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INTRACRANIAL TUMOUR *

Diagnosis, Prognosis, and Treatment of Brain Tumour—Fifty Years Ago and To-day

BY

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Fifty years ago, to be exact it was on November 25th, 1884, a tumour of the brain was operated upon and removed. This case, the first of its kind recorded in the literature, naturally aroused widespread interest. The present occasion would appear to be appropriate for a review of the steps which have marked the progress of our knowledge of intracranial tumours—with special reference to the practical advances—during the intervening period. It is well, indeed, that we should pause from time to time to take our bearings in order the better to visualize the possible lines of advance the future holds in store. A retrospect appeals to one who has had the good fortune to have been brought into contact with a number of those who have played a prominent part in the making of this chapter of medical history.

Tumours of the brain are referred to by the earliest medical writers, to be dismissed in a few sentences by them. Nor is this surprising, for while headache, fits, paralysis, loss of vision, etc., were observed in cases in which a tumour was found post mortem, it was recognized that these symptoms were met with in other conditions. It may be that on occasions the astute physician suspected or diagnosed a tumour within the cranium, but even if this were so, little could be done to relieve the distressing symptoms. The possibilities of surgery had not yet been conceived, and the unfortunate patient was doomed to certain death, usually preceded by a prolonged period of suffering.

The introduction of the ophthalmoscope by von Helmholtz in 1851 and the discovery of "optic neuritis" were notable diagnostic advances, for the clinician was now possessed of an objective sign which, although not pathognomonic, is present sooner or later in the great majority of cases of intracranial tumour. Von Graefe, whose observations upon optic neuritis were classical contributions, aptly emphasized this historical landmark when he designated the past as the "pre-ophthalmoscopic period."

A new era dawned with the establishment of the doctrine of cortical localization in the seventies of last century. Although the phrenological speculations of the brilliant anatomist Gall had been discredited, the suggestion that individual functions were located in different portions of the brain was "in the air" when Broca, in 1861, demonstrated three cases in which articulate speech had been abolished by a localized lesion of the left hemisphere in the region of the convolution now known by his name. It was not, however, until some years later that the experimental investigations of Fritsch and Hitzig (1870),

which were confirmed and amplified by Ferrier (1873), convinced the world that particular functions are represented in particular areas of the cortex. Hughlings Jackson, whose classical communication upon "Epileptiform Convulsions from Cerebral Disease" was read before the International Medical Congress in London in 1881, had, however, in the 'sixties, expressed views regarding the representation of function in the brain, based upon his clinical observations, which were far in advance of the existing state of knowledge.

The clinicians now applied themselves with assiduity to the correlation of the symptoms and signs presented by the patient during life with the pathological lesions met with post mortem, and a wealth of diagnostic data was thus accumulated. Diagnosis was making satisfactory progress, but the prognosis in cases of intracranial tumour, apart from the gummata, was still as hopeless as it had ever been.

The First Case and its Outcome

It was in the autumn of 1884 that a young farmer was admitted to hospital under the care of Alexander Hughes Bennett, complaining of severe headache and vomiting, progressive weakness of the left hand, and localized (Jacksonian) fits. There was, too, a "double optic neuritis" and some tenderness on deep pressure over the right parietal region. Hughes Bennett came to the conclusion that the symptoms were due to "an encephalic growth, probably of limited size, involving the cortex of the brain, and situated at the middle part of the fissure of Rolando," and he asked his colleague Rickman Godlee to operate on the patient. It is probable, I think, that Hughes Bennett visualized to an exceptional degree the possibilities of surgery; for his father, the distinguished physician and physiologist who held the chair of the Institutes of Medicine in Edinburgh, had died but a few years previously, and at the necropsy there was found an unsuspected tumour about the size of a hen's egg lying over the right temporal lobe, in which it had produced a deep depression. This incident must, I submit, have left a lasting impression upon the mind of his able son. Be this as it may, Hughes Bennett persuaded Godlee to operate, and the tumour was found and removed. Godlee's name is constantly referred to in connexion with this case, whereas Hughes Bennett's is seldom mentioned. Yet it was Hughes Bennett who diagnosed the growth, located it, and I think probably urged Godlee to operate. The credit accorded to the achievements of the surgeon often eclipses the part played by the physician. This case, which heralded the birth of the surgery of intracranial tumours, created a profound impression. A new

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field was thereby opened up to the surgeons, and the experimental researches of Ferrier and others, so severely criticized and condemned by the anti-vivisectionists, were vindicated in no uncertain manner.

The attention of the physicians was now concentrated more and more upon intracranial tumours, and contributions to the literature multiplied. But the spirit of optimism engendered by Hughes Bennett and Godlee's success was doomed to disappointment, for in many cases the tumour was not found, in others the growth proved to be irremovable, and the operative mortality was very high. Byrom Bramwell wrote in 1888, in what Cushing refers to as "his much neglected book on intracranial tumours":

"The following appear to me to be the most important conditions for successful operative interference: (1) satisfactory localization of the tumour; (2) the tumour must be accessible; and (3) the tumour must be single and of such a pathological character as to permit complete enucleation or removal."

Victor Horsley, in a paper read before the International Medical Congress in Berlin in August, 1890, was the first to advocate the operation of palliative decompression. To quote his words:

"Not only are the headache and vomiting relieved, but a most interesting arrest of the optic neuritis occurs, a phenomenon which I have now observed repeatedly during the last five years, and which, in many cases, is a source of much amelioration to the patient from the consequent recovery of sight."

Horsley's observation threw new light upon the nature of optic neuritis, to which the more appropriate term "papilloedema" is now applied. It is well to remember in this connexion that an intense papilloedema may exist without any visual impairment, and that if vision is to be saved operation should be advised before there is any evidence of failure.

But notwithstanding the strides which were being made in diagnosis, the surgical results in cases of intracranial tumour were very disappointing. David Ferrier, who opened a discussion on the treatment of intracranial tumours at the meeting of the British Medical Association held in Edinburgh in 1898, introduced his remarks with the words, "the treatment of intracranial tumours forms a rather melancholy chapter in therapeutics." He expressed the view that the great majority of brain tumours are so situated, or of such a nature, as to preclude the possibility of their successful removal, and after referring to the percentage of those operable, variously estimated by different observers, he concluded: "It is a fair estimate to say that only 7 per cent. are capable of being successfully dealt with." Of thirty-eight cases—thirty-one cerebral and seven cerebellar—in which a tumour was exposed and operated upon by Horsley or Ballance at the National Hospital during the previous ten years (no reference is made to cases in which the tumour was not found or in which its situation was not located and a palliative operation carried out), it had been wholly or partially removed in twenty-sixteen cerebral and four cerebellar. Six patients from whom a tumour had been removed—five cerebral and one cerebellar—had lived for a year or more after the operation. Oppenheim's results, to which he refers in his book *Tumours of the Brain*, published in 1902, were equally discouraging. Twenty-four of his patients had been operated upon. The diagnosis of brain tumour was proved to be correct, either at the operation or post mortem, in twenty-two cases, while in two no opportunity for corroboration was afforded. Although the tumour was not always found by the surgeon, the local diagnosis was confirmed in every case with the exception of one, in which the growth proved to be in the neighbourhood of the third ventricle and not, as

expected, in the frontal lobe. The diagnostic conclusions were satisfactory but the operative results very disappointing. Only one case could be regarded as a cure; in five there was definite improvement, in five a tumour cyst was evacuated or a tumour partially removed, and seven patients died as an immediate sequel to the operation. Oppenheim was of opinion that only 3 to 4 per cent. of brain tumours were favourable for removal, and that the operative outlook in subtentorial tumours was particularly unfavourable.

When, thirty-five years ago, I was a house-physician at the National Hospital, the diagnosis in cases of intracranial tumour had reached a high degree of excellence. The surgical side of the picture is, on the other hand, a gruesome one. Removal of a tumour and recovery of the patient was in those days a rare event and the operative mortality was very high. Operation, it is to be remembered, was often not undertaken until such time as the general pressure symptoms were pronounced, the headache unbearable, and the swelling of the optic disks such that rapid failure of vision was inevitable unless the intracranial pressure was relieved. When, in such circumstances, the surgeon removed the bone he met with a tense, bulging dura through which, when incised, the adjacent portion of brain protruded, and his manipulations were in consequence greatly handicapped. Though some of these patients, in whom a tumour was exposed or a palliative decompression carried out, lived for a year or more, their headache relieved and their sight preserved, one sometimes wondered whether death on the operating table would not have been a preferable ending.

Progress up to 1910

The first decade of the present century witnessed, I think I am right in saying, a remarkable expansion of the neurological horizon. Whereas the attention of the clinicians and neuropathologists had up to that time been largely focused upon the relationship between the symptoms and signs presented by the patient and the pathological appearances met with during life, and the differentiation of tracts of fibres connecting different parts of the nervous system with one another and with the periphery, new viewpoints were now emerging—the day of pathological anatomy was passing. The representation of function in the cortex continued, however, to engage the research workers, and in 1901 Sherrington and Leyton published their elaborate experimental observations upon the cortex of the higher apes. Studies upon the architectural cytology of the cortex by the Vogts (1902), Brodman (1903), and A. W. Campbell (1905) approached the same problem from another viewpoint. And here I would especially refer to the magnificent monograph in which Campbell embodied his personal researches and so admirably collected the pertinent data bearing upon the problem of cerebral localization, from the experimental, pathological, and clinical aspects. Increasing interest was now being taken in the pathological and diagnostic information which was to be derived from the examination of the cerebro-spinal fluid. In 1905 the *Spirochaeta pallida* was discovered, and the introduction of the Wassermann test in the following year opened up new lines of approach. With the appearance in 1905 of Sherrington's great work, *The Integrative Action of the Nervous System*, there dawned what may well be described as a new era, for from this time onwards the neurologist began to think more and more in physiological rather than in strictly anatomical terms.

Following upon Babinski's observations on the diagnostic significance of the plantar reflex in disease (1898), the clinicians interested themselves *inter alia* in the precise assessment of other reflexes and physical signs by the same

method of approach, with the result that much valuable diagnostic information was thereby obtained. All these advances served to promote diagnosis in cases of intracranial tumour, and the literature of this decade is rich in this connexion. To two contributions, coming from the National Hospital, I would particularly refer—James Collier's paper on "The False Localizing Symptoms of Intracranial Tumour" (1904) served to emphasize the importance of early signs and symptoms in regional diagnosis; and Gordon Holmes and T. Grainger Stewart, in their paper dealing with "Symptomatology of Cerebellar Tumours" (1904), indicated clearly for the first time the features which distinguished intra- from extra-cerebellar growths. Harvey Cushing's monographs upon "Diseases of the Pituitary Gland" (1912) and upon "Acoustic Tumours" (1917), were most valuable contributions to our knowledge of these particular disorders.

Surgery still lagged behind, but Cushing's results recorded in his Mitchell Banks Lecture of 1910 were encouraging, for they demonstrated the improvement that might be expected from advances in surgical technique. During the preceding ten months he reported that he had operated upon sixty-four cases of brain tumour. In twenty-three of these a solid tumour was removed or a cyst evacuated, and while six of these patients died very soon after, and as a sequel to, the operation, sixteen had recovered with more or less complete restoration of function, which he stated would probably in most be permanent. In forty-one a palliative operation was carried out: five of these patients died as an immediate consequence of the operation; fifteen had lived for various periods, some with considerable, others with little, improvement, while twenty-one were still living with symptoms in complete abeyance, and most of them had been able to resume work. These promising results were attributed to various factors. The fatal issue in several of the eight cases in which death had been directly attributable to the operation had, it was believed, been undoubtedly due to drawing off cerebro-spinal fluid by lumbar puncture to relieve the increased intracranial tension. Consequently, in all operations upon the posterior fossa a wide lateral decompression with removal of the posterior part of the foramen magnum was advised, for in this way the dura could be opened below the cerebellum and the cerebro-spinal fluid allowed to escape at the earliest possible moment. Finally, Cushing concluded:

"Earlier diagnosis and more prompt interference, a wider experience in overcoming the technical difficulties of these cases, coupled with the courage to work slowly and painstakingly—these things will lead to increasingly better results in this responsible work, the success of which depends so greatly upon detail, patience and the expenditure of time."

A discussion upon the treatment of tumours of the brain and the indications for operation at the meeting of the International Congress of Medicine held in London in 1913, which was opened by Bruns of Hanover and Howard Tooth, in the course of which the latter gave an elaborate and valuable analysis of the cases of brain tumour operated upon at the National Hospital during the preceding ten years, added little that was new. Victor Horsley, who spoke among others, urged that these cases should be operated upon before general pressure symptoms developed.

Recent Advances and Modern Diagnostic Aids

Since the great war there have been notable advances in various directions. Our knowledge of the histology and relative malignancy of brain tumours has made very definite progress; radiological developments of the greatest value in diagnosis have been introduced, and surgical technique has made rapid strides.

Recent histological observations have demonstrated that the most common tumours of the brain to which the term "gliomata" is generally applied may be subdivided into quite a number of groups according to the predominant type of cell of which they are composed, and Bailey has constructed an elaborate classification on this basis (1926). As many as 699 gliomata were analysed from Cushing's clinic and classified in accordance with their histological characteristics and in relation to the expectancy of life in the various types. The survival period in the astrocytomata (which constituted 37 per cent.) was seventy-six months or more, in the glioblastomata (30.2 per cent.) it was twelve months, and in the medulloblastomata (12.6 per cent.) fifteen months. Important prognostic information can thus be obtained when the tumour is exposed by the surgeon at operation and histologically examined.

The elaboration of radiological technique and the application of radiological procedures have during the past fifteen years done much to facilitate diagnosis. Stereoscopic photographs of the head are nowadays carried out as a matter of routine in every case of suspected intracranial tumour. Although it is only in exceptional instances, when calcification happens to be present, that the tumour itself throws a direct shadow, secondary changes in the bones often afford valuable diagnostic information. The digital impressions formed by the cerebral convolutions may be unduly pronounced when there is a general increase of the intracranial pressure; it is to be remembered, however, that a similar appearance is observed in children and sometimes in radiograms of the normal adult head. Rarefaction and erosion of the dorsum sellae is a common accompaniment, and when present affords definite evidence of increased intracranial pressure. Then again, changes in the bone, a direct consequence of the local pressure of the tumour, may be met with. Thus enlargement of the sella turcica is seen in pituitary and in some suprapituitary tumours, and enlargement of the corresponding internal auditory meatus may be observed in some cases in which a tumour arises from the eighth nerve. Meningiomata, too, may be associated with hypertrophy or absorption of bone, or with enlargement of the channels of the diploic veins or of the meningeal arteries in their immediate neighbourhood. Lateral displacement of the pineal body, which is calcified and consequently visible in many healthy individuals, may indicate the side of the tumour when this is uncertain.

Ventriculography—the radiography of the head after injection of air into the ventricles—a method introduced by Dandy in 1920, is now extensively used, and although not altogether free from danger is often of the greatest value in the information it affords as to the site and size of the tumour. Dandy's recent monograph upon *Benign Tumours in the Third Ventricle* (1934) affords a striking illustration of the diagnostic value of ventriculography in some types of brain tumour. He writes as follows:

"A series of twenty-one apparently benign, removable tumours arising within the third ventricle are reported. All have been disclosed at operation and removed. From the literature, forty-seven tumours of similar character have been assembled; all of these are post-mortem findings, none have been correctly diagnosed during life. . . . Tumours of the third ventricle are easily, safely, and unequivocally diagnosed and localized by ventriculography. . . . In the past two and a half years, fourteen of these tumours have been removed with a mortality of 14.3 per cent. Except for occasional minor effects, these patients make almost complete recovery of all functions."

The equally striking results which Dandy has obtained in benign tumours of the lateral ventricles are reported in a second monograph published a few months ago.

Encephalography is a procedure in which air is injected by the more convenient lumbar subarachnoid route. This method has been less extensively employed on the grounds that the air does not enter the ventricular system so satisfactorily, and that the attendant risk is greater, but it may be most informative and is practically free from danger if the correct technique is utilized. It should not be attempted if the intracranial pressure is increased.

Arterial encephalography—radiography of the cerebral arteries after the injection of thorotrast into the internal carotid in the neck—was introduced in 1931 by Moniz, who affirms that the abnormalities in the course and distribution of the arteries so demonstrated afford as useful information as does ventriculography, and that the procedure is quite free from risk.

The Present Position

A comparison of the operative results of to-day with those of the past necessitates a consideration of statistical data; and here we owe a special debt of gratitude to Harvey Cushing, the pioneer of the surgery of brain tumour, who has from time to time during the past three decades published his operative results. In his communication at the International Neurological Congress at Berne in 1931, entitled "The Surgical-Mortality Percentages pertaining to a Series of Two Thousand Verified Intracranial Tumours," Cushing analyses his unique experience. His figures are the more impressive since every death in hospital from any cause whatsoever, no matter how long the interval after operation, is regarded as a post-operative fatality. The facts, as the following table shows, are very striking.

Comparison of Operative Mortality Percentages for Verified Tumours of Four Major Groups Divided in Three Periods

	Hopkins Series to 1912	Brigham Series to 1929	July, 1928, to July, 1931
	per cent.	per cent.	per cent.
Gliomas (varia)...	30.9	17.8	11.0
Pituitary adenomas ...	13.5	5.3	5.7
Meningiomas ...	21.0	10.3	7.7
Acoustic tumours ...	25.0	11.5	4.4

Cushing points out that the improvement in the results is not due to a selection of relatively favourable lesions, for "the proportion of patients admitted as 'forlorn hopes' in the terminable stages of their malady, often after ill-judged procedures at the hands of surgeons with little or no neuro-surgical training, is as large as ever it was." The principal steps to which the more favourable results are to be attributed he enumerates chronologically as follows: (1) the generally accepted methods of decompression to relieve tension; (2) such irreproachable wound-healing that secondary infections are practically unknown; (3) the separate closure of the galea by buried fine black silk sutures, which has caused the once dreaded fungus cerebri to be well-nigh forgotten; (4) the introduction by de Martel, in place of ether inhalation, of local anaesthesia, now supplemented, when necessary, by the rectal administration of tribromethanol; (5) the more precise tumour localization which in obscure cases Dandy's ventriculography permits us to make; (6) the use of a motor-driven suction apparatus as an indispensable adjunct to every operation; and (7) the successive improvements in methods of haemostasis which since 1927 have been most advantageously supplemented by the introduction of electro-surgical devices. But the operation, he adds, is by no means the whole story. After-care is equally important, for unsuspected complications may arise.

Patients are not removed from the operating suite until the danger of a post-operative clot has passed. Many lives, too, he states, have undoubtedly been saved by the provision of a highly trained nurse, who may be expected to appreciate "the significance of symptoms which indicate that something is wrong with a patient recently operated upon for a brain tumour; and a few hours' delay due to the misinterpretation or neglect of a warning signal may mean the difference between a fatality and a recovery."

The operative risks in cases of intracranial tumour have been very materially reduced, and successful removal is now a commonplace. Surgical technique has indeed made great progress, and yet Cushing writes: "In another thirty years our present operative procedures will doubtless appear as crude to our successors as do those of thirty years ago to us." But while the operative results in the case of the extracerebral and encapsulated growths are so much more satisfactory, the same cannot be said of the infiltrating tumours. Some form of treatment is called for which will inhibit the reproduction of the neoplastic tissue and leave unscathed the functional elements of the nervous system. Deep x-ray therapy, which has been extensively employed of recent years, has an undoubtedly beneficial effect upon some forms of tumour, and notably upon the pituitary adenomata and some of the gliomata. This form of treatment is, however, still in the experimental stage, and time must elapse to permit of definite conclusions as to its efficacy and limitations. It is, too, a dangerous procedure, and should only be applied by those who are fully conversant with the method and its risks.

THE TREATMENT OF CHRONIC SUPPURATIVE OTITIS MEDIA *

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The successful treatment of chronic middle-ear suppuration remains one of our greatest problems. The reason is not far to seek when we consider the tortuous anatomy of the middle-ear cleft; our frequent inability by clinical methods to define accurately the nature and extent of the pathological lesion; the difficulty often confronting us when we attempt to eradicate the disease by surgical or other means of conserving the function of hearing; and the risks that may befall the patient. The latter concerns not only his hearing, but even his life if we delay too long a surgical intervention for which the necessity is not always plainly indicated.

Further, we may still have to encounter the indifference of a public that continues to regard a chronically discharging ear as merely a tiresome, if at times a somewhat distressing, complaint, and do not rightly appraise its grave potentialities as we see them—namely, at best a permanent impairment of hearing (and therefore a loss of both individual and national efficiency), or, maybe, the ever-impending disaster of an intracranial affection. For the latter reasons alone, apart from any feelings of pride in our specialty, it behoves us, in an age when such great scientific progress has been made in other fields of medicine and surgery, to devote our fullest energies towards a solution of this important problem.

* Read in opening a discussion in the Section of Oto-Rhino-Laryngology at the Annual Meeting of the British Medical Association, Melbourne, 1935.