineal gland were put into still another group named pineoblastomas and pinealomas, by Bailey and Cushing, (1), who pointed out their similarity to medulloblastomas.
(8) **Medulloepithelioma** and **Neuroepithelioma** form a very small group. According to Penfield, (8), they are the least differentiated of all the gliomas. Even in Bailey and Cushing's, (1), experience they are only occasionally encountered and develop from undifferentiated medullary epithelium.

(8) **Spongioblastoma Multiforme** constitute one of the largest groups of all gliomas, between 40 and 50%; this is the most malignant type and, consequently, presents the most difficult problem as regards treatment.

There is no definite line of demarcation between the tumor and the brain tissue. These tumors grow rapidly, are soft, and at times contain cysts which are small and usually multiple. The tumor may be pinkish or, in places where it degenerated, yellow soft and friable. There frequently are hemorrhagic areas in the tumor because of its great vascularity and the friability of the vessels. On this account, Bailey, (12), says, "massive hemorrhages may occur leading to sudden unconsciousness and death."

The name was proposed by Globus and Strauss, (13), who considered the multiforme character of these tumors their mass characteristic feature in some parts of the tumor, the cells are gathered palisade-like about areas of degeneration; in others there may be numerous giant
cells of every conceivable shape and size, while in still other portions the cells are closely packed together without any special architecture, giving the appearance of a sarcoma—the name that has frequently been applied to these tumors.

(10) Papillomas are not gliomas. They develop from the choroid plexus and reproduce the appearance of the plexus. They are well encapsulated and usually grow in or near the ventricle.

**Intracranial Telangiectosis and Other Angiomaticous Lesions**

There are a number of rare lesions found in the brain which clinically must be classed as tumors, though pathologically they are not true tumors. These are the vascular lesions variously spoken of as intracranial telangiectoses, and venous and arterial angiomatas. They are congenital and, therefore not true tumors. Clinically, however, they are frequently indistinguishable from tumors, though pressure symptoms are often absent and only irritative phenomena are present, such jacksonian convulsions.

**Hemangioblastomas** as pointed out by Bailey and Cushing, (14), have not been recognized in the past as a separate group. This is explained, in part, by the fact, that it was not known until recently that some of these
tumors undergo cystic degeneration. In these cases there is a nubbin of tumor in the wall of the cyst, just as in the astrocytomas. These tumors closely resemble the various types of angiomas that it is often very difficult to differentiate them. One of their most significant points of differentiation is that, in true angiomas which are not neoplasms, there is a glial tissue between the vascular channels, while in the tumors at present under consideration, the tissue is all developed from primordial blood channels.

3. Third Group---Inflammatory Lesions

(1) The acute lesions are caused by some form of puogenic organism, either staphylococcus or streptococcus. The staphylococcus more frequently produce a localized lesion, brain abscess, while the streptococcus produces a diffuse lesion—a meningitis.

(2) The chronic lesions are tuberculoma, gumma, and one of the rarer forms of granulomata.

BRAIN ABSCESS—Brain abscess may be metastatic following some focus elsewhere in the body, or they may result from direct extension of an infection in the scalp bone.

In the metastatic abscesses the infection is carried by the blood stream. Frequently these are multiple, and they are usually subcortical. Most commonly they are secondary to lung infections, though they may
follow infections elsewhere. The abscess that follow infection in the scalp or bone, if not traumatic in origin, most frequently are secondary to a chronic otitis media, which has extended into the mastoid, or to an infection in the nasal sinuses. These abscesses, in contradistinction to those of metastatic origin, are either near the surface or connected with the surface by a "stalk". If the infection is not to virulent, the abscess becomes walled off and a pyogenic membrane develops which, in long standing cases, may be a centimeter or more in thickness. If the infection is very virulent, the brain tissue is not able to form such a protecting membrane, and an encephalitis or meningitis develops.

Frequently a vein supplying the area affected is thrombosed. Some experimental work carried out in Sach's (10) laboratory some years ago suggested that a thrombosed vein is frequently, if not always, the first step in the formation of an abscess. "What happens is that an area of softening occurs as a result of thrombosis, and this area of lowered resistance then becomes the abscess. In no instance was it possible experimentally to produce an abscess unless the circulation was first impaired."

Tuberculoma--Tuberculosis may produce either a
diffuse or a localized lesion in the brain. Only the localized lesion is of importance to the neurosurgeon. According to Wagenen,(15), Surgery at present holds out no hope for the diffuse form—tuberculous meningitis. When tuberculosis becomes localized in the brain it forms a tuberculoma. These may be single or multiple, and when but a single lesion is present, it may attain great size. It may be well walled off, and, as long as the lesion will remain localized.

There is still considerable difference of opinion how best to deal with these lesions which can rarely be distinguished clinically from other brain tumors. After they have been exposed at operation some men advocate extirpation and others advocate letting them alone.

**Gumma—Syphilis,** occasionally may cause localized cerebral lesions. If the gumma becomes large enough, it gives rise to a clinical picture identical with that of a brain tumor and must be treated in the same way. Gumma must be suspected if the patient has a positive Wasserman. This is usually a hard mass with no tendency to break down, as does the tuberculoma. It is not well encapsulated, but can be dissected away from the brain tissue. Histologically it is difficult to distinguish
this from a tuberculosis lesion, as is the case elsewhere in the body. This gumma of the brain, however, contains much more connective tissue than the tuberculosis. After a gumma has been removed, strenuous antiluetic treatment should be instituted, but before the increased intracranial pressure in these cases has been relieved, antiluetic treatment has little effect. This was pointed out by Victor Horsley many years ago according to Sachs,(10).

4. Fourth Group--Pituitary Tumors

The pituitary gland is composed of three portions, the anterior lobe, the posterior lobe, and the pars intermedia. The first two develop from a pocket in the pharynx known as Rathke's pouch. The gland is surrounded by dura and arachnoid.

The anterior lobe, being the glandular portion, is the one which plays the role in the adenomatous changes that occur in the gland. It contains three types of cells:

(1) The chromophobe cells, which contain no specific granules.

(2) The chromophil cells, of two kinds,
   a. The acidophilic or eosinophilic cells, demonstrated with acid stains.
   b. The basophilic cells, which contain
granules taking a basophilic stain.

These different cells predominate in the different adenomatous changes that occur in the pituitary and are responsible for the different endocrinological pictures that occur. There is great variation in the gland during pregnancy, hibernation and the rutting season. During pregnancy there is an increase of the acidophilic cells, in the rutting season of all the chromophil cells, and during hibernation a decrease of all the chromophil cells.

The tumors of the pituitary all develop from one of these types of cells. Just what is the function of the posterior lobe is not understood. Removal of the posterior lobe produces definite physiological effects, while administration of posterior lobe extract produces exactly the opposite effect. This lobe has never, so far as is known, given rise to a new growth.

The Chromophobe Adenoma is the commonest type of pituitary tumor. It is the type that is found in cases of hypopituitarism. Dottr and Bailey, (16), have pointed out that the cells may be arranged in alveoli with connective tissue bands between them which closely resemble the normal gland, or there may be a formless mass of cells with little connective tissue stroma. When no glandular structure is present the tumor is spo-
ken of as a chromophobe struma.

The Chromophil Adenoma is the type that is found in cases of hyperpituitarism. In these tumors, glandular structure is not present, but the cells are packed together in a somewhat homogeneous mass so that the term struma is usually applied to this type of tumor. Dott and Bailey, (16), and Cushing and Davidoff, (17), found that chromophil adenomas always have symptoms of acromegaly or gigantism.

Basophilic Tumors are very rare. Evans and Simpson, (18), have shown clearly that the sex hormone is produced by the basophilic cells. In Cushing's, (19), monograph on the pituitary, two cases are described that might belong to this group: Case XLVI, "a case of infantilism with sexual precocity," and Case XLVI, "with precocious sexual adolescence."

Mixed type of Adenoma—Occasionally a pituitary tumor is encountered in which there are cells resembling those found in the chromophil and chromaphobe adenomas. Such cases show symptoms of both hypo-and hyperpituitarism.

When malignancy occurs it takes the form of adenocarcinoma. These tumors are invasive, and they metastasize as do carcinomas elsewhere in the body. They may present an alveolar structure or the cells may be
densely packed together.

**Hypophyseal Duct Tumors**—As pointed out before, the anterior portion of the pituitary gland develops from Rathke's pouch. The connection with the pharynx usually disappears, though at times remnants of a craniopharyngeal connection remain. These cells may give rise to epithelial tumors which lie above the sella, forming so-called "suprasellar tumors." The reason these tumors lie in that region is that the craniopharyngeal duct is drawn upward by the rotation of the pituitary gland during its development.

These suprasellar tumors frequently become cystic and project into the third ventricle obstructing the farsmina of Monro and thus causing an internal hydrocephalus. When cystic they may have calcium deposits in their wall and they always contain brownish fluid which is full of cholesterin crystals.

Jackson and Duffy,(20,21), have collected a large number of these cases from the literature and have classified them into several groups according to their histological appearance: 

1. **(a)benign cystic papillomas**;
2. **(b) adamantinomas**, which may be cystic or solid, and may contain calcification,
3. **(c) carcinomas**.
IV OUTLINE OF METHODS OF EXAMINATION

The study of a neurosurgical case may be divided into eight headings:

1. History
2. Neurological physical examination
3. Auscultation and percussion of the head
4. Eye fields
5. X-ray films (including pineal shift)
6. Air injection (pneumoventriculography)
7. Barany tests
8. Lipiodal injection

The entire plan of the study of such a case has an anatomical and physiological basis. The prime and ultimate purpose of the neurological surgeon, after diagnosing a pathological condition, must always be to make as accurate a localizing diagnosis as possible. As we are familiar with the first two headings a brief discussion of the remaining follows:

Auscultation and Percussion of the Head

This should be a part of every neurosurgical examination. There are at times vascular lesions of the brain which can be detected only by auscultation. Arteriovenous aneurysms, intracranial telangiectoses and hemangioblastomas, of all may give rise to a bruit.
Percussion of the skull may elicit a Macewen's note (tympanitic sound) which is characteristic of a thin skull and usually means an internal hydrocephalus. The sensation of vibration of the bone obtained on percussion of a thin skull is of even greater value than the actual note.

**EYE FIELDS**

A careful perimetric study is of great value, but a uniform lighting is essential as is also absolute quietness.

Lesions of the temporal lobes often give few localizing signs. This is particularly true of the right temporal lobe which, in right-handed individuals, has always been considered a "silent area". A carefully taken eye field, however, frequently enables one to locate a lesion in the temporal lobe. "The partial hemianopic defects that can be developed only with careful perimetric examinations are absolutely characteristic of a temporal lobe lesion". (10)

**X-RAY EXAMINATION**

Every suspected case of brain tumor should have x-ray pictures taken. These should always be taken stereoscopically with the side on which the lesion is suspected nearer the film. If there is nothing to
indicate the side of the lesion, stereoscopic pictures of both sides should be taken.

According to Davis (3) the x-ray changes that occur in tumor cases may be grouped under four headings:

1. **Tumor shadows**--In a certain number of cases, eight to ten per cent, brain tumors cast a shadow which can be seen on the x-ray picture. These shadows are usually caused by calcification in a portion of the tumor, and the deposits may be in the center of the tumor or they may be laid down at the edge in a curved line. Such curved lines usually indicate a cyst wall with calcification. They are most frequently observed in suprasellar cysts.

2. **Evidences of Increased Intracranial Pressure**

   Increased pressure may produce changes of various sorts. There may be general convolutional atrophic markings all over the skull, or these markings may be seen only in certain portions of the skull. Convolutional markings are evidence of bone or pressure atrophy. Whether or not the accumulation of cerebrospinal fluid alone—as is sometimes the case in fractures—can produce convolutional atrophy would be an interesting question to study.

3. **Areas of Thickening or Areas of Destruction**

   Tumors growing from the dura frequently produce
changes in the overlying bone. At times the bone hypertrophils, at other times it is destroyed by pressure atrophy. These bone changes may be caused by actual invasion of the bone by the tumor.

4. Other Changes Indicative of an Intracranial Lesion—The shape and size of the sella turcica and of the dorsum sellae may give most valuable information. The sella may show changes due to an intrasellar process, a pituitary tumor, or it may show changes resulting from the general intracranial pressure caused by a brain tumor.

5. Pineal Shift—In 1924 Naftziger (22) described a new observation. In a study of 215 x-ray pictures he found that shadows of the pineal gland were present in 50% of his cases. In the anteroposterior view of a normal skull this shadow always lies in the median line. When a cerebral tumor is present the pineal shadows is pushed to the side opposite the tumor. In cerebellar tumors, the pineal shadow is undisturbed and remains in the median line.

AIR INJECTION

In 1918, Walter E. Dandy (23), while trying out various methods of getting x-ray pictures of intracranial contents, discovered that by withdrawing cerebrospinal fluid and replacing it with air, he was
able to get extraordinary pictures of the ventricles. When he injected air by lumbar puncture, he found some of the air went into the ventricles and some into the subarachnoid space. Developing this method, he discovered that tumors in the cerebral hemispheres produced various types of deformities of the ventricles.

Recently there have been a number of excellent publications on encephalography—injecting air through the spinal canal.

Because of the danger and complications of air injection it should be made use of only when a diagnosis cannot be made by any of the other methods of examination. According to Sachs (10) a large proportion of cases, at least 70 and sometimes as high as 80%, a localizing diagnosis of brain tumor can be made without air injection. Therefore this method should be used only when all other methods of examination fail. In these cases air injection often gives startling and surprising information regarding the location of the tumor.

Both the Barany tests and the lipiodal injection are of doubtless value, the former having many chances for error in interpretation, and the latter giving a marked inflammatory reaction.
V GENERAL SYMPTOMS AND SIGNS OF INCREASED INTRACRANIAL PRESSURE

Until very recently brain tumors have been considered a rare occurrence. Pathologists have realized the fallacy of this idea but among the clinicians the view is still prevalent. Large series of autopsies have shown that the brain ranks fourth in the incidence of tumors—the uterus, stomach, and breast being the organs in which new growths occur more frequently.

Although the type of tumor, as well as its location, influences the symptoms to a marked degree, all brain tumors give rise, at some time, to symptoms which may be grouped under one of two headings:

1. General symptoms and signs of increased intracranial pressure.

2. Focal signs and symptoms.

The symptoms of group one are:

(1) Headache
(2) Vomiting
(3) Choked disc
(4) Unilateral sixth nerve paralysis
(5) Vertigo and dizziness
(6) Respiratory disturbances
(7) Yawning and sighing
(8) Convulsions (general)
(9) Mental dullness and deterioration
(10) Unconsciousness and coma
(11) Changes in the skull
(12) Slow pulse
(13) Blood pressure changes
Headache—No single symptom occurs more frequently than headache. It often is the first evidence the patient has of any intracranial trouble. The pain varies greatly in intensity in different individuals. It may be confined to one portion of the head or may be general.

In the earlier stages of brain tumor the headache may not be severe, but in the later stage it frequently is very intense. There is little doubt that it is due to tension on the dura, and as this may vary from day to day, or hour to hour, so may the headache. The evidence that tension, or pull on the dura, is the important factor in the causation of headache is confirmed by the striking way in which opening the dura, and thus removing tension by a decompression operation, relieves the headache.

Kolodny (24) says, "Undoubtedly the effect of the pressure on the flow of cerebrospinal fluid has much to do with headache. If there is no obstruction to the flow of cerebrospinal fluid, headaches are less severe. Thus a tumor in the frontal region may not cause headache, even though it may attain great size, while a tumor in the posterior fossa, around the aqueduct of Sylvius, which is readily compressed and thus dams back the fluid, may give rise to the most intense pain, even though the tumor be no larger than a lima bean."
Though headache caused by a brain tumor may occasionally have some localizing significance, in the vast majority of cases it is merely an evidence of increased intracranial pressure.

Headache, of course, may be produced by many other conditions and the question arises whether there is any way of distinguishing the headache due to intracranial pressure from other headaches. There is not. "They are absolutely indistinguishable", says Sachs.(10)

Vomiting--The classical description of vomiting caused by brain tumor is that it is projectile. According to (10) Sachs projectile vomiting is seen in many other conditions and he says it is not characteristic of cerebral vomiting. He concludes in saying, "that much more characteristic is the fact that cerebral vomiting is not associated with any nausea." It is believed that vomiting occurs much more frequently when the tumor is located in the posterior fossa.

Choked Disc--This is the most important single symptom that occurs. The majority of brain tumors, if they are present long enough, give rise to changes in the fundus of the eye. The origin of the choked disc as worked out by Paton and Holmes (25) after reviewing all present day theories is as follows: "The edema of the papilla that constitutes tumor papilledema(choked disc) is, in the first place, due to venous engorgement that results from
the rise of intravenous pressure that is necessary in order that circulation should be maintained on the intravaginal portion of the vein where this is subjected to an increased sheath pressure. The increased sheath pressure is also the origin of the second factor, the obstruction to the lymph drainage from the papilla."

There are many variations presented by a choked disc. The usual classical picture is well known; a swollen nerve-head with edges of the disc completely obliterated, the vessels dark, tortuous, and buried in edematous tissue, with exudate and hemorrhages radiating from the nerve-head. It is of great importance, however, to remember that this typical picture is frequently not present. The edges of the disc may be washed out and blurred by edema with no exudate or hemorrhages, and no tortuosity or fullness of the vessels. In other cases, there may be striking tortuosity of the vessels but little else. There may be other combinations and all these may be greatly altered by different tintings of the disc.

Ravdini says (26), "A patient may have a severe type of choked disc and yet have no impairment of vision. On the other hand, a much less "angry looking" choked disc may be associated with marked loss of vision." No good evidence has been advanced to explain why this occurs.
When intracranial pressure is relieved, a choked disc subsides and the swelling disappears. This, however, may be of little avail if vision has already been seriously impaired. Sometimes the eyesight becomes worse as a result of secondary atrophy. Occasionally it remains stationary and at other times it improves.

Unilateral Sixth Nerve Paralysis—When a patient has double vision, the result of paresis or paralysis of the sixth nerve on one side, a symptom is present which troubled neurologists for a long time because they endeavored to make use of this as a localizing sign. Today, however, as a result of the research of Cushing[27] it is interpreted as a general sign of pressure. Cushing pointed out that the transverse branches of the basilar artery generally overlie the nerves, and that these vessels frequently constrict the sixth nerve. As the pressure varies, the constriction may be greater or less, and this accounts for the daily, even hourly, fluctuations in a sixth nerve paresis. Bilateral sixth nerve paralysis, on the other hand, is usually of great localizing value, as it is caused by a pontine lesion.

Vertigo and Dizziness—These are two symptoms which frequently occur together. The patient may see objects turning before him or may feel as if he were whirling around. When vertigo is the result of disturbances of the semicircular canals, it may signify a localized
lesion, but, unless accompanied by other symptoms which can be ascribed to the canals, vertigo cannot be so interpreted.

Tumors situated in any portion of the brain may cause vertigo or dizziness, but undoubtedly lesions on the posterior fossa, which involve or press upon some portion of the vestibular mechanism, are much more apt to give rise to these symptoms. Nevertheless, vertigo does not occur in posterior fossa lesions often enough to justify calling this anything but a general sign of pressure.

Respiratory Disturbances—Whenever intracranial pressure is so great that the cerebellum tends to drop down into the foramen magnum, pressure is exerted on the medulla, and, as a result disturbances in respiration may occur; these may be merely irregularities, or they may assume the Biot type, in which the respirations vary in depth and length, but never actually cease. If the medulla is very seriously compromised, a sudden slight increase of pressure may produce respiratory failure.

Yawning and Sighing Respiration are very significant evidence of medullary compression and are of considerable prognostic value. Patients may not be tired, yet may yawn continually. They may show no other alarming signs
of increased pressure, yet the presence of yawning in a case of tumor should always be considered a very grave symptom. It indicates that medulla is being compressed and is in a precarious condition.

Convulsions may be a general sign of increased intracranial pressure, or they may be of great focal significance. The type of convulsion, even though general and not preceded by an aura, may have some localizing value. Thus tonic convulsions seem to arise from level in the brain than clonic convulsions according to Jackson. (28)

General convulsions may arise from irritation of both cortices simultaneously, or the irritative substance may be so powerful that it can set off the entire mechanism, even though it be applied at only one point. Whether a general convulsion originates in any particular portion of the brain is not known, but clinical observations have suggested that a lesion of the frontal lobe is accompanied sometimes by general convulsions. In conclusion Sacha(10) says, "It is safe to say that whenever a patient has a clonic convulsion due to a cerebellar tumor, the lesion is pressing on or involving the cortex."

Mental Dullness--When an individual has markedly increased intracranial pressure, one of the striking ways in which it may show itself is by a slowing of his cerebration. The degree of mental dullness may vary enormously.
The administration of hypertonic fluids, may enable one to differentiate mental dullness caused by general pressure from dullness caused by a focal lesion. The hypertonic fluids will clear up that due to general pressure, but not that due to a focal lesion. This is, of course, only a transient effect but sometimes is the only way of determining which of these causes is producing the dullness.

**Unconsciousness and Coma:**—When the intracranial pressure is very high, the patient may become unconscious and go into a deep coma. Repeated attacks of unconsciousness, often without convulsive movements, are not uncommon in brain tumor. If a patient becomes dull, stupid, and finally lapses into a comatose condition, it indicates, as a rule, a terminal stage in the course of advancing compression.

**Changes in the Skull:**—These were discussed under auscultation and percussion in preceding section on methods of examination.

**Slow Pulse:**—The pulse rate may be slowed in increased intracranial pressure and at times becomes very slow, 40-45. It is an evidence of medullary compression, and clears up as soon as the pressure is relieved. For some reason, for which no satisfactory explanation has been offered, a slow pulse occurs much more frequently in cases of brain abscess than in brain tumor.
Blood Pressure Changes:—There is a very general misconception regarding changes in blood pressure in cases of tumor. In rapidly developing intracranial pressure, as in hemorrhage, one of the characteristic signs is a progressive rise in blood pressure, while in tumor cases, in which increasing pressure extends over a period of weeks or months, a rise is not observed.
VI FOCAL SIGNS AND SYMPTOMS OF BRAIN TUMOR

As has been previously stated when a new growth encroaches upon the contents of the cranial cavity the pathologic changes which take place are determined mainly by two factors. First, the brain is a highly specialized structure with numerous and fairly definite physiologic functions whose impairment becomes immediately evident. Second, a bony capsule which permits no expansion surrounds the brain. Therefore, when a tumor grows within the skull it impairs the specific functions of various parts of the brain and gives rise to local or focal signs; it causes a disturbance in the very delicately balanced relations between the fixed capacity of the skull and its contents and gives rise to the general symptoms discussed in the former chapter. It has been shown that these general symptoms are probably due to interference with the two circulations within the cranial cavity, blood and cerebrospinal fluid, as a result of increased intracranial pressure.

The focal signs of tumors of the brain depend upon the direct and indirect impairment by the lesion of the specific function of the different parts of the brain, but the ultimate effect of this impairment, which localizes the lesion, does not differ from the effect of numerous other lesions of different etiology and
pathology. But the way the signs and symptoms arise, the chronologic order of their onset, the manner in which they progress serve, in many instances, to distinguish the focal signs of tumor of the brain from those of other pathologic origin. For localizing purposes it is important to bear in mind that it is mainly those signs which appear early that are of significance.

Therefore, depending on these two factors, a number of other changes take place which determine the symptomatology to a great extent. There may be internal hydrocephalus with dilatation of one or all the ventricles, or compression of one or more ventricles, the brain and cranial nerves may be directly or indirectly compressed. It may be edematous, softened, and its convolutions flattened out. The dura may be stretched and become very tense. Other secondary changes may lead to distortion of the brain, herniation under the tentorium cerebelli or into the foramen magnum. There may be distant pressure with erosion of the sells turcica or its clinoid processes. The tumor may compress the vessels and lead indirectly to hemorrhage or thrombosis, causing secondary or distant signs and symptoms. Those may be irritative or paralytic in nature.

Finally there may be hypertrophic changes in the skull which may be discovered on palpation or x-ray. Spiller (29) and Phemister (30) say that "hypertrophy
of exostosis of the bone due to an underlying tumor, is usually associated with a dural endothelioma or meningioma and at times these thickened areas of bone are invaded by the tumor cells."

CEREBRAL TUMORS

1. Frontal Lobes--This region of the brain probably is the seal of higher psychic functions, so that mental and psychic symptoms frequently occur. In every suspected frontal lobe lesion, it is important to determine first whether the patient is right of left handed, for in right handed individuals the speech mechanism is located in the left cerebral hemisphere, while in left handed individuals it is in the right hemisphere.

In a large series of cases of tumor of the frontal lobe, one encounters singular instances on which a distinction from subtentorial tumor is most difficult. As Cushing pointed out (31), "It is, of course, one of the traditions of neurosurgery that one may easily mistake a frontal for a cerebellar case or vice versa." However, in the long run, tumor of the frontal lobe is frequently accompanied by a train of symptoms that allows a localization.

Changes in Personality and Memory:--No more subtle yet more characteristic change than this may be observed. Koloňy (32) shows that definite subjective and objective evidences of defects of memory were present in thirteen
cases of his series, or in 43%, similar evidences were present in 50% of the cases in temporal lobe tumor. Kolodny (32) says, "Deterioration of memory, however, is a considerable earlier symptom in the cases of tumor of the frontal lobe." The outstanding features of the memory defect in these cases are, "loss of memory for recent events, general indifference, and a lack of interest in their own occupation and personal welfare."

Changes of mood were observed, and these changes may be grouped under the heads of "exaltation" and "depression". Changes in behavior were also observed the patient becoming self centered and extremely egotistical.

Unilateral Facial Weakness--Sachs (33) emphasized the diagnostic value of a weakness of the lower portion of the face on the side opposite the tumor. He observed this weakness in 32 out of 45 cases. It is best detected when talking with the patient, as it may not be apparent on voluntary movement (as showing the teeth).

Eye-Grounds--Both eye-grounds, in a frontal lesion, may show a high grade of choked disc, but it is not at all unusual to see patients with frontal lobe tumors who have normal eye-grounds according to Sachs. Paton (25) believes that the amount of swelling is greater on the side of the lesion.
Eye Fields—Eye fields may show a variety of changes. There may be a central scotoma on the side of the lesion with or without disc changes. As a rule, if there is a central ascotoma in an eye, that eye also presents the picture of a primary optic atrophy. The opposite eye may show a choked disc. In addition to these findings, there may be unilateral exophthalmos and paralysis of the external ocular muscles. Cushing (34) has drawn attention to this particular type of frontal lobe lesion. Ravdini (26) says, "that it is very important to remember that in no region of the brain do eye-fields change, choked disc, develop as late as they do in frontal lobe lesions."

Unilateral Tremor—About 20 years ago, Stewart (35) described a fine unilateral temor in the hand on the side of the lesion. Stewart (35) says, "I have never met with similar lesions in association with tumors situated in other regions of the brain." What its significance is, if any, or the mechanism of its production, neither Stewart nor anyone else has been able to explain.

Reflexes—According to Kolodny (34) the abnormality of the reflexes depends upon the extent of the lesion and its relation to the precentral gyrus. The reflex involvement may vary from a Babinski, Oppenheim, Gordon or Chaddock on the side opposite to the lesion to an
ankle and patellar clonus, and these may be associated with varying degrees of spasticity. With the increase in the deep reflexed, there may be an associated loss of the abdominal reflex on the side opposite the lesion. Not infrequently patients with frontal lobe lesions have incontinence of urine and sometimes also of feces. Whether this bladder disturbance is evidence of a bladder center in the frontal lobe, or of a mental disturbance, is very difficult to determine.

**Smell**—When a lesion is on the under surface of the frontal lobe, there may be loss of smell as a result of involvement of the olfactory nerve, but if the lesion presses on the temporal lobe, in which the cortical center for smell is located the patient may experience disturbance of smell, he thinks he smells odors which no one else can detect at the time.

**Speech Disturbance**—According to Sachs (33) when lesions occur on the left side, especially when they are in or near the region of the third frontal convolution, a disturbance in speech is often present. An aphasia arising in that region always is characterized by some impairment of the verbal component of speech. Although at times the patient loses all power of speech, far more interesting and much more difficult to analyze are the partial defects. Some patients show only
a slight slowing in speech or merely slight hesitancy.

**General Convulsions**—It has been pointed out by various observers that general convulsions occur in patients with frontal lobe lesions, months, and sometimes years, before there are any other evidences of a brain tumor. This has been so frequently observed that the possibility of a tumor should always be considered in every patient who has a convulsion.

In summary the most frequent and most dependable diagnostic signs of frontal lobe tumor were found to be facial weakness, personality changes, and, in left sided lesions, aphasia.

2. **Parietal Lobe**—A lesion in this region may occasionally give rise to focal epilepsy (jacksonian fits), and, depending upon the portion of the pre-central gyrus which is affected, the convulsion may begin in the face, arm, or leg. The convulsion according to Sachs (10) may be preceded by a motor aura, or if the portion irritated is behind the central fissure, the aura may be a sensory character—tingling or numbness. The cases in which convulsions occur, either have a lesion pressing upon the cortex or one involving the cortex itself. Such lesions must be irritative in character because a destructive lesion
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is not accompanied by convulsions. If the lesion involves the precentral gyrus, or the fibers coming from it, the patient will have a partial or complete hemiplegia.

Lesions of the precentral gyrus have the pathological reflexes that accompany an upper motor neurone lesion. If the lesion is behind the central fissure, there may be only subjective sensory disturbances. With such disturbances, the patient complains of tingling or a feeling of numbness, but the most careful sensory examinations may show no objective change in sensation. If there are any objective sensory disturbances they will be of a discriminatory nature, best demonstrated by compass points. This is the type of sensation that Head and Holmes (36) have called cortical loss of sensation. According to Mills (37) if the lesion is still farther back in the parietal lobe, there may be loss of the stereognostic sense. He also says "in testing for astereognosis, it is important to determine first whether the patient has any disturbance in sensation in the hand, for if he has, it vitiates the test. True astereognosis can be said to be present only if all cutaneous sensation is normal".

If a lesion is in the left cerebrum and near the sylvian fissure, asaphasia may be present. The aphasia that is produced from this region is what Head (38) has called nominal and semantic aphasia. Of the former
type Head (38) says, "This is essentially a loss of power, to use names and want of comprehension of the nominal value or meaning of words and other symbols." Head (38) says concerning semantic aphasia, "this form of aphasia is characterized by want of recognition of the ultimate significance and intention of words and phrases, apart from their direct meaning."

3. Temporal Lobe—Thompson (39) has recently reported five instances of focal bulging of the squamous portion of the temporal bone, due to an underlying brain tumor. Three of the tumors were large gliomatous cysts and two meningeal fibroblastoma.

Lesions in the temporal lobe are recognized primarily by the defects in the eye-fields—a partial homonymous defect with retention of central vision. In addition to these field defects, a patient may have a visual aura. Horrax (40) has studied a number of these cases from Cushing's clinic and points out that it is an aura of form, while an aura arising from occipital lobe is more frequently one of color.

According to Head (39) if the lesion is on the left side, there may be a definite aphasia, especially if the first temporal convolution is involved. If the anterior mesial surface of the temporal lobe is involved, there may be subjective disturbances of smell, so-called uncinate fits, first described by
Hughlings Jackson. If the lesion is farther back in region of Heschl's convolution, the patient may have an auditory disturbance according to Sachs (10). Kennedy (41) describes a condition of "dreamy state" where the patient has a sense of unreality, feels as if he were in a dream."

Finally Wechsler says (42), "Temporal lobe lesions may have mild contralateral hemiparesis, especially of the face, and even thalamic sensory disturbances. Should the tumor press downward and inward there may be trigeminal neuralgia with objective impairment of the function of the nerve and pupillary disturbances, such as fixed or dilated pupils, on the side of the lesion."

Schlesinger (43) reports a syndrome caused by fibrillary astrocytomas involving the deep parts of the temporal lobe. "The chief symptoms in chronological order are: various kinds of epileptic attacks, failing memory for recent events, and general mental insufficiency which proceeds to complete loss of memory and intellectual deterioration, motor and sensory disturbances on side opposite the lesion, particularly a definite weakness on the lower part of the face; aphasia and anisocorid."

4. Occipital Lobe:--The characteristic sign of tumors of the occipital lobe especially of the calcarine fissure, is contralateral homonymous hemianop-
sia. Holmes and Lester (44) show that the hemianopsia may be bilateral if the tumor lies between the occipital lobes and affects both calcarine areas. Also a lesion above the calcarine fissures results in a defect in the lower half of the visual fields and vice versa. Focal convulsions preceded by a visual aura arise from an occipital lobe lesion, the aura being one of color.

A tumor in the occipital lobe may sometimes, by direct pressure through the tentorum, give rise to cerebellar symptoms. In such an instance it may be difficult to determine whether the lesion is above or below the tentorum. Sachs (10) suggests the use of a ventriculogram to settle the point. He says, "The ventriculogram in an occipital lobe tumor, shows the posterior horn of the ventricle ablated."

5. Tumors of the Centrum Semiovale and Basal Ganglia. These tumors may exist for a long time without giving focal signs, and remain undiagnosed. Wechsler says(42), "large lesions of the basal ganglia may give bilateral symptoms. Lesions of the corpus striatum may give incontinence of urine, vasomotor and temperature disturbances. A hemiparkinson syndrome, hemianopsia may also occur. Tumors of the corpus callosum are both rare and difficult to localize and mental symptoms akin to those of general apresis are characteristic to these tumors."
6. Tumors of the Third Ventricle—Lesions of the third ventricle give very bizarre and variable symptoms. Dandy (45) shows that if the lesion is in the region of the foramen of Monro, the symptoms may be bilateral in character as a result of the associated dilatation of the two lateral ventricles. There may be bilateral pyramidal tract symptoms, and there may be symptoms suggesting both frontal and cerebellar involvement.

The most recent and most complete study of these tumors is that by Fulton and Bailey (46). They have grouped the symptoms under nine headings:

1. Infundibular syndrome (adiposity, polyuria)
2. Hypersomnia (the syndrome arising from the region of the aqueduct of Sylvius and central grey matter around the posterior end of the third ventricle).
3. The thalamic syndrome (central pain and painful hyperesthesia).
4. Extrapyramidal syndrome (bradykinesia, rigidity).
5. Paralysis of conjugate vertical movements of the eyeballs (Perinaud's syndrome).
6. Decerebrate rigidity.
8. Hypopituitarism (infantilism, hypotrichosis, lowered metabolism).

They contend that of all these symptoms the tendency to sleeplessness is perhaps the most characteristic, but, as this symptom may often be observed in other cases of marked increased intracranial pressure it still remains true that the most reliable method of diagnosing these cases is by ventriculography as introduced by Dandy.

Tumors of Cerebellum, Pons and Medulla

In tumors of the posterior fossa, general signs of increased intracranial pressure are particularly pronounced, and one rarely sees a tumor of the cerebellum in which in addition to the focal symptoms, the general symptoms are not well developed. The various terms used to describe the disturbed function which give rise to the focal symptoms are: asynery, ataxia, adiodokikinesis, hypermetria, atonia, asthenia, dysmetria and dysynergy. Weisengurg (47) believes that all are forms of asyneryg. A discussion of cerebellar tumor symptoms follows:

1) **Ataxia**—When the patient walks he staggers like a drunken man, and walks with his feet far apart. He may be so unsteady that he falls unless he is supported, and he tends to fall to the side of the lesion. If the lesion is in the vermis he may fall forward or backward.
(2) **Adiodokokinesis** is the inability to carry out coordinated movements. When movements are combined or coordinated they are synergized movements.

(3) **Attitude of the Head**—Patients with cerebellar lesions sometimes hold their heads in a characteristic attitude. The head is flexed to the shoulder on the side of the lesion and the chin is turned to the opposite side. Horsley (48) believes it is due to the pressure in the superior peduncle.

(4) **Nystagmus**—According to Grey (49) when one of the lateral lobes of the cerebellum is involved, the patient may show lateral nystagmus either on looking to the side of the lesion or on looking straight ahead. He says, "True cerebellar nystagmus has a quick component to the side to which the patient is looking, and a slower recovery to the other side." When the median lobe of the cerebellum is involved, the patient may have a vertical nystagmus.

Weisenburg (47) in concluding his article says, "There is functional localization in the cerebellum." In the vermis are represented the synergic activities of the trunk; in a superior vermis the movements of the shoulder girdle of the upper trunk, in the inferior vermis the pelvic girdle or the lower trunk. Synergic activities concerned in talking and movements of the eye are located in the vermis, in all probability in the superior vermis. Synergic control of the limbs is in the lateral hemispheres, for lower in
the inferior."

1. Cerebellopontine Angle and Acoustic Tumors—

Certain tumors in the posterior fossa are located in the cerebellopontine angle or lateral recess. They may be of two kinds (1) those that originate in the cerebellum and (2) those that have their origin in the eighth nerve, and, very rarely, in the fifth nerve.

According to Stewart and Holmes (50) the history of cerebellar tumors extending into the angle is quite different from the history of acoustic neuromata. The outstanding points of difference are these: In the first group, cerebellar symptoms appear at the onset of the disease, and involvement of either portion of the eighth nerve, if it occurs at all, appears later. In the eighth nerve tumor cases, however, the earliest symptoms are all due to interference with the functions of the eighth nerve, either the cochlear or vestibular portions. Usually the patient first complains of tinnitus, diminution of hearing and vertigo and dizziness. These are followed later by cerebellar symptoms and general signs of pressure. As an eighth nerve tumor develops it may involve the fifth nerve and cause hypesthesia or anesthesia of the cornea. Frequently the entire sensory branch of the fifth nerve becomes involved, and sometimes the motor branch. Cushing (4)
has drawn attention to the point that, in some cases, the involvement of the eighth nerve is but a part of a general disease, neurofibromatosis, or von Recklinghausen's disease. Clinically, these cases can be recognized only by the presence of fibromatous nodules elsewhere on the body.

2. Pontine Tumors--Horrax (51) has described a group of symptoms which he considers characteristic of pontine tumors. They are he says, "Absence of evidence of increased intracranial pressure, absence of choked disc, rapid development of symptoms and cranial palsies, particularly of the fifth, sixth, ninth and tenth nerves." Perhaps the most striking single symptom of pontine involvement is complete bilateral sixth nerve paralysis. While unilateral sixth nerve paresis is a general sign of intracranial pressure, bilateral involvement is an important focal symptom. Horrax (51) also points out that if the tumor surrounds the aqueduct of Sylvius, an obstruction will be caused early giving choked disc and internal hydrocephalus.

3. Pineal Tumors--Pineal tumors are operable while tumors of the pons are not. A tumor in the pineal region is almost certain to produce visual disturbances since the anterior corpora quadrigemina lie directly ventral to it. The type of visual defect is
usually a homonymous one which, according to Sachs (10) cannot be distinguished from the homonymous defect that occurs when there is an injury in the optic radiation or occipital lobe. Dandy (45) first advanced the idea that these tumors could be recognized and differentiated from occipital lobe tumors by air injection.

4. Tumors of the Medulla--These tumors are quite rare and like those of the pons, also give alternating hemiplegias, with the cranial nerves (eighth to twelfth) impaired on the side of the lesion and the pyramidal tract signs on the other. As the medulla is a small structure the symptoms are often bilateral. Tumors are rapidly fatal because of the many vital structures involved, especially the pulse and respiratory centers. According to Wechsler (42) the outstanding symptoms are: Paralysis of the vocal cords, dysarthria, atrophy of the tongue, nystagmus ataxia, vertigo, vomiting, crossed anesthesia and Horner's syndrome.

Tumors of the Pituitary Body--

Tumors of the pituitary body may be divided into those which are infrasellar, and do not at all invade the cranial fossa, and those which push up the tentorium sellae, or break through it and grow into the middle fossa. According to Cushing (19) the pituitary adenomas are generally intrasellar, while craniopharyngeal duct and cystic tumors are extrasellar and
intracranial. As long as the tumor remains within the limits of the sella the only symptom present may be headache and the signs of either acromegoly or dystrophia adiposogenitalis. But as soon as the growth begins to press upward, the optic chiasm and tract begin to show signs of involvement. In a summary of the symptoms described by Cushing (19) we find that bitemporal hemianopsia and optic atrophy are the characteristic signs. The hemianopsin may be homonymous, or the blindness be limited to one eye. The headache is often severe and constant. Somnolence is an occasional symptom. Cushing (19) says, "It has become increasingly probable that what passed hitherto for pituitary symptoms alone are also found in lesions of the infundibulum, the tuber cinereum, the anterior perforated space, and the third ventricle." These symptoms are polyuria, polydipsia (diabetes insipidus) and disturbed sugar tolerance. Choked disc is very rare in pituitary tumors and if it occurs at all, is a later sign, showing that the tumor has invaded the cranial cavity sufficiently to compress the third ventricle. In craniopharyngeal duct suprasellar tumors, which occur earlier in life, choked disc is more common. According to Davis (3) in intrasellar tumors the sella is ballooned out, while in suprasellar it is flattened, he also shows that in Rathke's pouch tumors there generally is found suprasellar calcification; not so in suprasellar endotheliomas.
While gliomas of the chiasm may give rise to signs and symptoms more or less like those caused by tumors of Rathke's pouch, they are not nearly so typical and show no calcification.

Cushing (17) has shown that the clinical syndrome of pituitary adenoma in the adult is that of acromegaly due to hyperfunction of the anterior lobe and the long bones may increase in length and somewhat in diameter, the bones of the face also may show enlargement. There is a prominent lower jaw, prominent frontal eminences and large feet and hands. All gradations from pure gigantism to almost pure acromegaly may be encountered but it is important to remember that while gigantism, or a tendency in that direction, may be physiological. Acromegaly is always due to a pathological change in the pituitary gland—achromiophil adenoma.

Dystrophia adiposogenitalis (Frohlich's syndrome) due to pituitary deficiency caused by a destruction of the gland. The syndrome occurs mainly in the young, in pre or postadolescent period. There are areas of Frohlich's syndrome which show no involvement of the pituitary at necrospy; conversely, the pituitary may be severely compromised without giving rise to any symptoms. The syndrome is seen frequently though in cases of chromaphobe adenoma which is the most common type of pituitary tumor." The syndrome is characterized
by a enuchoidal obesity, alteration of the secondary sex characters, change in bodily growth, gigantism, metabolic disturbances. The sex glands are small, the genital hypoplastic. Menstruation, and libido are lost if the disease sets in after puberty and fail to appear if the syndrome is present before puberty. In males there is loss of facial and pubic hair, or a feminine pubic hair line is present. In addition there may be polyuria, polydysia and increased sugar tolerance. The optic atrophy and other cranial nerve plasies, the headache, somnolence, and so forth, may be the same as in any other tumor of the pituitary.
SUMMARY

In summarizing this article we find that the diagnosis of tumor of the brain is at the same time the simplest and most difficult in the whole domain of neurology. It should embrace not only the general fact, but also, if possible, the site and nature of the lesion. With the possible exception of choked disc there are no "classical" signs of tumors of the brain. But a syndrome which is characterized by the slowly progressing headache, occasional vomiting, dizziness, mental dullness, and one or more focal signs should at once arouse suspicion of tumor. The gradual onset of choked disc lends almost certainty to the diagnoses, although this can often be made without its presence. Localized headache, possibly accompanied by percussion tenderness, and especially by vomiting without nausea, is very significant. Nevertheless one must exclude headaches due to syphilis, migraine, hysteria, sinus involvement, uremia, or other general causes. Jacksonian convulsions, particularly in young people, are very suggestive of tumor of the brain, and so is a generalized convulsion coming on in the middle life or later. General paralysis, other forms of neurosyphilis, and arteriosclerosis must, however, be borne in mind.
In the differential diagnosis of brain tumors, we find that ordinarily abscess of the brain causes no difficulty. It is usually preceded by disease of the ear and sinuses, abscess of the lung, or fracture of the skull. Fever is more often present in abscess, there is usually a slow pulse, choked disc is less common, the course is more rapid, there is apt to be more than one focus, and the spinal fluid, if the abscess is near the surface, may show signs of meningeal reaction. Progressive softening of the brain, due to vascular disease in older people, at times offers insurmountable difficulties. Progressive hemiplegia, with headache and stupor and mild optic nerve changes, may closely simulate tumor. The general condition of the patient, evidence of arteriosclerosis or hypertension, the previous history, and the progress of the case should help in the diagnosis. At times only an encephalogram, an exploratory operation or necropsy can establish the diagnosis. General paresis very seldom offers difficulties. This is possible, however, if the disease is heralded by epileptiform attacks alone. But the history, the general mental picture, the pupillary signs, the course of the disease, and especially the serology usually attest the diagnosis.
Chronic recurrent hydrocephalus offers great, frequently insurmountable, difficulties. While there may be all the symptoms of increased intracranial pressure, there are few or no localizing signs. Acute hydrocephalus usually follows some infectious or inflammatory disease. The history, the onset, the absence of focal signs, the hydrocephalic head, and the typical cry point to the diagnosis. Optic atrophy is also more common in hydrocephalus. Acute or subacute encephalitis may be accompanied by choked disc and be mistaken for tumor. Usually the history, the presence of fever, ophthalmoplegia, radicular pains, evidence of basal ganglion involvements, multiplicity of signs, and the spinal fluid findings point to encephalitis. Multiple sclerosis, if it begins with optic neuritis and the first patch is in the pons and the cerebellum, may for a while lead to an erroneous diagnosis. Hysteria may, very rarely, simulate tumor of the brain. The absence of gross neurologic signs obviously rules out tumor.

X-ray of the skull, except in pituitary tumors, offers little diagnostic evidence. Growths within the sella greatly enlarge it, and erode the floor and the clinoid processes. But even x-ray of the sella may be incorrectly interpreted. The general signs of intra-
cranial pressure are not altogether reliable. Increased vascularity of the skull and the enlargement of the diploic veins may show on the x-ray plate in some meningiomas. Ventriculography or pneumography, introduced by Dandy, and encephalography give decided help in selected cases.

Pathologic diagnosis is important alike for treatment and for prognosis. Tumors of the cortex (meningeal) are apt to be endotheliomas or sarcomas. Gliomas are as a rule deep-seated. In the angle one usually finds neurofibromas or acoustic neuromas. Tumors of the pituitary are apt to be adenomas or cysts. In children glioma and tubercle are the most common tumors, and frequently are cerebellar. The latter are usually secondary to other tuberculous foci in the body. Carcinoma is practically always metastatic. Bony tumors often show on the x-ray plate. Endotheliomas, neuromas, and gliomas, as a rule, run a slow course. The last occasionally runs a very rapid one, especially the spongioblastomas.

In conclusion, it may be stated that an accurate localizing diagnosis is not only a test of the skill of the neurologist, but is essential alike for palliative and for radical operations. An accurate history, regard for the chronological onset of signs and symptoms, and a meticulous examination are absolutely necessary. It may be emphasized once more that only the signs and symptoms which occur early are of greatest value in localization.
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