BRAIN TUMOR: ITS CONTRIBUTION TO NEUROLOGY
IN THE REMOTE AND RECENT PAST*

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A prophecy as to the future of Neurology would seem to be an appropriate
topic for the address which, in accordance with tradition, I am about to make as
your incoming President. However, on recalling that a prophet is said to be
not the wisest of men, and for other and obvious reasons, I have chosen Brain
Tumor as a more suitable subject. Here, to some extent, future progress can be
projected against the background of the remote as well as the more recent past.
It is also possible to compare the periodic, decade by decade, accumulations of
this special knowledge, noting particularly the pace of progress, whether
accelerated or retarded, as medical art and science advanced.

It was the latter half of the 18th century when those engaged in the art of
healing caught up with the other forces of the Renaissance. In that time, we
find Morgagni and Bonet (quoted by Morgagni) as reliable current informants
about the external form of, and the disturbances produced by, brain tumors.

The former in his letters on “The Diseases of the Head” offers a fair inventory
of the prevalent knowledge of brain tumor accumulated up to their publication.
But, before quoting from these and other sources it would be well to devise some
convenient scheme for tracing the steps in the march of the advancing knowledge
of brain tumor, by distributing the more significant events into a series of selected
epochs.

The first epoch encompasses the greater part of the 18th century, when ex-
anding intracranial lesions came to be more readily recognized clinically, but
only when they made their appearance through a defect in the skull, resulting
from the effects of the tumor.

A second epoch followed at the end of that century, when it became apparent
that such tumors took origin from the coverings of the brain, the skull cap, the
dura and leptomeninges.

During the third epoch in the early part of the 19th century manifestations of
increased intracranial tension were found to have as their cause deep seated
lesions of the brain. During the same period careful investigation of the ac-
cumulated material served to identify some of the more obvious features related
to the size, form, consistency and color of such lesions, but there was no under-
standing of their true structural character or correlation of their location with
symptoms. Attempts made to correlate the more obvious morphologic features

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of such tumors with the clinical manifestation yielded almost nothing in the nature of sound scientific observations.

A fourth epoch during the later half of the 19th century was productive of the first scientific results, as correlation between the location of the expanding lesion and the clinical expression was more successfully established. A closer approach was made to the modern understanding of the effect of brain tumor on the functions of the intracranial contents.

The final and modern epoch at the opening of the 20th century may be said to have begun when the early foundation was laid for a workable hypothesis of localization of function.

It would be well to remember that the opening epoch, at the beginning of the 18th century, received from the preceding years an exceedingly poor heritage, the recording of which will require but a few remarks with the mention of but a few names. Among them is that of Marcus Aurelius Severinus, (1580–1656), (see Courville) who recorded the exposure by trepanation of a fungoid growth in the head with the result that the patient was relieved of headache. Vigier, in 1657, (mentioned by Peaucqut) had recorded a case of what he termed “fungus cerebri.” It is safe to assume, that under this term, he described a meningeal tumor which probably decompressed itself through a defect in the skull. Camerarius, (see Courville) in 1687, described a tumor of the right frontal region which grew very rapidly and terminated in the death of the patient. He found the tumor to involve the dura as well as the underlying leptomeninges and to implicate the brain.

At about the same time (1679) the Sepulchretum of Bonet made its appearance. Morgagni drew liberally from the abundance of informative material in this treasure of pathological observations. Bonet's observations on one case and Francois Pourfour du Petit's (quoted by Newburger) (1710) studies of four cases laid the foundation of the concept of the sensory motor function of the cerebral cortex, a good beginning for our present understanding of localization of function.

A significant observation was made by Weissman, in 1692 (p. 133). He described an intracranial tumor in a patient who manifested among other symptoms: mental changes, some form of speech disturbance, and a mimetic disorder. The lesion as he described it, "an edematous tumor, occupying all of the upper of the cerebrum between it and the pia mater..." was probably a meningioma of the frontal lobe.

MORGAGNI

Morgagni in his letters on "The Diseases of the Head" provides an excellent inventory of the knowledge of brain tumor accumulated up to their publication. The first and the third volumes consist of several important subdivisions, each one considering a series of topics in the form of letters. One of the most significant letters deals at great length with Pain in the Head; several letters discuss Apoplexies; still another is concerned with Paralysis; and one with Convulsions and Convulsive Motions. The reader of these letters is impressed with the thoroughness with which this keen observer recorded his findings. Indeed, ex-
ception may be taken to the deductions and conclusions he drew, but it must be realized that he was still under the influence of the medieval metaphysical interpretations of the normal and abnormal functions of the human organism. It seems that he himself was aware of these shortcomings, as revealed by the fact that he seldom attempted to predict the character of the probable organic lesion from the observed symptomatology. Only on discovery of some related anatomical anomaly would he undertake to interpret the related symptoms, and then only in the light of the then prevailing teachings. Yet, we are indebted to him for many classic descriptions of pathologic findings, some of which I should like to quote verbatim. A tumor, very probably gliogenous in nature, found in the depth of the longitudinal fissure was described by him (vol. 1; p. 474):

“The anterior lobes of the cerebrum where they are contiguous to one another, had, in the middle of their height, part of their surface convolutions in a manner of intestines; so formed that the one was received and the other was recipient in that part.”

His interpretation of the clinical manifestations of the case are, of course, in keeping with the concepts of his day:

“What effects even a vain terror can produce, is shown by the history in question. You see that instantly, both the clinic and tonic convulsions, as those at the mouth, arose from disturbed motion of the spirits; and by detaining the blood in the vessels subserved to the brain, and by this means bring on an effusion of serum, certainly brought on new causes for which these very convulsions continued even to the death.”

When the foregoing lines are compared with other observations, one can still admire a man whose appreciation of pathologic alterations was not impaired by his mystical considerations of cerebral function. Nor was his clinical sense dulled by it. For instance, that headache with progressive loss of vision is likely to be caused by a “scirrhus” suprasellar tumor was a condition already known to him. In this connection, he quotes (vol. 3; p. 499) a case reported in the “Acta Eruditorum” of Leipsig, of “a female who was seized with obscurity of vision, following intense headache with terminal loss of vision.” The postmortem revealed a “scirrhous” pituitary with a “fungus” growing above the sella in the optic chiasm.

In commenting upon Valsalva’s concept that one half of the brain controls the contralateral musculature, he recalls (vol. 1; p. 235) that Wepfer, who, as recorded in the Sepulchretum, observed a “hemiplegic virgin” whose brain when dissected disclosed two cyst-like tumors within the right ventricle which he thought “conspired to produce a hemiplegia of the left side.” Morgagni finds it necessary to note that Wepfer “attributes too little to these tumors which had compressed the right side of the brain so long, and consequently prevented, or at least diminished, the influx of animal spirit into the left part of the spinal marrow for a long time... which for that reason seemed less (smaller) than the right.” This may be considered as the earliest observation on pyramidal tract atrophy in the cord as the result of cerebral implication.

Another highly suggestive observation by Morgagni (vol. 1; p. 203), is on “A woman aged 60 years, who had for almost two years been subject to epilepsy, by falling down in one of her fits had got a blow upon her head. At first no external signs of injury appeared
upon the cranium, nor yet any internal symptoms of the brain's being injured." The epilepsy did not change its character. There was a slight fever before she died. "The meninges were everywhere sound... but scarcely was the dura mater taken off when we observed, that in the left hemisphere of the brain, the third and anterior lobe was much lower than its fellow, and much softer; and not only in the upper part, but entirely throughout the substance, the brain as well as the other parts, not excepted... softness which was very evident in the cortical substance, but much more so in the medullary. For this last, in particular, was changed into a kind of jelly, in the greatest part of it, which was of cineritious color, degenerating into brown, and yet almost transparent. And this disorder had also affected the anterior part of the lateral ventricle,... There was nowhere anything of a disagreeable smell; nowhere any pus, or anything bloody, in this jelly, so that it seemed to be a disorder of a peculiar kind. In the remainder of the cerebrum, cerebellum, everything was sound..."

This case is in all probability an instance of brain tumor in spite of the presence of softened tissue. In favor of this assumption is the fact that Morgagni, as can be gathered from his descriptions elsewhere of cerebral softening and cerebral hemorrhage, was fully aware of the character of such lesions and would have recognized their existence of this case. Instead he chose to describe it as "a disorder of a peculiar kind."

Of unusual interest is the description of anatomical findings in another case (vol. 3; p. 480):

"A man of 48 had begun to complain of very acute pains in the head. To these pains was added a debility of both the lower limbs likewise, to so great a degree, that he could no longer support himself upon them... And although the lower limbs, as far as motion was concerned, were paralytic; yet neither the upper limbs nor any other parts of the body were attacked with an affection of that kind. It happened that he died... it was suddenly observed that he was giving up his ghost..." To a lengthy account of alterations in the cerebral hemisphere, he added: "The third ventricle seemed to be shorter than it naturally should be; but the fourth ventricle certainly appeared to be longer than it generally is, after the cerebellum had been cut through the middle, in the usual manner; and laid aside on one hand and on the other. And in cutting this substance in the manner I have said; I found a circumstance of disease, which the surface thereof, that was similar to what it generally has, did not so much as suffer me to suspect. This is to say, no sooner had I proceeded, with the knife, to the depth of a finger breadth, but perceiving an unusual resistance, I stood still and drawing asunder that part which I had cut into, was very much surprised that no mark of the medullary tree or shrub appeared; but that in its place were parallel medullary striae drawn betwixt the cortical substance; from which striae no small branches were, in any place, sent forth. Then attempting the division with a sharper and stronger knife; whatever remained of the middle substance of the cerebellum, I cut quite down to the fourth ventricle and began to see that disorder... It was a substance not soft, not of two colors, nor cut betwixt with deep and frequent sulci; but a scirrhous substance and of one color, which approached pretty nearly to that of a very dilute flesh color, being made up of roundish corpuscles, as it were, so compacted one with another, that there nowhere occurred any interstice, no membrane, no sanguiferous vessels. A disorder of this kind extended itself on the one hand, towards the right side, in some measure; and, on the other hand, through almost the whole left lobe of the cerebellum. For if you excepted the surface of this lobe, which was made up of its natural substance; that was in some places very little, and at the lower part none at all; all the remaining part was occupied by just the same disorder; and at the lower part in particular it was closely connected with the dura mater; so that the disorder might be supposed to have taken its origin from that place and to have been propagated, from thence, into the other parts whereof I have spoken. And the right lobe,
although it consisted of a soft substance, and that double also; I mean a cortical and a medullary substance; nevertheless did not show, when cut into transversely, that disposition of both these substances, which it is wont to do in other bodies; but a disposition evidently different therefrom: although not to such a degree as that middle part of the cerebellum; which where it was soft, and made up of a double substance, of old sections so very different from what we have always seen."

The foregoing description of an infiltrating cerebellar tumor is so vivid that it tempts one to offer a definite pathologic diagnosis. However, I shall not venture to do more than to express an opinion based on Morgagni's observations on its consistence, surface appearance and relation to the overlying dura. These features would suggest the diagnosis of a sarcomatous menigioma.

The pineal body, which in the days of Morgagni was still considered as "the seat of the soul," was, wherever possible, subjected to careful investigation. References to the state of this organ as well as attempts to correlate some neurologic disorders with its altered conditions are frequently encountered. And so Morgagni at every opportunity similarly directs attention to this structure. He describes what was in all probability a pinealoma as a "pineal body of unusual magnitude" found in a boy of 13 years. From his account of the neurologic manifestation we see that he was apparently unaware of the diagnostic implications. He lists but a few findings, such as fixed gaze, headache, convulsive seizures, without commenting on their clinical significance (vol. 1; p. 1).

Also of interest is the clinical observation by Morgagni (vol. 1; p. 18) of a patient in whom "pain in the head" was the most troublesome symptom. He notes "there was no disorder in the belly, although there were signs of obstruction." On death, on opening the cranium, the dura was found to be firmly attached to the skull and for some space this meninx had degenerated into "the middle state betwixt a bone and a ligament and formed the figure of an ellipse." Apparently, he was not aware that he was dealing here with a well-defined menigioma. He offers a most interesting explanation for the clinical signs manifested by the patient. They were caused, in his opinion, by some obstruction of the circulation. This in turn, he continues, "caused obstruction of circulation of juices in the meninges" and thus caused headache. The latter, he assumes, was provoked by contraction of fibers resulting from irritation, caused by the described lesion in the meninx.

The occurrence of convulsive disorders in patients with expanding lesions who did not display paralysis, was another clinical feature which did not escape Morgagni's observation. He predicated that tumors on the outside of the brain may irritate the meninges and thus cause convulsions, but, "failing to compress the brain, do not lead to paralysis."

He described a case (vol. 1; p. 211), which may now be identified as a frontal menigioma, but did not relate the location to the clinical picture. In a patient, aged 35, pain of the head was the first symptom. It was followed by loss of weight in the course of two years. Then loss of smell, epileptic seizures and frequent bleeding from his nose ensued. He died shortly thereafter. A tumor, hard and callous, connecting with the dura near the crista galli was found. Of
interest is his comment on the physiological deviation which resulted from this
tumor. He says:

"It is probable that the animal spirits are put out of their course, and reflected in tumultuous motions, as often as being more swiftly agitated, from any cause whatever, they come to some certain place in the brain, which by reason of callous hardness, or an interposed abscess, are altogether impervious; although, indeed, it seems that even the abscess alone may be emitting something from itself into neighboring parts to excite tumults of the brain."

All that is necessary is to supplant his references to the circulating spirits by the more logical and now fairly well accepted understanding of the cerebral vascular mechanism, and a more charitable interpretation may then be placed on his remarks.

This somewhat sketchy review of Morgagni's observations on brain tumors would be incomplete without reference to his views on the causes of blindness. He mentions four: "extenuation of optic nerves; subsiding of ventricles of the brain; wasting of nerves; and detraction of nerves." All of them we would now recognize as causes or results of optic atrophy.

Thus, it seems that by the end of the 18th century some knowledge, though vague and of meagre scientific value, had accumulated as the first of the indicated epochs was opened by Louis (1774), the famous secretary of the French Royal Academy of Surgery. In his equally famous memoires he drew attention to his predecessor, Quesnay and his published observations on "Trepanation in doubtful cases," on "Multiple trepanations" and on a case of "Trepanation for a carcinoma cerebri." As for himself, Louis assembled in these memoires a series of lesions, mainly neoplastic, resulting in destruction of a localized portion of the skull. He and his contemporaries were restricted in their studies to the morphologic character of these lesions. For this reason his "tumeurs fungueuses de la dure mère" do not represent a single anatomical entity, but comprise expanding lesions of various origin and character. Nevertheless, his observations, no matter how faulty, served to lay the foundation for subsequent and more fruitful studies. In fact, almost everyone who undertakes the study of meningeal tumors begins with a consideration of his material.

In direct succession to Louis, there are encountered the names of Conrad (1778), Loder (1779), Sandsfort (1786), Abernethy and Siebold, Wenzel (1811), and finally Bell (1821) who have added well observed instances of fungoid neoplasm of brain and cranium, without departing from their prevailing interpretations.

ABERCROMBIE

A bold move toward a more systematic grouping of disease forms in the central nervous system with emphasis on brain tumors, is made by Abercrombie. In his Pathological and Practical Researches on the Diseases of the Brain," published in 1831, he defined organic diseases of the brain as permanent changes in the cerebral substance itself. Among them he found new formations in the head which are either embedded in the substance of the brain or attached to its surface. With
the latter he included those that were formed by thickening of membranes of the brain, or by deposition of new matter between their laminae.

He was apparently first to offer a classification of tumors in accordance with their external appearance and consistency and recognized several types: One type was characterized by the deposition of "a pellucid or semi-pellucid substance" bearing the character of albumin, which may be formed in undefined masses under the membranes of the brain, particularly under the arachnoid, or contained in distinct cysts in various parts of the brain. A second type was a very dense tumor of a whitish ash color, exhibiting the properties of coagulated albumin. These tumors were distinctly rounded and generally attached to the dura. He found them to arise from the outer surface of the dura; then they frequently eroded the bone. Abercrombie further made the observation that when such tumors were rashly meddled with by incision, death was generally the consequence. He noted that some small similar tumors were attached to the choroid plexus. He saw one in each lateral ventricle of the brain of a man who died after having had repeated epileptic attacks at long intervals and had been affected with symptoms threatening apoplexy for some time. The third type of tumors resembled externally those of the second type, but showed an "organized appearance, a reddish or flesh color, resembling the substance of the kidney." In addition to the foregoing three types of tumors, he pointed to tuberculoma, ossification of either the inner surface of the cranium or that of the falx cerebri.

In his endeavor to correlate the leading symptoms with the pathologic findings, he was, for obvious reasons, unable to find any uniformity "by which particular symptoms can be distinctly referred to the various forms of the morbid affections." Praiseworthy, though unsuccessful was his attempt in this direction, when he postulated as a pathognomonic sign for tumors of the first type: long continued headache and for those of the second type: headache, mental changes, vision-hearing disturbances, disturbances of taste and smell, and speech impairment. He was vaguely aware of the symptoms on varied localization. He singled out the optic nerves, the corpora quadrigemina, the lower part of the anterior lobe, the posterior part of the left hemisphere, and the pineal gland as sites which determine the deflection from uniformity of symptomology. He mentioned, as an example, one case of deafness in which the tumor rested between the brain and cerebellum, apparently an angle tumor.

Tumors of this third type, he found to manifest the same symptoms as those of the second type, but to cause also convulsions without affecting the sense organs and to give rise to little pain.

The greatness of Abercrombie lies in his keen sense of morphologic observations as exhibited in a most artful description of a tumor. It appears at the end of his thesis on brain tumors and is presented to the reader without suggesting its significance. He apparently relied upon later observers to discover its true character, that of spongioblastoma (Case CXL; p. 317).

"... the left hemisphere of the brain... to be diseased throughout in a very singular manner. Some parts of the mass were indurated others softened; and it presented a variety of colours, chiefly a rose-colour, grey and yellow; and the more diseased portions were
highly vascular. In some places there were distinct inculcated masses, enclosed in vascular cysts; these were generally indurated, but some were softened, and they were of a rose or flesh-colour passing into grey. The change from those parts which retained a natural appearance to these degenerated portions was abrupt, and marked by a rose coloured line. These rose coloured portions were chiefly in the parts nearest the surface; in the central parts this passed into the yellow or the grey, and many portions were in a state of ramollissement. The whole left hemisphere in fact, presented little else than a mass of concentric induration with softenings of the various colours, which have been mentioned. On the upper part of the hemisphere, the disease did not extend entirely to the surface of the convolutions, but at the base of the anterior and middle lobes, it did. "... and on one place there was a well defined spot of superficial ulceration, size of a split pea."

Cruveilhier earned a prominent place in connection with meningeal tumors by being first to put on record a case which he termed tumeur cancreuse of the dura which he correctly localized in vivo and verified at postmortem. This opened the epoch in which constellations of signs and symptoms formed the subject of careful clinical analysis. The recognition of one of these constellations is credited to Rayer (1823) who was apparently among the first, if not the first, to outline the focal and general signs and symptoms of pituitary neoplasm, stressing the loss of vision due to direct pressure on the optic chiasm.

ANDRAL

Of still greater prominence is the name of Andral whose most significant contribution is a concise summary of manifestations of focal disease of the central nervous system, published in 1838. The material upon which he made his observations is not extensive, but well studied. His main contribution is a systematic plan for the allocation of signs and symptoms in accordance with the seat of the lesion. He was among the first to recognize the cerebral hemisphere as the site of intellectual activity, without overshadowing motility as its leading function. He assigned a prominent place to headache, vomiting, nausea, circulatory and respiratory difficulties as manifestations of brain tumor. No less significant is his observation that a cancerous lesion in the cerebellum is capable of causing, in addition to other signs, unsteadiness, ataxia and retroflexion of trunk and head. He sensed already the significance of anoma, but described it in rather vague terms. Describing a case which at autopsy revealed a tumor in the pons and recording its clinical features, he took note of such disturbances as we would now recognize as nystagmus, sensory and motor disturbances, and dysarthria.

W. H. WALSHE

At the approach of the middle of the 19th century, we find an unusually keen observer in the person of Walter Hoyle Walshe. A chapter in his book "The Nature and Treatment of Cancer" on brain tumors reflects the deep interest clinicians of that day displayed in the symptomatology and other features of this type of lesion. He opened the chapter by the somewhat conservative but provoking statement that "it is not possible during life to distinguish with any degree of certainty the precise seat, cerebral or meningeal, from which a cancerous tumor
springs; but assuredly it is not by adhering to a vicious mode of anatomical arrangement that future correct clinical inferences are to be hoped for.” As to the structural character of brain tumors, he adhered to the old concepts by saying “three species of cancer occur in the brain and are: encephaloid, by far the most frequently; true scirrhus, excessively rare, although the term is very frequently to be found in description by the older writers, and chronic induration of the simple kind, following a state of previous softening, has evidently been spoken of under that title.”

He was quite unhappy with the available criteria as to the origin of such tumors for he says, “It is to be noted that in no organ are tumors more frequently deficient in those well-marked characters, which to the practiced eye at once assign them their place in the series of morbid formation.” He took issue with those who claim trauma and inflammation as probable causes of cancer of the brain, and says, “the brain is one of those organs in which the influence of predisposition must be admitted to be strongest in the generation of the disease, as it is excessively rare to discover any immediate and direct cause for its development.” He discounted injury to the head as an important etiologic factor by saying, “Of 31 cases collected by Andral, there were but two, at the most, in which the disease followed external injury.” The affirmation of Bouillaud that the cases he has collected show that the disease originated amid the symptoms characteristic of acute or chronic inflammation, was met by the statement “I have examined these cases without discovering any evidence of the alleged fact.”

In his discussion of the more prominent symptoms and signs of brain tumor he presented them in a way that would make some of our present observers almost old-fashioned. Speaking of headache he said this: “Cephalgia varies in all its characters in different cases. In some instances constituting the main phenomenon of the disease, in others it is so slight as scarcely to attract the patient’s attention; while in a third class of cases it is wholly absent. Its total absence, however, is extremely rare. It may be constant, and of uniform intensity, almost from its first development; or it may be remittent, or irregularly remittent. The periods of intermission vary extremely in length, for instance, from some hours to a few days, or even months; and the violence and duration of successive paroxysms are subject to similar irregularity in duration and severity.”

Concerning focal signs, Walshe held that in “the presence of a tumor within the brain, we should expect to be necessarily productive of some form of paralysis. The paralysis may be hemiplegic, or as is much more curious, paraplegia may be the form observed. Andral quotes from Esquirol a case in which the anterior extremity of each hemisphere contained a cancerous mass, while the lower limbs only were paralysed...” Walshe apparently did not recognize the importance of paracentral lobules.

“The paralysis may be established gradually or suddenly, the former being by far the more common fact. The paralysis may be simple or attended with tonic, clonic or persistent contraction. Partial or general convulsive movements are not uncommon and fits having the epileptic character have in a considerable number of instances, depended on a cancerous tumor in the brain. In some patients local convulsions have assumed the tetanic form.
Generally speaking, convulsions do not occur unless in parts already paralysed; but it is important to observe, that they do exist independently of that state, and have sometimes ceased permanently."

These keen observations on the character of epileptiform seizures in organic disease of the brain were not entirely new, as Richard Bright had already drawn attention to them. However, they may be regarded as the forerunners of later studies by Hughlings Jackson.

Walshe apparently was not certain of the effect of tumor on the intellectual capacities of the victim and relied mainly on the observations of Andral and Durand-Fardel who infer, from the cases analyzed, that the intellect undergoes no obvious change in the greater number of instances. On the other hand he quoted Calmeil who found the intellectual faculties impaired in half his cases of organic diseases of the encephalon. Durand-Fardel questions whether this high ratio may not depend upon Calmeil having chiefly observed cases in lunatic establishments without recognizing that many cases of brain tumors, with secondary psychoses, found their way to an asylum because of diagnostic errors.

Regarding speech disturbances, Walshe noted that "in certain cases, but these are rare, the faculty of speech has been especially affected; in others, all power of memory has been completely lost, and all observers agree in noting the frequency with which the sight of these patients suffer, Calmeil calculates that vision is considerably weakened, or altogether lost in three of every eight cases. Diplopia has not infrequently been observed; some patients imagine objects turn around them; others, Calmeil observes, experience actual hallucinations of vision. One out of nine persons, Calmeil found, had become deaf; the sense of smell and taste do not appear to suffer except in extremely rare instances, independently of implication of their special nerves. These various affections of the organs of sense do not always persist, or increase progressively, when once established; cases are related in which alternate loss and recovery of sight and hearing occurred."

Localization of function, a doctrine then still in its infancy, drew from Walshe the following observation: "The attempt has been made to attach particular symptoms to affection of particular parts of the cerebrum. Bouillaud is of the opinion that disturbance, or loss, of the faculty of speech or of memory (a form of idiocy) announces the anterior part of the organ to be affected; while paralysis of the limbs shows that the cancerous growth is either seated in, or presses upon, the middle or posterior lobes, or the corpora striata and optic thalami. Cases supporting, so far as this goes, the system of localization, may no doubt be quoted; but as certainly there are others totally at variance with its provisions, even in respect of the connexion of the anterior lobes with the faculty of speech." He nevertheless favored the doctrine of localization of function in accepting the cerebellum as the seat of a coordinating center as gathered from the following statement: "The doctrines taught by certain physiologists concerning the influence exercised by the alteration of that function is of particular interest. Now it appears that among thirty cases of morbid product developed in the cerebellum, Andral found eight in which no affection of the function in question had been observed. In some of these eight cases the disease was cancerous; and either one or both lateral lobes of the cerebellum was affected." He continues and points out that "Defective co-ordination of muscular action (producing in some cases a 'tremulous and unsteady walk, like that of a person balancing a burden on the
head,' Latham's case) has been observed in very few instances; yet this is the mode of morbid condition of motility, which the doctrines above alluded to would teach us to expect."

In support of these doctrines Walshe quoted a case of Gall. "The chief symptoms observed by Gall (1813) in a case were pain on changing in position, but particularly severe at the back of the head, neck and between the shoulders; occasional vertigo and nausea without vomiting... The palpebrae were more than half closed; vision imperfect and almost limited to the left eye; imperfect paralysis of the left side; vertigo; tinnitus aurium; constipation; diminution of the cephalgia; fits of stupor occurring 20 times a day, universal muscular debility, eventually paraplegia; pulse 60; death by gradual exhaustion." Some of the foregoing symptoms are most typical of a cerebellar neoplasm.

Walshe cited an observation by Scipion Pinel, that in certain cases of cancer of the pons, singular movements of the eyes, numbness of the limbs, sharp pains in the soles of the feet, in the calves of the legs and the knees, and total loss of sight, taste and smell, (while the intellect and the faculty of hearing remained sound), have been found. He devoted much attention to the discussion of visual impairment as will be noted from the following,

"The only one of the senses which appears from recorded cases to have been impaired, independently of implication of its special nerve, is that of vision. Complete or incomplete amaurosis has been observed in a sufficient number of cases to render this symptom one of deep interest; but it cannot be connected with affection of any particular part of the cerebellum rather than of others; nor, as may be gathered from the description of cancer affecting other portions of the encephalon, does it, taken alone, by any means localize the disease in the cerebellum."

He recognized this as well as the occurrence of blindness secondary to hydrocephalus caused by a posterior fossa tumor.

In spite of this long array of significant data in support of the concept of localization of functions as a highly serviceable guide in the identification of the seat of suspected tumors, Walshe concluded that, "The diagnosis of cerebral cancer is in its infancy; this is sufficiently obvious from the excessive rarity of cases in which the existence of the disease has been announced with any degree of confidence during life." However, he adds that,

"The circumstances most distinctly permitting the physician to affirm that a tumor exists within the cranium are, the existence or a considerable period of intense cephalgia, especially if limited to a fixed point, or even to one side of the head, and if attended with repeated vomiting; of convulsive movements without paralysis but followed by mere weakness or actual paralysis of the affected parts; or different affections of the organs of sense, especially alteration of sight; and of disturbance of intellect, while the general health does not very materially suffer."

"What part of the hemisphere the new growth may occupy, or even whether it be seated in the brain itself or the meninges, are problems insoluble in the majority of cases, in the existing state of knowledge."

LEBERT

Unusually rich in highly illuminating observations, bearing the earmarks of pioneering work, is the comprehensive monograph on "Über Krebs und die mit
Krebs verwechselten Geschwulste im Gehirn und seinem Huellen,” by Lebert, published in Virchow’s Archiv, in 1851. He recognized the basic character of meningeal tumors, when he said: “Unjustly were many solitary tumors (of the brain and its coverings) considered as cancers. In accordance with our investigations they are just as often of fibroplastic character; in this category belong most of the solitary tumors of meninges at the base of the brain.” In reaching this conclusion he made use of microscopic observations on such tumors. He noted spherical and crystalline bodies, in all probability phases in psammoma body formations. He traced the fibroplastic tumors to the dura, others to the arachnoid and some to the pia mater. He stressed their independence from the adjoining brain tissue, and noted that the fibroplastic tumors do not metastasize, while he was aware that metastasis into the brain takes place from other sites or viscera.

In discussing the symptomatology of brain tumors, he re-emphasized the constellation of cardinal symptoms and of signs of the early onset of headache, followed by paresis, later to be accompanied by convulsive seizures, and as the progress of the clinical course advances, sense disturbances of sensory organs appear. Mental changes and visceral disturbances, including what we now consider the result of brain stem involvement, he recognized as manifestations of the disease. Significantly, he points to the observation that motor and sensory disturbances occur with tumors on the convexity, while sense organ impairments place the lesion at the base of the brain. Neurokeratitis was already observed by him in the course of implication of the trigeminal nerve.

A pioneer in localization of functions, he pointed out that tumors on the convexity give rise to contralateral gradual hemiparesis and headache and disturbances of the intellect; that tumors, deep seated in the brain display gravely impaired motility, but the sensibility is less affected with some impairment of the intellect, sense organ and visceral disturbances; that tumors of the falk cerebri have a tendency to bilateral implication; that in tumors of the anterior part of the base the first and second nerves are affected; that pituitary tumors cause visceral disturbances and third nerve involvement; that pontile tumors cause among other symptoms, decerebrate rigidity. He concluded his observations by declaring the prognosis in brain tumors to be generally unfavorable, and especially so for pontile tumors and more favorable for meningeal fibroplastic tumors.

VIRCHOW

Apparently, a distinction was already made in this period between extramedullary tumors and those within the substance of the brain, variously termed fungus medullaris by Monnoir in 1820, medullary sarcoma by Abernethy (1809), and encephaloid by Laeneck. But it was to the lot of Virchow to discover the existence of a special supporting tissue in the brain, which he termed neuroglia, and to be first to identify some of the deep seated brain tumors as primary, and neuroglial in character, for which he coined the term glioma.

Careful search led Virchow to older observers who had already by mere gross inspection found a strong similarity between tumors, such as he termed glioma
and the brain substance. This was particularly true of Burns (1810), Mounoir (1820) and to some extent of Abernethy (1809). It, however, does not in the least minimize the importance of Virchow's contribution to the modern understanding of the biology of primary brain tumors. His distinction between false and true brain tumors was and still is a most valuable guide in the classification of expanding intracranial tumors.

LADAME

A much more difficult task was undertaken by Ladame. Although the study of the clinical manifestations of brain tumor was then further advanced than the contemporary understanding of the form and substance of such lesions, Ladame had to deal with a great array of variants and obscurities in devising a diagnostic scheme for coordinating the location of tumors with their clinical manifestations. In fact, he had gone far beyond Walsh in categorizing tumors according to location, subdividing the brain into a larger number of districts. Thus he tried to correlate symptoms such as those arising from disturbances in sensibility, mobility, sense organs, intellectual potencies, visceral and other somatic disturbances with the location of the expanding lesion. He may be looked upon as one who made the first sound approach to the modern establishment of syndromes.

His relative success in this attempt is shown in a summary of his observations. Intellectual disorders, including hypomania with ideas of grandeur, recurrent epileptiform seizures, in the absence of motor or sensory loss he attributed to tumors on the convexity of the brain. Visual and olfactory impairment, occasional speech disturbances, and mental alterations were considered manifestations of frontoparietal lobe tumors, whereas mental alterations and speech impairment were attributed by him to tumors of the corpus striatum; the syndrome of tic douloureux (prosopalgia) and anaesthesia in the distribution of the trigeminal nerve to middle fossa tumors; double ambylopia, amaurosis (asymmetrically developed) to pituitary tumors; alternating paralysis of the oculomotor nerve to tumors of a cerebral peduncle; sensory, motor alteration and, above all, dysarthria and dysphagia to pontile tumors and finally, to the probable existence of sugar and even levulose in the urine to fourth ventricle tumors.

THE MODERN CONCEPT OF LOCALIZATION OF FUNCTIONS

It is somewhat platitudinous to say that Broca opened the way to the modern concept of localization of function. But, though foreshadowed by Gall's phrenology and antedated by Bouillaud's recognition that injuries to the third frontal convolution cause speech disturbances as well as by Bright's observations on focal convulsive seizures, he, nevertheless, initiated a decided turn towards the doctrine which identifies certain territorial division of the brain with some specialized functions.

This shift away from the previously prevailing view of indivisibility of function of the brain was accelerated by the experimental evidence obtained by Hitzig and Fritsch. It was tempered by the warnings of Schiff, who pointed out in 1859 that focal lesions do not necessarily cause manifestations referable to the site
of the lesion and that postmortem findings often show a lesion remote from the seat of the dysfunction; and Brown-Sequard, who also believed that loss of function in the demonstrable site of the disease does not necessarily point to that lesion as the sole cause of the dysfunction. On the other hand, it was aided by Griesinger, who held that, while localization of function in the strict sense is a promising field of investigation, even the "remote influences" have a definite pattern, constancy and a mechanism which provides that under similar circumstances there are similar results. The absence of certain symptoms is also of significance as it often aids in the formulation of a correct diagnosis. It made itself felt slowly at first, in the field of brain tumor localization. Progress in this direction gained momentum with the development of the ophthalmoscope by Helmholtz and its utilization by V. Graefe in establishing the significance of papilledema in instances of increased intracranial pressure particularly when caused by brain tumor.

**WERNICKE**

This period presents a large array of keen observers and resourceful investigators. Among them is Wernicke (1874) whose recognition of the anatomical bases for the sensory aphasia and impairment of stereognostic sense placed further emphasis on the newly tested theory of localization of function. What is still more significant, is that he led the way for earmarking more specifically the several diverse intellectual functions and for the recognition of the idea that, while each of them contributes toward a unified mental effort, a structural disruption of one or more of them may cause the loss of one or more of such functions with or without affecting the whole. This view found support in the observations of Charcot on the existence of a graphic centre and those of Kausmal and Berlin who independently identified a word reading centre.

**NEUROLOGY AT THE END OF THE 19TH CENTURY**

At this point it is advantageous to take stock of neurology as it existed at the end of the foregoing epoch. As will be seen from the account given by Bernhardt in 1881 this discipline including the symptomatology of brain tumors had already climbed to greater heights. It is illustrated by his list of recorded disorders of the central nervous system which were properly localized and evaluated; his recognition of the law of spread of focal convulsions, of monoparesis as a manifestation of cerebral cortical disease; his observations on accentuation of paralysis by recurrent convulsions, on the innervation of the upper extremities by the middle part of the central gyrus—lower extremities by the upper part, on the tolerance of brain to mechanical pressure, on the presence and significance of choked disks without impairment of vision in brain tumor, or aphasia in left handed individuals being caused by a lesion in the right hemisphere, on mental changes as manifestations predominantly of frontal lobe tumors, on photopsia, hemianopsia, signs of occipital lobe lesions, on festination, tremor with hemiparesis in tumors of the corpus striatum; swaying gait, vertigo, tilting of the head and forced attitudes in cerebellar lesions, on Gubler's paralysis (paralysis alter-
nans abducenti) and conjugate deviation of the head in tumors of the pons, on sensory involvement accompanying motor in capsular lesions, on sudden death in bulbar tumors, and on infantilism in pituitary tumors.

BRAMWELL

A still better inventory of the state of neurology at the end of the 19th century, is found in the comprehensive volume on intracranial tumors by Byron Bramwell, published in 1888. A new trend becomes already evident in his introductory sentences "the subject of intracranial tumors is of great interest, from a clinical, physiological and pathological point of view." An adherent to the concept of cerebral localization, he was aware of the pseudolocalizing symptoms, which he ascribed to alterations in the vascular blood supply to distant (to the tumor) centres and parts (note that he speaks already of centres); to indirect irritation or inhibition of distant centres. He regarded as certain the possibility that "the function of a part of the brain which is itself free from disease may be deranged (excited or inhibited) in consequence of disease in some other and distant part." He illustrated this occurrence by drawing attention to "phenomena of certain cases of aphasia which seem to show that lesions on the sensory side of the speech mechanism (sensory speech centres) almost of necessity produce derangements in the motor (speech) centres." He minimizes, however, the significance of this observation by saying that the "risk of erroneous diagnosis (localization) from this cause has been exaggerated."

His clinical classification of brain tumors may serve to measure the degree of understanding of brain tumor at that period. It is the manner in which he grouped cases of brain tumor that engages one's attention and admiration. In group one he placed "cases ... in which the presence of the tumor is not indicated by any characteristic symptoms during life." In group two he put "cases in which the characteristic symptoms indicative of the presence of tumor in some part of the intracranial cavity, are present, but in which there are no symptoms indicative of its exact site." A third group included "cases in which symptoms show that not only a tumor is present in some part of the intracranial cavity, but in which they indicate, more or less closely, its exact locality or site;" and finally he reserved for a fourth group "cases in which there are distinct indications or derangement or disease of the intracranial contents, and in which the symptoms may be due to the presence of an intracranial tumor, but are not typical and characteristic of that condition."

He disclosed the remarkable progress which was made during the preceding decade. There was already a satisfactory understanding of the mechanics and causes of papilledema, based upon microscopic studies; the disturbances in visual fields as demonstrated by perimetry were correlated with a fair understanding of the anatomical arrangement of fibers in the optic nerves, optic chiasm and optic tracts in their relationship to the visual centres. Several forms of hemianopsia, with or without retention of central vision were already noted and fairly adequately explained. He called attention to the view that "deafness is not often caused by an intracranial lesion; when it does occur it is usually due to
involvement of the trunk of the auditory nerve, either by the tumor itself or by
the inflammatory products in its neighborhood."

He noted that "in the great majority of cases of intracranial tumor some im-
pairment or derangement of mental faculties exists. They are often so slight as
to escape detection. In some, these changes are due to widespread derangement
of brain function—in others, to localized lesions in special parts. In the first
instance irritative material due to metabolism of tumor tissue, or in an area of
softening which surrounds the tumor, or oedema of tissue caused by dyspsy of the
ventricles. In the second instance frontal lobe tumors may be more frequently
attended with mental symptoms."

Discussing tumors in various locations he made several significant observations.
Tumors in the region of the pituitary body may involve one or both olfactory
nerves, causing unilateral or bilateral loss of smell. Quoting Rosenthal, he
pointed out that diabetes may be of central origin and due to irritation in the
third ventricle, and that this irritation may travel along the gray matter which
connects the third and fourth ventricles, producing secondary changes in the
latter. He foreshadowed Frolich's observation that an excessive development
of subcutaneous fat is often found in disturbance of the pituitary body, in some
cases accompanied by glycosuria and polyuria (diabetes insipidus). He signifi-
cantly added, "If we consider, in addition, that the tuber cinereum is found in
the immediate neighborhood of, and in advance of the pituitary gland, and that
the infundibulum merely represents a prolongation of the grey substance of the
third ventricle, and by continuity of the fourth ventricle into the medulla
oblongata, by an increase of pressure, may give rise to a paralysis of the medul-
I ar centres of hepatic innervation, and to consequent hyperaemia of the liver,
resulting in diabetes."

He credits Nothnagel with the idea that "irritation (mechanical or chemical) of
a localized spot in the head of the corpus striatum (nucleus caudatus) produced an
irresistible tendency to run or jump, which movements continued until the
animal became exhausted. . ."

He made it a point to distinguish diagnostically between cerebellar tumors and
Ménière's disease. He showed already greater familiarity with the histological
features of primary and secondary brain tumors. He spoke of gliomata con-
taining giant cells and cited Klebs (quoted by Osler) on the existence of brain
tumors derived from nerve cells, and on the observation that in the development
of some gliomata all elements of the nerve tissue may participate. He thus pointed
to the existence of a type of tumor which was recently described as spongio-
nueoblastoma or as gliomeuroma when in a more advanced state of differentiation
of its cellular elements.

SIR VICTOR HORSLEY

From the foregoing brief summary of Bramwell's contribution to the subject
of brain tumor, it is obvious that the stage was now set for the final phase in
which brain tumor no longer was to be merely the recipient of a windfall from
active neurological and neurophysiological research, but would itself contribute
to the general pool of neurologic data. In this transition, neurosurgeons played a dominant role. Foremost among them was Sir Victor Horsley. While entering upon, if not to say opening, the field of intracranial surgery, he retained a most active interest in experimental neurophysiology. This is attested by his contributions on such matters as experiments upon the functions of cerebral cortex; minute analysis of the various movements produced by stimulating in the monkey different regions of the cortical center for the upper limb; minute analysis by electric stimulation of the so-called motor region of the cortex cerebri and experimental investigation into the arrangement of the excitable fibres of the internal capsule of the monkey; electrical excitation of the so-called motor cortex and internal capsule in an orang-outang; experimental investigation of the central motor innervation of the larynx; and changes produced in the circulation and respiration by increase of the intracranial pressure or tension. The mammalian nervous system, its functions, and their localization determined by an electrical method was the subject of a Croonian lecture based upon his studies of the passage of nerve impulses between the cortex and the cord, as well as between many other levels of the nervous system. All this supported, modified and amplified earlier observations of Hitzig and Fritsch, and particularly those of Ferrier, and constituted a "memorable achievement in research," the work of a pioneer.

His appointment as Surgeon to the National Hospital for the Paralyzed and Epileptic, Queen's Square, London, in a sense marked the beginning of modern neurosurgery. His contribution to the development of skillful technique in this branch of surgery held but second place to what he had accomplished and was still doing in the field of neurology and neurophysiology. He thus continued his investigations (with R. H. Clarke) of the intrinsic fibres of the cerebellum, its nuclei and its efferent tracts. With Dr. C. E. Beevor he published observations on the excitable fibres of the crus cerebri, on the cerebellum and its relation to special orientation and to locomotion. With Dr. Otto May he recorded his views on the mesencephalic root of the fifth nerve. Alone, he published notes on sense organs in muscles, and on the preservation of muscle spindles in conditions of extreme muscular atrophy following section of the motor nerve. Topognostic sense was another subject of investigation.

In his substantial contributions to topographical diagnosis of tumors in the cerebral hemisphere and other related problems, and his utterances, he reflected his adherence to some of Hughlings Jackson's doctrines. This is well illustrated in part by the following quotations from an address he made before a learned lay society:

"The true method of regarding the anatomical construction of the cortex cerebri should begin by accepting the principle first enunciated, by Hughlings Jackson, from the consideration of the nervous system from the evolutionary standpoint—namely, that every centre in the nervous system must be sensori-motor. Such a thing as a pure motor centre could not exist; since it would be unfurnished with the causative sensory mechanism essential to the occurrence and production of the motor or efferent impulse; and, in fact, a muscular action would be an effect without a cause—an absurdity which indeed the old idea of psychic spontaneity of action involved."
In spite of the immense work and thought he devoted to devising ways and means of localizing and removing brain tumors and in spite of his relatively great success in this direction, he did not hold out much hope for ultimate complete success in surgery when employed for primary gliogenous brain tumors. This became apparent when he addressed a section of neuropathology of the International Medical Congress (1910). Analyzing the results of Tooth’s study of 500 brain tumors he said: “If these appearances are to be accepted—and I offer them with the greatest possible diffidence—one is forced to infer, on pathological grounds alone, that surgical interference, exploration, or manipulation, with few notable exceptions, is liable to awake into greater activity an exuberance which perhaps may be almost latent at the time. . . . There may be some hope of treatment in the future by some application of ultra rays after removal of the bone, such as has given results in some other vascular growths. . . . It seems that in the present state of our knowledge we must be content with relieving pressure by decompression in all gliomata, lest worst befall.” Somewhat later he said:

“There must always be a high mortality, with or without operation; but every surgeon must agree, and perhaps still more after study of the preceding pages, that the mortality is probably capable of reduction, not by shrinking from operation, but by judicious choice of the form of operation, and modification of procedure. I go so far as to say that the period of surgical activity, of which this report has been the survey, has been a necessary stage in the development of cerebral surgery, as it has been in abdominal, rectal, and other branches. On the other hand, the survivals also present many brilliant results, lives not only saved but rendered useful and indefinitely prolonged. But close consideration of the state of the patient in the less fortunate survivals may well raise the question as to whether, by less energetic and extensive surgical treatment, as good or even better results could not have been obtained. . . . The fact is that most cases of declared intracranial tumor need operation, perhaps sooner than later, and the risk has to be taken. The question is rather what class of operation shall be selected.”

HARVEY CUSHING

When death struck down Horsley in “the fulness of the powers” which he had planned to use not only in his chosen field, but also for the promotion of social reform, the mantle of this great neurologist, skilled in surgery, fell upon the deserving shoulders of another giant: our own Harvey Cushing. Here again a surgeon, indoctrinated in biologic sciences and particularly in those concerning the nervous system, devoted himself to the development of skill and precision in neurosurgery. He made, as did his predecessor Horsley, substantial contributions to the doctrine of localization of function and to numerous other subdivisions of neurology. Mention of only a few of his legacies to the science of neurology sufficiently establishes the immense value of his contributions. He made observations on the relationship between blood pressure and intracranial tension, produced the so-called Froelich syndrome in an experimental animal (the dog) by excision of part of the anterior lobe of the pituitary, demonstrated the relation of pituitary disorders to diabetes, and completed basic studies on disorders of the visual fields including color and quadratic defects, tracing the latter to involvement of Meyer’s loop.
MILLS

While these two great minds in modern neurology were engaged in their epoch making discoveries and were opening the way to further advances, other workers though less spectacular in their accomplishments were equally industrious and productive in the fertile field of neurology. Among them was Charles K. Mills. Mills, by his constant drive toward the revision of older concepts in the light of newly acquired information, enriched the understanding of localization of function by placing greater emphasis on the role the frontal region of the cerebrum plays in mediating emotional and intellectual activity. "Aphasia, agraphia in some of their practical surgical relations" formed another subject of his investigation. The significance of the Barany tests in the early stage of their application received his careful attention and his interest in the thalamus resulted in the comprehensive discussion of a thalamic syndrome.

Mills' colleagues and associates, Spiller and Weisenberg, followed in his footsteps and made valuable additions to localization of function and particularly toward the understanding of the aphasias.

Allen Starr, another important figure of this period, contributed much to the subject of brain tumor by his lucid interpretations and wide popularization of cerebral and cerebellar localization.

More recently Foster Kennedy described the now well known syndrome which bears his name, and called attention to certain dream states which he could relate to lesions of the temporal lobe. Brun described his fourth ventricle syndrome; Lipman contributed studies of apraxia; Gerstman advanced a concept of finger agnosia; Bailey, Ranson, and Hinsey in well planned experiments threw light on the function of the hypothalamus; and Horrax comprehensively described visual hallucination.

The work of "neuropathologic clinicians" and "surgical neuropathologists," whose names you probably will know without their being mentioned, is certainly not unimportant because of its far-reaching significance in anatomical, physiological and embryological implications. I will be forgiven, I am sure, when I bring to the fore these contributions, for in my opinion they have been, and continue to be, a major stimulus to clinical and neuro-physiological advances.

Clinical neuropathological studies are in the last analysis, the basis on which the many important contributions made by experimental physiologists are integrated into the sum total of neurological experience. Clinical neuropathology and experimental physiology remain the two disciplines upon which we must rely, now and in the future, for major advances in the field of neurobiology.

We are now passing through a most critical moment in the history of brain tumor. It began with the discovery of pneumonencephalography, a procedure with which the name of Dandy is inseparably connected, and the introduction of electroencephalography as a diagnostic aid. These discoveries, indeed, eased the burden of the neurologist and the surgeon alike, but unfortunately steadily deprived them of the incentive to search for the yet undiscovered functions of the brain, by substituting "mechanical" diagnostic means for the more difficult process of correlating structural defects with functional inadequacy.
At this point I cannot do better than to quote and in part paraphrase Sir Charles A. Ballance in his history of surgery of the brain:

"I have an uneasy feeling," (probably shared by some of you) "that during the last two decades the cult of localizing lesions by mechanical means has displaced in part the sacred duty, laid upon each one of us, of adding one more stone to the building of the understanding of the brain and its functions. Every man is in debt to his profession. Each one of us is but a pilgrim of neurology and psychiatry who have reached only to the threshold of truth. A vast field of our art and science remains unmapped and unexplored."

It now seems that increased mechanical facilities in diagnosis have led us to stray from the path upon which the older investigators brought us out of utter darkness to this age of relative neurologic enlightenment. Some of us are being carried far afield, tempted by quick and illusory returns of the mechanical age, to discover now or later, that there is no substitute for a sound grounding in structure-function relationships.

Of course, the accessory mechanical diagnostic procedures have their useful place when employed to provide additional avenues of investigation but they should not be allowed to lead us into a blind alley from which there will be no going forward.

Greater promise for lasting success in pushing back the barriers of the unknown rests with the return to the older and well trodden road of thorough clinical study and anatomico-physiologic structure-function relationships, correlating the data from the bedside and those from the laboratory for the continued progress of neurology as a medical art and a scientific discipline.

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