STUDIES ON
THE TREATMENT OF INTRACRANIAL
MENINGIOMAS.

Surgical and pathological considerations determining mortality, operability, recurrence after operation, and residual disability.

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CONTENTS.

I think it may be true that fortune is the ruler of half our actions, but that she allows the other half or thereabouts to be governed by us.

Niccolo Machiavelli : The Prince.

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The clinician's first demand of the pathologist who examines the tumour he has removed is, "Is it innocent or malignant?" This habitual query has engendered the notion that every tumour must be innocent or malignant. A more enlightened modification of the question, and one which pathologists should encourage clinicians to ask, is "How innocent or malignant is this tumour?"

R.A. Willis : Pathology of Tumours (3rd ed.; 1960)

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CHAPTER I

INTRODUCTION

It was recognised many years ago that the intracranial tumours now usually known as meningiomas present a special challenge to the surgeon. On the one hand they are clearly far more suitable for surgical treatment than most other types of cerebral tumour, and it was early evident that operative cure is often possible. On the other hand, their removal can be dangerous in the highest degree. Furthermore, even after apparently successful operations, the results may be in various ways disappointing.

Consequently, these tumours have been studied with great thoroughness. Their peculiar pathology has received much attention, from surgeons as well as from neuropathologists close to surgical work, and many excellent studies have been written. More exact knowledge has allowed general plans of management to be formulated, and these have become standardised to a remarkable degree. Advances in diagnostic method and new techniques in operation and in anaesthesia have been applied with great benefit.

Today, many of the problems presented by the meningiomas have been wholly or partially solved.

There is general agreement on most aspects of their pathology and natural history. Diagnosis is usually easy and precise. Operative hazards, such as haemorrhage, brain swelling, and infection, have been greatly reduced. When contrasted with other cerebral tumours, the meningiomas present a pleasing picture, and it is not surprising that several contemporary neurosurgeons have written of them in highly optimistic terms.

Unfortunately, however, common experience and most published reports show that this optimism must be qualified. Even in the most skilful hands, surgery fails in a significant minority of cases. In large series, the operative mortality is still considerable, and so also is the incidence of serious residual disability. Furthermore, it is usually (though not invariably) admitted that some meningiomas are inoperable: a partial, palliative resection is of them all that can be achieved. Finally, most surgeons have experienced the disappointment of a tumour that recurs after seemingly complete removal.

The causes of these surgical failures have been much discussed. Some result from delay in diagnosis, a cause to which great prominence is usually given.

Some represent the non-specific dangers of major intracranial operations, often necessarily performed on the elderly and infirm. But in many instances, and it is with these that the present study is concerned, the operative failure expresses the peculiar pathology of the meningiomas.

Surgical pathology is a utilitarian branch of knowledge: applied to tumours in any situation, it can be reduced to a few pragmatic questions. Can the tumour be removed? If it can, will it recur? If it cannot, what will be the course of events? The meningiomas have been said by many great authorities to be benign tumours. If this were entirely true, the answers to these questions could be given easily. In fact, however, the meningiomas are often locally invasive; they tend to infiltrate contiguous tissues, and in doing so they show tissue predilections that seem to come from a definite biological tropism. It is here submitted that this invasive potentiality has been given insufficient emphasis, both in regard to operative difficulties, and as a cause of delayed recurrence.

The survey upon which this thesis is based was begun some eight years ago. It was undertaken from

concern at the apparent frequency of recurrence, especially with meningiomas in the parasagittal situation. Investigation showed that recurrence was more frequent than had been supposed, and that in most instances it resulted from unnoticed residues of infiltrative meningioma, though other causes were also noted. The same survey also demonstrated the frequency of conditions which forbade complete extirpation of the tumour. In most instances, dangerous proximity of the tumour to vital structures was responsible; in a considerable number, invasive growth was present.

The conclusions reached from this survey were published (Simpson, 1957: Appendix A). They aroused some comment; several critics endorsed certain parts of the argument, but not the whole, and others considered that undue emphasis had been given to the unfavourable aspects of meningioma biology.

The subject is clearly one of great importance. It has seemed therefore desirable to review the cases originally studied, with particular regard to their subsequent fates, and to consider again the interpretations given to the pathology of their tumours. This review has been supplemented with observations made more recently in the course of routine neurosurgical and

neuropathological practice in another country. The original study was concerned specifically with the problem of post-operative recurrence. In planning the present investigation, however, it seemed that the pathological processes leading to recurrence were also largely responsible for inoperability, and for at least some of the operative deaths and post-operative disabilities. Therefore, statistics concerning these related problems are also presented, and an attempt is made to analyse the treatment of intracranial meningiomas in terms of their surgical pathology.

CHAPTER II

REVIEW OF LITERATURE

i. Early Concepts:

The tumours now usually designated as meningiomas have been known under various names for at least two hundred years. Cruveilhier (1829-1835) and before him Louis (1774) described new growths arising from the dura mater; when Virchow (1864) gave his well-known lectures on neoplasms, there was already a great, confused body of literature on so-called fungus durae matris. Until surgical treatment became practicable however, this branch of pathology was of only academic moment, and the problems under present consideration could not arise. Abercrombie (1834), whose once popular little book contains several descriptions of tumours which must have been meningiomas, says bleakly of operative intervention: "When these tumours have been rashly meddled with by incision, death has generally been the consequence". He wrote this in discussing cerebral tumours, with external spread, palpable as subcutaneous masses; in the absence of reliable neurological methods of localisation it was only with such tumours that the possibility of operation could even be

considered.

In the latter part of the nineteenth century, however, neurology became a reasonably exact science. The new knowledge of cortical localisation was applied by Hughlings Jackson and others to the diagnosis of brain tumours, and it became possible to consider the removal of masses not externally visible. Concurrently, the Listerian revolution in surgical methods was reducing the risks of sepsis. Advances along these different paths converged in 1884 when, for the first time, an intra-cerebral tumour was localised solely by its neurological manifestations, and removed surgically: appropriately, the neurologist, Bennett, was assisted by Hughlings Jackson, and the surgeon, Godlee, was Lister's disciple.

The story of the evolution of neurological surgery is well known. For the present purpose, it is only relevant to note that several of the pioneer surgeons were fortunate enough to encounter meningiomas, and their favourable nature was at once realised.

In 1879, Macewen (Anderson 1879; Macewen 1888) removed a dural tumour which may have been a meningioma, though the descriptions are equivocal. In 1883 he removed a parasagittal tumour, said by him to be a

gumma, but considered by Jefferson (1960) to have been "very possibly" a meningioma. In 1885+ Professor Durante, of Rome, successfully removed a large subfrontal tumour, termed a "sarcoma of "multiform fibrocellular structure". This was probably an olfactory groove meningioma (Cushing, 1938: p.270). Access was by a frontal craniotomy, and the tumour was dealt with quite radically; it had invaded the ethmoid air cells, but nevertheless removal was considered to have been complete (Durante, 1887). In 1887, Keen (Keen & Ellis, 1918) removed a "fibroma" from the fronto-parietal region, and this patient lived thirty years.

These felicitous operations encouraged surgical endeavour. In the last decade of the century, many neurologists incited surgeons to attack cerebral tumours of every kind. A few successes are recorded. It is pleasant to find that a "dural sarcoma" was successfully removed in Melbourne as early as 1894, by Syme (1895). (An account of this historic case is given in appendix B). The operative hazards were however

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+ This is apparently the correct date. Durante (1887) and other writers have said that the year was 1884, and priority over the Bennett-Godlee case has been claimed. Cushing & Eisenhardt (1938a) however state on private evidence that Durante, for some now obscure reason, gave an incorrect year.

enormous, and soon only enthusiasts persisted in this murderous branch of surgery. Exsanguination, meningitis, and cerebral fungus were common events, and so was failure to locate the lesion.

Moreover, at this period, knowledge of the pathology and natural history of cerebral tumours was confused, and inadequate as a guide to surgical management. Following Virchow (1865), most pathologists identified tumours of glial origin correctly, terming them gliomas if well-differentiated and gliosarcomas if anaplastic. The extracerebral tumours were less well understood. Virchow (1863) had coined the name "psammoma", and some of the better-differentiated meningiomas appear to have gone under this designation. More commonly, the tumours which would now be called meningiomas were regarded as dural sarcomas or fibrosarcomas; Golgi's term endothelioma was also used. In Bramwell's interesting monograph (1888) there was careful mention of sarcomas of meningeal, osseous, or metastatic origin. The circumscribed primary sarcoma was considered to be benign and potentially curable by operation. But separate identification was made of primary carcinoma of the dura, which term probably comprehended some examples of meningioma; of endothelioma or plexiform

angiosarcoma; and of psammomata, "of little or no clinical interest, for they very rarely give rise to symptoms". Other contemporary authors gave equally confused terminologies and review of the cases of so-called sarcomas suggests that in some instances gliomas were included in this category - especially medulloblastomas. Detecting the meningiomas in these early reports is, as Jefferson (1960) says, an excellent guessing game. When one considers the great variations in histology exhibited by the meningiomas, and the still uncertain status of the primary intracranial sarcomas, all these errors appear very natural.

At first, surgeons operated with indiscriminate hope on all apparently circumscribed tumours, irrespective of their pathology. It was, however, not long before bitter experience showed how deceptive are the appearances of circumscription sometimes seen with gliomas. As early as 1893 Horsley noted that in every case of this disease referred to him the tumour was inoperable and had recurred after a palliative resection. In consequence, attention was directed to the more amenable growths, and chiefly to the encapsulated tumours with dural attachment: the meningiomas.

The comparative innocence of such growths was

emphasized, and there are many optimistic comments in contemporary writings. "Innocent tumours which are encapsulated, and which shell out, such as fibroma, &c... are curable by the operation" (Horsley, 1893). "A well-defined and accessible tumour such as fibroma or endothelioma of the meninges can, and should, be completely removed. No time need be spent in arguing the value of such an operation". (Ballance, 1907: p.168). "Die Sarkome bilden die eigentliche pièce de resistance für die Anhänger und Förderer der operativen Entfernung der Hirngeschwülste". (The sarcomas are the very pièce de resistance for those who support and promote the operative removal of brain tumours) (Bruns, 1908: p.27). Such statements are entirely justifiable even today, with some qualifications, and no doubt they gave a needed incentive to the early neurosurgeon faced with the appalling technical problems of his time. It appears, however, that the invasive capacity of these tumours was gravely underestimated, and it is likely that many of the resections carried out were in consequence inadequate by present standards. Krause (1910: p.71) gave a clear description of his concept of the surgical pathology of the tumours which he called fibromas or fibrosarcomas. This is worth brief summary, for it

seems to be fairly representative of contemporary opinion, and was presented in a well-known and influential book. According to Krause, these "fibrosarcomas" arise from the inner table of the skull, the dura, or the leptomeninges. They compress the brain, but do not invade it. They may involve the outer layer of the dura, but only by "chronic inflammation due to irritation from the tumour". Similarly, he considered that they may sometimes, though rarely, be associated with thickening of the overlying bone: but this Krause, following Virchow, also attributed to irritation rather than to neoplastic permeation. Even when the intradural tumour was associated with a large externally visible bony tumour, as in the cases of so-called hemicraniosis, reported by Brissaud and Lereboullet (1903) and by Krause himself, it was not always realised that the disease-process was a locally invasive neoplasm. Admittedly, some workers were better informed. Taylor reported a case with a skull tumour infiltrated by a subjacent endothelioma as early as 1896. Horsley and Ballance, then working at the National Hospital, Queen Square, appear also to have been somewhat ahead of their time in comprehension of the bony changes associated with meningeal tumours.

Horsley, when resecting a massive bony tumour which would now be recognized as the hyperostosis overlying a meningioma en plaque, was careful to remove the dura beneath it, and to rongeur away even the walls of the orbit if they seemed abnormal, which is evidence that he regarded these bony changes as something worse than a reactive proliferation (Penfield, 1923). Ballance (1907: p.324) reported the important case of a so-called sarcoma of the frontal lobe, which had penetrated the dura and the skull, causing a massive external hyperostosis. He considered this growth to be malignant, and noticed elsewhere that mesoblastic intracranial tumours have a general tendency to infiltrate outwards rather than inwards, an observation of fundamental importance. In Germany, too, there were some pathologists and clinicians who even at this time appreciated correctly the peculiar properties of the extracerebral tumours. Bruns (1908) especially, must be credited with some very judicious views. His optimism over the operability of these tumours has been quoted: but he was also well aware of their capacity to infiltrate bone (p.19) and even brain (p.25). (It is, however, impossible to say whether he made the latter observation on an infiltrative meningioma, or whether he was

describing some more common malignant disease. His "Hirnsarkome" probably constitute a heterogeneous group, including some tumours which would not now be regarded as meningiomas".)

These writers did provide a pathological basis for the correct understanding of the meningiomas. They were unfortunately opposed by other authorities of equal influence, who exaggerated the innocence of these tumours and misinterpreted the evidence of infiltration seen with them. Spiller (1907, 1929) reported a case with an "endothelioma", subdural in site, which had an associated bony thickening. Both tumour and bone had been resected by Frazier, and no microscopic osseous infiltration was found. This patient was presented as cured, though in fact he later developed recurrences. Spiller taught for many years that the hyperostosis was primary and the tumour a reactive secondary development (Cushing, 1922). Further difficulty arose because the (comparative) homogeneity of the tumours now known as meningiomas was not appreciated. Their diverse microscopic appearances naturally led to confusion: but Engert (1900) had already seen the basic unity underlying these and had grouped together tumours of fibromatous, sarcomatous, and even angiomatous histology.

More confusing, it would seem, was the variation in gross anatomy; and the relationship between meningiomas wholly intradural and meningiomas with massive bony involvement was very commonly missed. This is evident in the descriptions given by Senn (1900: pp. 587 & 616) and later Rawling (1912: pp. 211 & 330). Clarification of these problems in surgical pathology was not attained until the publication of Cushing's experiences.

Nevertheless, the practical problems at present under consideration slowly took shape. It became evident that these benign lesions could be inoperable for reasons other than mere difficulty of access, and that even when removed with apparent success, they might occasionally recur. There are isolated references by the writers of this time to the recurrence of tumours which would now be regarded as meningiomas. Durante's famous case developed a local recurrence involving the falx some twelve years after the initial operation. It is possible that this arose from invaded dura: the drawing of the excised specimen is compatible with such an interpretation, though Durante had been careful to remove the affected dura at the original resection. The patient survived a second operation and lived at least seven years. (Roncali, 1903: p.252. Cushing (1938:

p.270) gives the impression that the second operation was unsuccessful, but he appears to have been misinformed). Spiller's case, as has been observed, developed a recurrence within a year of the seemingly successful resection. Ballance (1907: p.179) mentions an occipital "angeiolithic sarcoma", which recurred after an enucleation. There is a good drawing of the histological appearance of this tumour, and it is clearly a meningioma. In Fedor Krause's great test-book (1910) there are several incidental comments on the prevention of recurrence by surgical precautions, which suggest that the author treated the extrinsic intracranial tumours with greater respect than one would expect from his belief in their benignity, as summarised earlier. His advice is indeed still very pertinent. Any dura to which such tumours adhere should be excised; this policy was applied even with a spinal "psammoma" (p.1001). After an enuncleation, the cavity in the brain should be carefully searched for residual nodules of tumour. Krause describes (Observation IV) an interesting recurrent "fibrosarcoma" which may have been a meningioma; unfortunately, the histology is not illustrated. It was an encapsulated growth, adherent to dura and embedded in the Sylvian fissure. It recurred after an initial,

seemingly complete, resection, and the recurrence was excised nine months after the first operation. It recurred yet again. A third operation was done some eight months after the second; following this the patient remained well for another year, and then developed a final recurrence. This herniated through the craniectomy opening, and ultimately grew to gargantuan size. At autopsy, it was larger than a cerebral hemisphere, and still in part circumscribed, though it is said to have been infiltrative in one region. In the absence of convincing histological evidence, it is impossible to be certain that this formidable tumour was a meningioma. The gross appearances suggest that it was, however, and, if so, it must have been a meningioma of exceptionally rapid growth. Another interesting case of this time, also relevant to the problem of recurrence, was reported by Barling (1906). This was a parasagittal tumour, undoubtedly a meningioma, and it had invaded the overlying bone. It was termed an endotheliomatous sarcoma, related both to the psammoma and the perithelioma, and thought to originate in the pia mater. Barling emphasized the necessity of excising the invaded bone, to prevent recurrence, and discussed also the treatment of invaded dura, over which he was evidently less concerned.

However, despite such observations, the surgeons of this period seem to have had no qualms about the ultimate results obtainable with the extracerebral tumours, which were universally regarded as benign, or, at worst, feebly malignant. (Barling, 1906). The possible development of delayed recurrences must have appeared to be of little moment, when compared with the immediate dangers of the operation. Tooth (1913), after reviewing Horsley's then unrivalled material, did not hesitate to describe the recurrence of endotheliomas as "so unusual as almost to be negligible", though he did mention an instance, thought to have arisen from invaded bone. The operative mortality with these tumours was about 50%, and attention was at first, very properly, concentrated on this. It was not until the evolution of a better surgical discipline gave substantial numbers of survivals that the problem of recurrence became important: and it was only then that the surgical pathology of these tumours was elucidated.

ii. <u>The Work of Cushing.</u>

Cushing's contributions to neurological surgery are very numerous, and it would be hard to say what will be his most enduring memorial. But certainly his name will always be associated with the meningiomas.

Between 1903, when he first operated on a tumour of this kind, and 1932, when he retired from active practice, he collected a series of 313 intracranial and spinal meningiomas. This was then an unequalled number. His numerous writings concerning these tumours have a value beyond the mere bulk of experience behind them, because of the meticulous clinical and pathological analysis devoted to each case. No study of the meningiomas can be begun without full consideration of Cushing's classic papers (Cushing, 1908, 1922, 1922a, 1925 & 1930) and his great monograph (Cushing, 1938).

Nevertheless, he began his acquaintance with these tumours without any clear concept of their pathology. His first important publication (Cushing, 1908) is very revealing. This was the section, "Surgery of the Head", published in Keen's large surgical text-book. In it, Cushing was concerned to promote the operative cure of cerebral tumours, and said firmly that partial removal was to be condemned. He realised that the superficial encapsulated tumours, and especially those arising from the meninges, were easiest to localise, and to remove. But his account of the pathology of these tumours is remarkably naïve and confused even by the standards of the day. He regarded the endothelioma, or fibrosarcoma,

as the most frequent type of cerebral neoplasm, and highly benign. A favoured site was said to be the cerebellopontine recess; evidently confusion with the acoustic neurinoma was responsible for this observation, since acoustic tumours were not separately considered. He was aware that meningeal sarcomas might invade bone, and regarded this as evidence of intense malignancy: "no form of new growth arising from any of the tissues is more serious than these bone sarcomata". There is a photograph of a patient with one of these cranial tumours, called a round cell sarcoma, which is stated to have been inoperable. It is amusing to see the same photograph published by Cushing thirty years later (Cushing, 1938: figure 382), as an example of hyperostosing meningioma, without reference to its earlier appearance in another guise. (This patient was reported by Taylor in 1896; Cushing had seen the case and performed the autopsy).

His first experience was with a spinal meningioma, which recurred two years after an excision

believed to have been complete. It was again excised; at neither operation was any attention given to the dural attachment. Cushing was doubtless unaware that some European surgeons had been excising such potentially invaded dura as early as 1900 (Krause, 1910). In the ten years following this initial experience, he collected eighteen cases of dural endothelioma, as he then termed them, and remained firmly convinced that they were highly benign tumours. Nine of these patients died following the primary operation; the chief causes were exsanguination and failure to relieve pressure. But the results with the survivors were initially most encouraging. The fourth patient in the series is worth particular mention, because his fate greatly influenced Cushing's assessment of these tumours in general. He was a noted (in some circles, notorious) American soldier and colonial administrator, who came to Cushing in 1910, with a complaint of focal epilepsy and left-sided hemiparesis. There was initially a palpable skull tumour, which had been excised five years earlier: in the terminology of the day, it had been designated as a psammoma of the diploë. Cushing was already aware of the occasional association of such external tumours with underlying intradural tumours: the so-called round-celled sarcoma mentioned earlier had been of this type, as were those reported

by Barling (1906) and Spiller (1907). (As has been noted, such knowledge was by no means universal at this time, and in fact Cushing's patient had fruitlessly consulted a number of European neurologists before coming to Baltimore). Cushing therefore advised operation, and succeeded in removing a large (198 gm) parasagittal tumour, histologically well differentiated and having many whorls and psammoma bodies. Convinced of the innocence of such tumours, he did not tamper with the small dural attachment, nor did he resect bone widely, as Horsley would probably have done. All went well, and for many years Cushing regarded this felicitous issue as warrant for avoiding a more radical operation. Not long after this operation, he successfully removed his first tumour of the sphenoidal ridge, and also three massive tumours of the hyperostosing variety, in which there were large exostoses, associated with clinical evidence of intracranial extension, the significance of which was however missed. In these cases, Cushing subsequently condemned his operative procedures as inadequate, though in view of the fearful difficulties attending neurosurgery in those days, the marvel must be that so much was achieved. The sphenoidal ridge tumour he completely removed, but paid no attention to its

dural attachment. The bony components of the hyperostosing tumours were likewise removed completely, but the dura was not incised. The existence of intradural tumours was not suspected. In fact, Cushing had then only in part seized the relationship of bone and meningioma. It is of extreme complexity, and still somewhat controversial. While Cushing, unlike Spiller, had realised the true meaning of such bony swellings as the one overlying the parasagittal tumour mentioned above, he was still unaware of the significance of the more massive hyperostoses. Horsley and Gowers were at that time better informed (Penfield, 1923). In 1908 Horsley had indeed successfully removed such a hyperostosis together with its associated asymptomatic subdural meningioma-en-plaque: but this important case was then unpublished.

In 1913 Cushing went to the newly-established Peter Bent Brigham Hospital. In the next ten years he slowly discovered how prone to recur these tumours are. In 1915 one of his earliest successes developed recurrences, from two foci; these were excised in another clinic (Heuer and Dandy, 1916). In the same year one of his three patients with massive hyperostosing tumours died, and he recalled the other two for reoperation, to find in both unsuspected subdural plaques of neoplasm. It was

from this experience that Cushing learnt that the smaller hyperostoses seen with globular tumours differed only in degree from the large bony swellings then still often called hemicraniosis. Presumably he also began to regard invasion of bone more seriously, for some of his operation notes of this time mention the deliberate excision of hyperostoses. It was, however, not until after his return from the War that he began to encounter recurrences in such numbers as to make him wholly recast his concepts.

In 1919 he first operated on Timothy Donovan and Dorothy Russell, two patients whose tragedies he has made immortal in a classic chapter. (Cushing, 1938: chapter 31). Both had parasagittal tumours of unusual histology, ultimately considered as malignant epithelioid meningiomas (Type V varient 1 in the scheme of Cushing and Eisenhardt). In both cases the tumours recurred repeatedly, and both patients eventually died, in 1931 and 1932 respectively. Donovan endured eleven separate operations; his tumour first recurred in 1923 and continued to recur after each of a series of seemingly radical resections, despite a course of X-irradiation. Miss Russell endured even more, having seventeen operations. Her tumour was of a very peculiar character, and varied in

its microscopic appearances with different biopsies. It recurred in the cerebral operation field, and also in the scalp wound, no doubt by implant; and at autopsy there were pulmonary metastases. These two unfortunates display the behaviour of the cytologically malignant meningioma at its worst. In 1927 Cushing had a still more mortifying experience: the fatal recurrence of a cytologically innocent tumour. This occurred in the fourth patient in his series, mentioned earlier, a man now very eminent in American public life and a personal friend of Cushing (Fulton, 1946: p.551). It seems that this disaster particularly influenced Cushing's assessment of the liability to recurrence, for the tumour in question was very well differentiated, and "as favourable a lesion as one could hope for" (Cushing, 1938:p.415). Another recurrence developing at this time also seems to have been influential in the revision of his operative strategy: this was in the seventy-seventh case in the series, and arose from a tumour-invaded bone flap.

With the growth of his experience, Cushing had become more concerned with the diverse natural histories of cerebral tumours of all kinds, and detailed histopathological studies were instituted. Cushing himself was no histopathologist (Fulton, 1946: p.410), but his

pupils Percival Bailey and Louise Eisenhardt undertook tumour classification by microscopy. Very elaborate systems were evolved, and precise clinico-pathological correlation was attempted. The meningiomas naturally received particular attention, and in 1922, Cushing (1922a) discussed them at length in his well-known Cavendish lecture. This very important contribution focused attention on the peculiar pathology of the extra-cerebral tumours. The name "meningioma" was now first used, to comprehend all the circumscribed, extra-cerebral tumours of pachy-meningeal attachment whose histology suggested an arachnoidal origin or at least excluded origin from other structures. (No better name has yet been found, and over the next few years the many rival terms, notably "dural endothelioma" and "arachnoidal fibroblastoma" (Mallory, 1920) slowly became rarer in the surgical literature). In this lecture, Cushing gave publicity to the theory that these tumours were of arachnoidal rather than dural origin, and this led to much debate on their histogenesis. Further, he gave an admirable system of regional classification, now universally accepted. Finally, and of more relevance in the present study, Cushing's brief notes on the surgical pathology of the meningiomas were

followed by, and partly inspired, a number of more minute investigations.

Concurrently, methods of diagnosis became more precise, and operative management safer and more radical. With the introduction of the diathermy cautery, the removal of basal meningiomas became comparatively easy. In the first year of electrosurgery, as it was regrettably termed, Cushing had 31 new cases of meningioma, 26 of whom survived operation (Cairns, 1936); total removal was found possible in a remarkable number. Tumours in the subfrontal region, inner sphenoidal ridge, and posterior fossa were attacked in this year, as well as the more familiar tumours on the convexity. It became evident that with these deeper tumours the greatest problem was the preservation of major cerebral vessels, and Cushing's case protocols show that the occasional preferability of partial removal was becoming clearer. Nevertheless, every effort was made to achieve a radical cure. Involved bone and dura were now excised whenever possible. After 1927 Bovie's electric cautery was employed to coagulate destructively any bone or dura not excisable. Attempts were made to effect clean removals, several recurrences being attributed either to free implants or to broken-off nodules embedded in brain.

Resections of bone, dura and tumour en bloc were even attempted, as Horsley had advised many years earlier. Even these measures did not eliminate the occasional development of recurrence.

When Cushing presented his final dicta on the tumours by then (1938) widely known as meningiomas he drew upon the voluminous notes of 295 cases. Operation had been carried out on 281 patients, with a case death rate of 19.6 per cent, reduced in his last five years to 11.8 per cent. In 43 instances re-operation for "actual or symptomatic" recurrence was necessary, and 76 patients died at home from incompletely removed tumours; many of the latter had had temporary relief of symptoms, and it would therefore be reasonable to regard their terminal illnesses as recurrences in the clinical sense. Cushing unfortunately did not state the incidence of inoperability, or of recurrence after operations which had appeared to be total removals, the figures of prime interest in the present study. It is, however, possible, by analysing his tabulated case summaries, to make a rough estimate. There were about one hundred cases in which the first resection appeared a complete extirpation, and in this group the incidence of recurrence was about 15 per cent. If one includes the seemingly radical operations done on

recurrent tumours, the incidence is still higher. In some seventy cases the primary operation was less extensive, consisting of total intradural ablation with no treatment of actual or potential dural and extradural infiltration. In this group the incidence of recurrence was 35-40 per cent; and several patients lived twenty-five years or more, despite the retention of probably invaded dura. Even where the intradural tumour itself was incompletely excised there were a few patients who survived many years, illustrating the unpredictable natural history of the disease. These figures can be compared with those reported in this paper, but only with some reservation: in the majority the operation summaries are not so detailed as to justify exact analysis.

Cushing was aware that the biological nature of the meningiomas is variable: their growth patterns and rates are diverse. He laid considerable stress on the special liability of certain histological variants to recurrence. Earlier writers, notably Engert (1900), had noted the histological diversity of the meningiomas, but Bailey, Cushing and Eisenhardt (1928) appear to have been the first to attempt a limited correlation between clinical behaviour and the specific tissue-formative properties of the tumour. Cushing (1938) and Eisenhardt ultimately

evolved a very complex system, to which further mention will be made: in essence, it was a compound, based both on these histological differentiations and on the purely cytological evidence of rapid or slow growth. (See table I, page 42). The disposition to recurrence was considered to be greatest with the angioblastic tumours of Type IV, variant 1 (but not those of variants 2 and 3); the epithelioid tumours with many mitoses and bizarre nuclei (Type V); and the fibroblastic tumours with similar cellular abnormalities (Type VI, variant 1), these last being the worst. Cushing was, however, aware that recurrence could follow the excision of tumours of more favourable type, whether epithelioid and cellular (Types I and II), or fibroblastic (Type III). He described recurrence from unnoticed nodules broken off the enucleated tumour, from invaded dura and invaded bone, and also from seedling implants dropped in the wounds, which were seen in five patients, one of whom had a quite benign tumour. (Cushing, 1938: p.252). "Recurrences" due to multiple primary tumours, sometimes in association with neuro-fibromatosis, were given detailed consideration. His views on the prevention of recurrence have been already mentioned: it must, however, be said that he does not appear ever to have decided how

much can in practice be done. It had become evident to him that in some regions the surgical ideal is unattainable. He observed (p.498) that the logical treatment of parasagittal tumours invading the superior longitudinal sinus must include a block resection of falx and sinus, but the obvious dangers of this procedure deterred him, and he was obliged to leave its proper indications undecided.

It has been needful to give Cushing's experiences at considerable length, and to present the evolution of his knowledge without regard to the work done by others simultaneously, because his writings are still of great importance to a proper comprehension of the behaviour of the meningiomas, and must be considered as a whole. Moreover, in the historical perspective, Cushing influenced his contemporaries much more than they him. However, his work was paralleled to some degree throughout the world. Many surgeons were now operating on intracranial meningiomas, and the pathological conditions hindering successful surgical extirpation now received the fullest consideration. (cf. Lindon, 1932; Olivecrona, 1934). Penfield (1923), Phemister (1923), Cushing himself (1922), Kolodny (1929), and many others presented studies on the invasion of bone. It became evident that in as many as

25 per cent of cases the meningiomas evoke hyperostosis in the overlying bone, and although the precise mechanism of this was contested it was agreed that such hyperostoses were usually invaded by tumour cells. Rowbotham's important paper (1939) gave a clear description of all forms of bony reaction, including not only the common hyperostoses, but also the rarer osteolytic changes. Bruns (1908) had noted the latter, but Penfield (1923 & 1932: p.967) had denied their association with the ordinary meningeal tumours, supposing them to be produced only by the malignant so-called dural sarcomas. (This erroneous distinction has died hard). The question whether a hyperostosis may be evoked without neoplastic permeation of the bone was not, however, fairly answered, though Rowbotham and also Spiller (1929) reported single specimens in which careful examination showed no tumour cells. The frequent finding of bony invasion led Julian Taylor (1928) to present the thesis that meningiomas are not benign but frankly malignant, and analogous to the periosteal fibro-sarcomas. This spirited paper has less meaning today, for it is now realised that innocence and malignancy are but relative terms: but it was doubtless valuable in combating the prevalent excessive optimism about the behaviour of meningiomas after extirpation.

Less obvious forms of infiltration also became known in this period. Invasion of the great venous sinuses assumed increasing importance as more and more radical operations were attempted. Cushing (1922a) and Phemister (1923) had recorded this, and Towne (1926) added two cases in one of which venous permeation had reached the superior vena cava. It soon became evident that in many cases of parasagittal tumour recurrence was likely if the invaded sinus was not resected. But most surgeons were, like Cushing, reluctant to venture such a resection, and as late as 1940 Dandy could find only nine published examples, to which he added four.

Invasion of brain had been denied by earlier writers (e.g. Mallory, 1920), and Penfield (1932: p.965) categorically rejected the possibility. However, cases in which there was at least a local penetration were soon encountered. Globus (1937) went so far as to say that some penetration of the leptomeningeal barrier was evident in the majority of cases. The cases reported by Kalbfleisch and Grebe (1937) are relevant in this context. These were five autopsy findings of indubitable meningiomas, all with definite invasion of brain, and the authors emphasized that in several a total excision might have been very difficult.

In the two decades following Cushing's Cavendish Lecture some notable discoveries were made in the purely histological study of the meningiomas. When the tumours of this group became recognised as an entity, attempts were made to classify them on the basis of their microscopic appearances. Engert's (1900) pioneer study has been mentioned. A number of workers now followed him in presenting systems based on the identification of specific tissues: formations of epithelioid cells resembling arachnoid villi, blood bessels, fibrous tissue, bone, and so on. The most notable of these were the system of Bailey and Bucy (1931), and the similar but simpler scheme of Bland and Russell (1938). There were also del Rio-Hortega's (1934) architectural classification based on the cellular patterns and relationships, and Globus' (1937) embryological classification, still popular in some centres (cf. Bertrand et al., 1948).

Any system of classification is, however, of purely academic value if it does not furnish an index of the biological character of the tumour, and in particular its disposition to recur. It became evident that these morphological systems do not do this, and the pathologists responsible usually admitted that the histological type of the meningioma so determined was no real guide to

its behaviour. An exception was, however, made by some authorities concerning the angioblastic tumours. Bailey regarded them all as highly malignant, and indeed said that they invariably recur (Bailey & Bucy, 1931). This doctrine has lingered, despite its vigorous rejection by Bergstrand and Olivecrona (1935), and the demonstration by Cushing (1938: p.45) and Eisenhardt of several distinct varieties of angioblastic meningioma, not all of evil prognosis.

There were, however, some attempts to obtain more fundamental histological criteria of biological behaviour at this time, and these deserve careful consideration, being very relevant to the problem of recurrence. The first was probably Craig's (1927) well-known paper. Here it was postulated that the ordinary cytological criteria of rapid growth, anaplasia, frequency of mitosis, &c., could be applied to the meningiomas, and a definitely malignant form thereby identified. It was further contended that a grading like that used by Bröders for epitheliomas could be established, and that this was a guide to the biological behaviour of the "malignant" tumours, eleven examples of which were described. In four instances cytological malignancy was accompanied by some degree of cerebral

invasion; but in others the tumours were well encapsulated. In two there were said to have been multiple implant metastases in the meninges, but the alternative explanation of multiple primary tumours was not discussed. The cases are well described, but unfortunately there is no account of their ultimate fates. Nevertheless, the writer emphasized, I think justly, the likelihood of recurrence with such tumours and the importance of assessing histology with this in view. Craig was criticized for this paper by Penfield (1932: p.985) who suggested that some of the so-called endotheliomas might have been metastatic carcinomas, and also by Cushing (1938: p.48). It is indeed a rather naïve work, and the analogy with Bröders' system is not happy, since it ignores the many meningiomas that do not remotely resemble epithelial tumours. But the conception of a simple grading based on the ordinary standards of general pathology is surely a good one. It is certainly preferable to the practice resorted to by Bailey and Bucy (1931), and by others, of retaining a morphological classification but segregating as sarcomas those tumours microscopically of malignant appearance. This made a rigid identification with formidable clinical implications, and moreover obscured

the fact that any of the morphological types may show changes suggesting malignancy. The other outstanding effort to achieve a biological and microscopic correlation was that made by Cushing (1938) and Eisenhardt, to which reference has been made. The great drawback attaching to this system is its immense complexity. It comprises nine types, with twenty-two variants, some of them wholly arbitrary. As has been noted, it was prepared with the specific problem of recurrence in mind, however, and is therefore of considerable interest.

The year 1938 may be given to date the end of one phase in the history of the meningiomas. In the great years between the delivery of Cushing's Cavendish Lecture and the publication of his superb monograph a clear conception of the surgical pathology of these tumours had been attained. It was realised that, although undoubtedly the meningiomas are among the most favourable cerebral tumours, they are nevertheless capable of infiltrating dura, bone, rarely brain, and other tissues. It was seen that, while they are fundamentally a fairly homogeneous group, there are yet important variations in structure and behaviour. Some pathologists used the Cushing-Eisenhardt system of

classification system, with its behavioral implications, and others employed one of the simpler descriptive classifications with an additional report on the tumour's probable liability to recurrence. Surgeons, aware now of the penalties attending an incomplete excision, were universally at pains to carry out truly radical operations. Improvements in operative technique, and especially in blood replacement, now made these more ambitious procedures possible, and they were practiced throughout the world in comparatively uniform manner.

iii. Modern concepts of pathology.

Since 1938, much has been written about the meningiomas, and notable advances have been made in their diagnosis and management. However, there have been few major increments in knowledge of their surgical pathology, which is of chief relevance in the present study.

Today, the leading synoptic pathologists, Kernohan (Kernohan & Sayre, 1952), Henschen (1955), Zülch (1956), and Russell (Russell, 1950 & 1950a, Northfield & Russell, 1951; Russell & Rubinstein, 1959) give concordant accounts. It is now usually agreed that meningiomas are of arachnoidal origin; Turner (1961) is one of the few dissenters. It is also agreed (with certain reservations) that they can be regarded as a clinical and indeed a biological entity. This acceptance of a common histogenesis, and recognition of a reasonably uniform natural history, has been hard to reconcile with the remarkable diversity of the histological appearances. Some interesting hypotheses have been advanced to explain this paradox (cf. Wolman, 1952 & 1953; Diezel, 1954). Of more practical importance are the numerous attempts to classify the meningiomas histologically, and to relate their behaviour with their histology. Table 1 shows some of these systems of

classification and terminology, presented with their approximate homologies. (The method employed in the present study is also given).

Taxonomic debates are rarely rewarding, but the systems listed are broadly in agreement, and they have this relevance: they set the terms of reference in any consideration of the nature of the meningiomas. It is accepted that neoplastic cells derived from the arachnoid villi may assume various differentiations. They may resemble the parent arachnoidal cells, as in the common endotheliomatous type, or they may become fibroblastic; as Bland & Russell (1938) early noted, there are many intermediate transitional forms. Less commonly they may exhibit angioblastic potentialities, or may form other specialised mesoblastic tissues such as bone. Certain authorities, notably Kernohan and Sayre (1952) & McWhirter & Dott (1955), question the propriety of designating the angioblastic meningiomas as such, considering them to be capillary haemangioblastomas allied to the similar tumours commonly found in the cerebellum. This however is not the general belief, and there are probably good grounds to include angioblastic meningiomas in the general group (cf. Corradini & Browder, 1948; Jones, 1960).

TABLE 1. Systems of classification of meningiomas, some apparent homologies.

GLOBUS 1937	BLAND & RUSSELL	CUSHING & EISENHARDT, 1938	COURVILLE 1945	HENSCHEN 1955	SIMPSON 1957
1. Meningioma indifferentials.	-	-	-	-	Undifferentiated
2. M. omniforme	-	-	-	-	-
3. M. pachymeningeal	II Fibroblastic	III Fibroblastic (3 variants)	Fibroblastic	Fibroplastic	Fibroblastic
-	-	II Meningothelial, with tendency to form reticulin or collagen (4 varian	Transitional	-	Fibro-endotheliomatous
4. M. leptomeningeale	I Endotheliomatous	I Meningothelial, with no reticulin or collagen (4 variants)	Syncitial	Cytoplastic	Endotheliomatous
5. M. piale (with subgroups including angiomatous psannomatous & melanomatous types)	III Angioblastic	IV Angioblastic (3 variants, variant 1 being malignant) V Epithelioid (2 variants: often malignant)	Angioblastic	Angioplastic	Angioblastic
6. Sarcomatous M.	-	VI Malignant fibroblastic	Sarcomatous	Malignant	-
-	-	VII Osteoblastic	-	Osteoplastic	-
		VIII Chondroblastic	-	Chondroplastic	-
	IV Xanthomatous	XI Lipoblastic	-	Lipoplastic	-
	V Myxomatous				-

This remarkable diversity of histological appearances, complicated by the existence of many hybrid forms, makes it no easy matter to define what is a meningioma. Cushing's (1922) original definition was admirably non-committal. Although it has often been criticised, no better term has been found, and no more exact histological identification has been achieved. Most modern writers would accept as meningiomas those circumscribed tumours with meningeal or choroidal attachment, whose histology is compatible with origin from the cells of the arachnoid villi. The term is so used in this study. With well differentiated neoplasms, identification is easy, but inevitably many difficulties arise when the meningeal tumour is anaplastic.

Many writers, as is shown in table I, have identified malignant meningiomas, and several speak of them synonymously as sarcomatous. Since there is a strong tendency towards mesoblastic activity in many of these tumours, this is not unjustifiable. Unfortunately, it makes for much confusion, in that there are other sarcomatous intracranial tumours, not necessarily derived from the leptomeninx. Some can be identified as arising in bone or from the dura mater. Others are sarcomas of microglial origin (Russell & Rubinstein, 1959: p.66).

There are also sarcomas arising from blood vessels (Zülch, 1956: p.162), and allegedly sarcomas arising from the cerebellum, resembling medulloblastoma and distinguishable therefrom only by special stains (Hsü, 1940). None of these sarcomas resemble in their surgical anatomy the ordinary meningiomas. Nevertheless certain pathologists (e.g. Nichols & Wagner, 1952) in describing primary intracranial sarcomas, have evidently comprehended in that term some rapidly growing meningiomas; conversely others (e.g. Globus et al., 1944) have described as sarcomatous meningiomas certain very malignant tumours having little in common with meningiomas as surgeons know them. Further difficulty arises from the recent recognition of cerebral gliosarcomas (Rubinstein, 1956); these tumours certainly contain mesoblastic elements, but their biological affinities are with the gliomas.

It must be recognised that some tumours of arachnoidal origin may be so anaplastic as to defy exact classification. Nevertheless, for clinical purposes, it seems desirable to attempt to separate the anaplastic meningiomas from the heterogenous group of intracranial sarcomas. This is the policy pursued by Henschen (1955: p.482) and Russell & Rubinstein (1959: p.56). In

practice the distinction is usually possible, though it must be admitted that the microscopic diagnosis of meningioma is not always easy. Kepes & Kernohan (1959) have pointed out the errors that can be made, especially with small biopsies; some reports are vitiated by failure to allow for this.

Also to be distinguished are the rare diffuse meningeal neoplasias, described by Black & Kernohan (1950) Lundh (1952) & others. In these, the histological evidence supports the concept of a generalised neoplastic change throughout the leptomeninges. The term diffuse meningioma is therefore legitimate, but a condition of this kind has little biological or clinical affinity with the ordinary meningiomas, and transitional forms are excessively rare.

If these exclusions are accepted, as they are by most contemporary neuropathologists of note, it is possible to regard the meningiomas as a reasonably homogeneous group, exhibiting however a spectrum in cytology that extends from excellent differentiation to marked anaplasia. Since the clinical behaviour also varies, many pathologists have tried to establish cytological criteria of malignancy, and to correlate this with prognosis. These endeavours are of extreme

importance in the present study.

Since the classic, but not wholly felicitous, clinico-pathological studies of Cushing & Eisenhardt (Cushing, 1938), there have been diverse estimations of the significance of histology. Turner et al. (1942) reported 36 malignant meningiomas in the Mayo Clinic material, then amounting to 370 cases of meningeal tumours, exclusive of diffuse meningiomas and perithelial cerebellar sarcomas. Their criteria were cytological, as in Craig's (1927) earlier paper; though the attempt at a Bröders-type grading was abandoned, it was found possible to distinguish between moderate or low grade malignancy (22 tumours) and high grade malignancy (14 tumours). None metastasized, but mention is made of the great liability to invade bone and to recurrence. The average time between operation and recurrence was only 7½ months, which well supports the thesis that these tumours are clinically malignant. Unfortunately, it is not made clear how radical were the surgical procedures, nor is the incidence of recurrence with cytologically innocent meningiomas reported. In this analysis, no special prominence was given to any one histological type: the criteria were those of the general pathologist. This has been reiterated by Kernohan &

Sayre (1952: p.116): the evidences of malignancy are "presence of giant cells, cellularity, mitosis, and architecture of the tumour", in that order.

Bertrand et al. (1948), from the Salpetriere, have nevertheless endeavoured to correlate malignancy and histology. Using the method of Globus (1937), they analysed 130 tumours, and considered that, while no type had a monopoly of malignant predisposition, the meningiome piale was especially unfavourable. In a more recent report on a larger material, Guillaume et al. (1957) (with Bertrand's assistance) again incriminated this type, together with the meningioma indifferentiale and omniforme. The fibroblastic tumours, on the contrary, appeared to be of better prognosis, although it appears that at least two recurred.

Against these findings stands a considerable body of opinion, especially in the German literature. Peters (1952) denied that there is any definite relation between histological type and biological behaviour. He emphasized that some of the bizarre cellular forms seen in meningiomas represent degeneration rather than anaplasia; this may well explain the case reported by Marcos (1954), in which an extreme cellular polymorphism was associated with a very long history. A very

judicious warning is given by Folke Henschen which is worth quotation. "Zwischen diesen biologisch-klinischen Zeichen der Malignität und den histologischen scheinen keine konstanten Beziehungen vorzuliegen. Histologisch maligne Meningome brauchen nicht klinische bösartig zu sein, anderseits zeigen histologisch vollkommen gutartige Meningome nicht selten ein Wachstum, dass man doch als invasiv bezeichnen müss". (There seems to be no constant relationship between the biological-clinical and the histological signs of malignancy. Histologically malignant meningiomas need not be malignant clinically; on the other hand, meningiomas which are histologically entirely innocent not uncommonly show a pattern of growth which one has to call invasive). Henschen, 1955: p.486). It seems likely that failure to appreciate this fundamental limitation of microscopic studies underlies some of the present confusion, especially evident among clinicians, on the infiltrative potentialities of the meningioma. That such confusion exists, is evident in many case reports of "unusual" behaviour by meningiomas. A typical example is that of Pertuiset et al (1958): these authors described massive extracranial spread, with muscular infiltration, by a cytologically

innocent meningioma, and regarded this as so extraordinary that they felt obliged to postulate a local alteration in vascularity to promote the invasive spread.

Nevertheless, it has become increasingly evident that some meningiomas may be malignant in the most definite manner possible. Cushing's (1938) famous patient Dorothy May Russell died with extracranial metastases; when this was reported ti was probably unique, but in subsequent years many additional reports were published. Winkelman et al. (1952) reviewed those then available and considered ten to be acceptable; to these may be added the cases reported by Christensen et al. (1949: two cases), Swingle (1949), Laymon & Becker (1949), Lima (1951 & 1955), Cross & Cooper (1952), Shozawa (1952), Zulch et al. (1954), Rosen & Branch (1954), Simpson (1957: two cases), Baumann (1958), Vlachos & Prose (1958), Gibbs (1958), Ringsted (1958), Meredith & Belter (1959), Hukill & Lowman (1960), Oifa (1960), Robertson (1960), Rossman (1960), Kruse (1960: two cases), and Arnould et al. (1961), the last being a metastasizing spinal tumour.

The total is thus thirty-three and there are several other reports in less accessible languages. To be

sure, there are some extremely disputable cases in this list. Not all were verified at autopsy; not every author appears aware of the diagnostic pitfalls presented by metastatic carcinomas, as Willis (1960: p.731) & Kepes & Kernohan (1959) have well observed. But, notwithstanding all these reservations, it must be agreed that meningiomas can metastasize, especially after repeated operations. Such metastases are usually haematogenous; metastasis by lymphatic paths is much rarer, but has occurred (Lima, 1951 & 1955; Laymon & Becker: 1941). Dissemination by the cerebrospinal fluid, so common with gliomas, is also rare; cases were reported by Kalm (1950) Schöpe (1951) Winkelman (1954) & Hoffman & Earle (1960), and more debatably by Globus et al. (1944).

It is clearly difficult to distinguish cerebrospinal fluid metastases from the commoner condition of multiple meningiomas. The tendency of the meningiomatous neoplastic change to take place in multiple foci is well known; it has obvious clinical implications, and has received much attention in recent years. Although in no way a manifestation of malignancy, it can be as fatal. Diagnosis can be difficult; the neoplasms can be too widespread to be removeable; in less generalised

forms, the operating surgeon may overlook a small satellite tumour which will ultimately give rise to a clinical recurrence. (Petit-Dutaillis & Ectors, 1936). Cushing's patient Edith Mindes, reported by him in 1938 and by Raskin in 1950, illustrates these problems. There have been many papers dealing with multiple meningiomas and with the meningiomas associated with neurofibromatosis (Vestergaard, 1944; Mufson & Davidoff, 1944; Le Besnerais & Messimy, 1960; Ectors & Achslogh, 1960; Lazorthes et al, 1960). It is difficult to determine how common the condition is: Luyendijk, (1953) reviewing the literature, reported an incidence of 1.9 per cent, but his material, resting often on clinical and operative impressions, is not acceptable, and only autopsy statistics can give a reliable estimate. Wood et al. (1957) report an incidence of 16% in one hundred patients in whom asymptomatic meningiomas were found post mortem! It seems that very widespread meningiomatosis is much rarer than the occurrence of multiple meningiomas in a circumscribed distribution; consequently, surgical intervention is well worth while, and there have been many encouraging reports (Raaf & Craig, 1934; Woltman & Love, 1935; Stepién, 1949). Ectors and Achslogh

(1960) emphasize this, and report four successfully operated cases of "méningiomes multiples non associés focalisés", a good term for this important group. No recurrences have taken place after these resections, the maximum survival being eight years.

Metastasis and multiplicity are dramatic events, and receive disproportionate attention. Few writers give so much notice to the commoner problem of local invasion, and still fewer attempt to assess its frequency. Courville (1947) accepts as the frequency of hyperostosis the astonishingly low figure of 4.5%, apparently derived from Cushing's statistics, and this estimate is quoted by Russell and Rubinstein (1959: p.47). Traub (1961: p.57), however, examining radiological material, found hyperostoses in 22.9% of cases. But there can be invasion without hyperostosis; an additional 10% of Traub's cases showed an osteolytic change, and these tumours were "classified histologically as benign". Conversely, there can, though rarely, be hyperostosis without actual neoplastic invasion, as is confirmed by Russell & Rubinstein (1959: p.48).

The incidence and significance of dural, transdural and cerebral invasion is of extreme surgical importance, and was discussed, at some length, by me in an earlier

report (Simpson 1957: appendix A). Although the figures given in this paper are high, the opinions expressed have not as yet been challenged, and seem in general to have been acceptable to pathologists: Russell quotes the general conclusions in her recent monograph (Russell & Rubinstein, 1959: p.55). In this already celebrated book, she describes, without statistics, the propensity of meningiomas to invade dura, dural venous sinuses, pericranium, muscle, and air sinuses. Other authorities (Kernohan & Sayre, 1952; Zülch 1956) have given briefer, but comparable, accounts, again without attempting any numerical estimates of the frequency of these invasive tendencies. Henschen (1955) in his encyclopaedic study gives the fullest statement. He describes invasion of bone, and of extracranial structures: he emphasizes that this may occur with histologically typical meningiomas. He also describes invasion of brain, emphasizing that this is not invasion by dissociated tumour cells, but merely a marginal extension by continuous cords of meningioma, rarely penetrating to a great distance. This is a vital distinction, from a therapeutic viewpoint; however, more distant infiltration, along the Virchow-Robin spaces, has been reported, as a rarity, by Schöpe (1951).

Although there is thus an authoritative body of opinion on the invasive behaviour of meningiomas, even those histologically not peculiar, it appears that there is still a widespread ignorance of its frequency and even its nature. Bonnal et al. (1961) in an excellent study of eleven invasive basal meningiomas, to be discussed further, express surprise at their seemingly unpredictable natural history. "On serait tenté a priori de dire que ces méningiomes ne sont envahissants que parce qu'on les a laissé évoluer". (One will be tempted to say, a priori, that these meningiomas are only invasive because they have been left to grow). But the rapidity of post-operative recurrence appeared incompatible with this belief, nor was any correlation between histological type and rate of evolution established. "Le dogme donc de l'évolution lente des méningiomes semble à revoir". (The dogma, therefore, of the slow growth of meningiomas seems to need review). These authors do not publish any account of the cytology of their tumours, other than their histological typing; it is perhaps a little disappointing that they, and indeed other contemporary writers, should fail to exploit the cytological assessment of growth rate, which has

appeared in the present survey to be of definite though restricted significance.

In a wider perspective, contemporary neuropathologists have become especially concerned with the general effects of intracranial masses. The abnormal physiology of intracranial hypertension, and the dynamics of brain displacement, have been extensively studied; herniations, especially transtentorial, so often caused by meningiomas, have attracted particular notice. The large literature is reviewed by Finney & Walker (1962). This new knowledge is vital in considering the proper treatment of the meningiomas: but, curiously, their specific peculiarities as space occupying lesions have received little attention from pathologists. Notable exceptions are Scherer (1936), Greenfield (1939), & Noetzel (1951), whose observations are considered on page 120.

iv. Modern practice in surgical management.

Since Cushing died, the diagnosis of meningiomas by clinical neurology has advanced little. So excellent was his analysis of the regional groups, with their correlated clinical syndromes, that later writers have found little to add and less to alter. Certain tumour groups have however received more detailed consideration than his material allowed. The posterior fossa meningiomas have been reviewed by a number of clinicians, notably Petit-Dutaillis & Daum (1949 & 1950), D'Errico (1950), & Castellano & Ruggiero (1953). The intraventricular meningiomas, diagnostically so difficult, have been the subject of several articles, the most recent and comprehensive being that of Gassell and Davies (1961). Meningiomas in rare sites, such as the pineal region (Heppner, 1955), or the nasal cavity (Belal, 1955; Pertuiset & Beciric, 1955) have received attention. Recognition of these rarities will doubtless aid diagnosis in particular cases. But the great diagnostic advances have been in the field of radiology.

With Sosman's assistance, Cushing fully exploited the potentialities of plain radiography, but as is well known he was slow to resort to ventriculography. He

never employed angiography, though his later writings contain references to its utility, which was shown as early as 1929 by Moniz (Moniz et al., 1929) in the specific diagnosis of meningiomas. The safety and value of the procedure soon became accepted. There is now a vast literature on the neuroradiology of meningiomas, and this has recently been reviewed in some detail by Traub (1961). For the present purposes, certain applications of these investigations are relevant.

Nowadays, most cerebral tumours can be localised quite precisely, and often their nature can be predicted before operation. Consequently, few meningiomas escape surgical treatment; even tumours presenting in atypical manner are today likely to be detected. Modern series are therefore less selective than those of early writers, and the incidence of highly benign, slow growing tumours is relatively less.

With exact knowledge, or strong suspicion, before operation, it is possible to plan the attack more nicely; extreme vascularity can be anticipated, as also can the proximity of major cerebral arteries. (Guillaume et al. 1957, MacCarty 1959, 1961). Inoperability can sometimes be predicted, when there is for example local

constriction of a major artery, as in one of the cases reported by Bickerstaff et al. (1958). It is possible even that the more malignant meningiomas may be identified by their vascular patterns, as Lorenz (1940) suggested, though this has not been generally verified (cf. Reichel & Wockel, 1961).

These radiological aids simplify the surgeon's work, and should lower the mortality. So, likewise, should the modern improvements in supportive therapy, and the advances in anaesthetic methods. The ready availability of blood transfusion now makes it possible to contemplate operation even on the most vascular tumours. The use of hypothermia and of intravenous urea make exposure of deeply placed tumours much less hazardous; it is fair to say that today no sites of origin are by definition inaccessible, save perhaps the clivus (Castellano & Ruggiero, 1953: p.118). The value to the neurosurgeon of antibiotic therapy needs no elaboration. With these many advances, one might expect to find in published series a considerable reduction in operative mortality, a greater number of curative operations, and a fall in the incidence of serious morbidity. Today, operative proceedures are in a measure standardised: different surgeons will employ different procedures, but there is

enough common ground for generalisations on the results of surgical treatment.

Unfortunately the published data are not so exact as one could wish. Among North American writers, Francis Grant (1947, 1954, 1958) has especially interested himself in the meningiomas. He has reiterated his belief that these "are benign tumours, and total extirpation will effect a cure". With 128 meningiomas of the vault, comprising those tumours usually designated as parasagittal, falx, and convexity, his operative mortality was 14% (Grant, 1954). Complete removal was achieved in 95, and of these about a third are said to have been crippled. No mention is made of recurrence in this group. Incomplete removals were carried out in 14, and of these four had died of recurrence. The chief cause of failure to achieve a complete removal appears to have been the involvement of the superior longitudinal sinus; this was not removed unless demonstrated to be occluded (by aspiration or sinogram). With 74 basilar (subfrontal and subtemporal) meningiomas, the operative mortality was 23%. There were 39 complete removals, and 18 incomplete; again, the post-operative disability rate was considerable, and there were 7 fatal recurrences after incomplete removal. With 17 subtentorial meningiomas, the operative

mortality was 20%. and there were two delayed fatalities after incomplete removals. These tumours were encountered in the period 1931 to 1954, and it is reasonable to suppose that the high mortality (18% in the entire group) may have fallen in later years. However from his most recent publication (Grant, 1958), which deals especially with the basal meningiomas, but mentions a total experience of 407 cases, it appears that Grant has become somewhat less optimistic. Though still emphasizing that meningiomas are benign and curable, he lays greater stress on the disabling results of a too radical operation, especially when major cerebral arteries have been injured. In this paper it is said that of 110 subfrontal meningiomas, only 44 were completely extirpated, with 16 operative fatalities. The mortality rate after incomplete removal was only slightly lower. In these papers, it is at times difficult to determine exactly what were the criteria of complete removal; little mention is made of extradural infiltrations. Similarly, the indications of inoperability are not wholly apparent: for example, it is stated (Grant, 1958) of subfrontal meningiomas that "the only way I know to determine the possibilities for removing a tumour of this type in this area is to swing a finger about it". There is in these papers little special

mention of recurrence after apparently complete removal; it is however stated that 11 tumours, described as fibroblastic, did recur with untoward rapidity because they grew in a confined situation.

Horrax & Strain (1952), reporting an experience of 168 meningiomas, stress the benign nature of these tumours, and say that, with rare exceptions, they can be completely removed. Their operative mortality was 13.6%, falling in recent years to 7.9%. There were only fifteen incomplete resections - but again the treatment of extradural infiltrations is not described in detail. Of 114 patients known to have survived five years or more, 85% were in good health, a creditably low incidence of disability. Nine fatal recurrences had occurred; no mention was made of non-fatal recurrence, nor are there any details of the circumstances under which recurrence took place. In a later report on a slightly larger series, Horrax (1954) states that 77.3% of patients surviving operation more than five years were living useful lives.

Fincher (1954) is one of the few contemporary American surgeons to express sharp disappointment over the results achieved with meningiomas, and he especially emphasizes their occasional tendency to recur. Nine

fatal recurrences took place in a series of 99 cases; four followed seemingly complete removals, and in several instances, repeated recurrence took place, despite very radical surgery, including block resection of the underlying brain. In the present context it is regrettable that fuller pathological studies of these recurring meningiomas are not given. Fincher also reports a high post-operative morbidity: more than half his survivors had residual deficits. His principal recommendation for the prophylaxis of recurrence is to make the first operation as radical as is possible: "one is likely to do his best first".

Olivecrona's experience of meningiomas is probably unrivalled: by 1956, his clinic could report a series of 1070 cases (Schisano & Olivecrona, 1960). Three of his publications concern the parasagittal (and falcial) meningiomas (Olivecrona, 1934; Olivecrona, 1947; Hoessly & Olivecrona, 1955), of which he had 280 by the end of 1954. Of these, 276 patients had undergone operation: the over-all operative mortality was 12.3%, but in the period 1947-54 it had fallen to 10.8%. A year after operation, 47% of these patients were alive and working; 19.5% were "partially well"; 11.2% were invalids. This series is of extreme importance in

determining the criteria of operability. Olivecrona stated, and has reiterated this in personal conversation, that increasing experience made him ever more conservative. In the last report, the number of complete tumour removals was said to be 266. However, bloc resection of the superior longitudinal sinus was accomplished in only 64 patients; marginal resection (which may or may not represent a radical cure) was performed in 80 patients; in the remainder, presumably, the dural attachment of the tumour was either excisable without sinus resection or was treated by thermal coagulation. The dangers and indications of sinus resection are given very clearly. Olivecrona has found that bloc resection of the patent sinus is ill tolerated, both in terms of mortality and residual morbidity. Even anterior to the rolandic region, such resections may inflict permanent mental disability. The obliterated sinus is clearly more amenable to resection, and in 1947, Olivecrona recommended that it could always be safely resected; more recently, however, he has come to doubt this, because there may be a valuable collateral venous circulation in the falx (Hoessly & Olivecrona, 1955). It is very significant that in his last 74 cases, total resection of the patent

sinus was performed only once and resection of the obliterated sinus only ten times.

Admittedly this policy increases the incidence of recurrence: Olivecrona is prepared to accept this, and to resect the recurrences as need arises. It is unfortunate that the Swedish material does not permit an exact estimate of the incidence of recurrence: many patients have not been traced (19.2% of those surviving ten years or more) and many have died at home of unknown causes. It is however known that in sixteen patients, recurrences have occurred, demanding one or more further operations. The greatest number (ten) of these occurred between three and ten years after operation. No details of the cytology of the recurrent tumours are given.

Olivecrona's practice with meningiomas of the posterior fossa is reported by Castellano and Ruggiero (1953). These writers do not explicitly state the incidences of inoperability recurrence and mortality, but the full case protocols give a guide. It appears that 53 of 71 tumours were "extirpated", with an operative mortality of about 30%. However the term extirpation seemingly covers operations in which the dural attachment was not resected: it is clear that

resections of dura involving the great venous sinuses were considered hazardous. The sigmoid sinus was found difficult of access, and it was considered that the straight sinus was irremoveable; the transverse sinuses however were resected, even when patent, on four occasions. (In parenthesis, these recommendations are more precise than those given earlier by Arnvig, 1944, and accord with the opinions of Petit-Dutaillis and Daum, 1950). No recurrences seem to have followed operations classed as extirpations, but the protocols indicate an incomplete follow-up, especially with foreign (i.e. non-Swedish) patients. After operations known to have been incomplete, there have naturally been recurrences, often fatal, but it is worth noting that in several instances there was a valuable and prolonged remission. This admirable monograph considers the posterior fossa tumours in five regional groups, with very different operative risks and opportunities: further references to this report are made in chapter V.

Olivecrona's experiences with the sphenoidal ridge meningiomas en plaque are also on record (Castellano, et al., 1952). Fifteen patients underwent operation: three died post-operatively, and two of subsequent recurrences. The difficulty, often the impossibility,

of wholly excising the invaded bone is emphasized in this report; moreover, the indolent growth of these tumours encourages expectant management, and ten patients were in fact not operated upon. One of these had survived 24 years, a duration surpassed by the patient of Abbot & Glass (1955) whose symptoms had begun 39 years earlier.

Second, perhaps, in size to Olivecrona's series is the material collected since 1914 in the Mayo Clinic; this now comprises a number of meningiomas "considerably in excess of 1,000" (MacCarty, 1961:p.4). Unfortunately, the statistics of this experience are not readily available. Operative policies have however been published in MacCarty's (1961) recent monograph. It is stated that parasagittal tumours are removed with the longitudinal sinus, whether "thrombosed" or not, if anterior to the rolandic vein: posterior thereto, the sinus is resected if occluded, but if it is patent, reliance is placed on coagulation. The outer sphenoidal ridge tumours are readily excised; the inner ridge tumours may be inoperable by reason of their intimate relation to the middle cerebral and internal carotid arteries. (This group of tumours has also been briefly reported by Horning & Kernohan, 1950). The olfactory

groove meningiomas are removed "relatively easily": their dural attachment is also removed, and the related "osteoma" is cauterised. With the posterior fossa meningiomas, treatment is more conservative: if the transverse sinus is patent, it is not resected, the electric cautery being employed to destroy residual cells. It is evident from references in the text (e.g. p.41) that recurrences may follow these procedures; unfortunately, no indication is given of the frequency of recurrences, nor indeed of other untoward complications. Neurosurgeons in the Mayo Clinic have also devoted attention to the orbital meningiomas; the important papers of Craig and Gogela (1949, 1950) are briefly mentioned in chapter V.

Two large series of meningiomas have been reported by French authorities. From the Salpetriere comes the monograph of Guillaume et al. (1957). This is based on a material of 340 cases, collected between 1941 and 1956. The tumours have been classified histologically by the method of Globus (loc. cit., p.7), and regionally by a system based on that of Cushing. The monograph deals fully with the clinical and radiological diagnosis of meningiomas, but for the present purposes, chief interest lies in the surgical policies and their results. Believing, as is

explicitly stated (p. 53) that the meningiomas are benign tumours, Guillaume has been concerned to remove them with the minimum possible disturbance of cerebral function. With parasagittal and falcial meningiomas, primary resection of the superior longitudinal sinus was never performed (p. 80); seven recurrences in situ were attributed to this, for one of which a secondary sinus resection was performed. With basal meningiomas, emphasis was laid on the need for cautious piece-meal removals; the dural attachments were fulgurated, but there is little reference to osseous invasion. In one patient, such fulguration apparently caused a cranionasal fistula, with death from meningitis. In the posterior fossa, equal caution and delicacy were enjoined, but the resectability of the transverse sinus was noted, which doubtless implies a radical surgical policy for the tentorial meningiomas. However, there is little special reference to the detection of transtentorial, or indeed transfalcial spread; brief mention is made of these problems on pages 81 and 91 . The operative mortality in this large series has fallen from 20.8% to 10%, an achievement especially attributed to improved anaesthesia and resuscitation. Even more impressive is the high operability rate: there are references to only two

incomplete removals! Nevertheless, even in the short time-span of the study - seventy patients had been treated in the previous two years - there had been a number of recurrences. It is stated (p. 66) that two of these were after the operations known to have been incomplete, but that twenty (6%) followed operations which to the authors were apparently complete ablations. In view of Guillaume's reluctance to resect the superior longitudinal sinus and falx, it is not surprising that twelve of these recurrences were parasagittal or falcial; there were five recurrent sphenoidal ridge tumours, and this relatively high incidence may perhaps reflect failure to excise the "ostéome régional". Histologically three of the recurrent tumours were considered malignant, and several others showed suspicious cellular activity. These figures scarcely justify the conclusive statement (p. 147) that "si l'ablation totale d'un méningioma a pu être réalisés, la guérison definitive est assurée" (if total ablation of a meningioma has been achieved, the definitive cure is assured), though reservations are expressed when there are histological evidences of predisposition to recurrence. This monograph contains also valuable general observations on postoperative disability. Although statistics are not

given in detail, it is evident that postoperative epilepsy was a common problem, especially with parasagittal and falcial tumours, and also when (as with suprasellar tumours) it was found necessary to ablate a portion of the frontal lobe. Postoperative motor and psychic disabilities are also discussed.

From Lyons, Dechaume et al. (1949) reported 114 cases of intracranial meningioma, studied over the period 1931-1949. The case mortality rate was 41.22%; of those who survived, a number could not be traced, but among the survivors there were at least three tumour recurrences. The writers were naturally concerned with the high death rate and considerable incidence of residual disability, and were at this time not impressed with the risk of recurrence: "ils ne recidivent pas après une exérèse complete". (They do not recur after a total excision). This view the writers have since had to modify, as is noted below, and their changed attitude is significant. (Wertheimer et al., 1959).

Among German neurosurgeons, Tönnis is pre eminent in his experience of the meningiomas: by 1960, his clinic had treated 604 cases (El-Banhawy, 1961). Unfortunately, the surgical policies adopted by him have only been reported in the context of meningiomas of the sphenoidal

ridge. (Tönnis and Schürmann, 1951). This paper suffers from the difficulty experienced in tracing the patients, consequent on the partition of Germany; however, in a limited follow-up, there was a significant incidence of disability and recurrence. Tönnis (1953) has indeed expressed great concern over the high incidence of residual disability; after resection of meningiomas, only 50-60% of his patients have returned to work.

Peters (1952) of Bonn has reported a clinico-pathological study of 50 surgically treated meningiomas, with no postoperative recurrences. His average post-operative follow-up was less than three years, and his series is of more interest from the pathological viewpoint. Of greater relevance is the report of Holub (1956) from Vienna. This is based on a careful analysis of 328 cases, treated in the period 1939-1952. The over-all mortality was 23.37%; it is explained that this high figure partly results from the policy of performing operation even in very unfavourable conditions. Detailed accounts of the operative statistics are given, and it is of great interest that (contrary to the experience of Guillaume et al, 1957) it was very frequently necessary to accept an incomplete surgical ablation as the safer procedure. The recurrence rate, so far, has not been

high, and of patients whose state is known, 72.4% are working. Unfortunately, this excellent study is partly vitiated by failure to trace many of the patients: in the disturbed state of wartime Austria, it is not surprising that about a 30% third of patients have been lost.

Finally, Lima (1955), from Lisbon, has written on a series of about 200 cases. This article is noteworthy for its relatively pessimistic tone. The operative mortality was considered high (about 10%). The incidence of sarcomatous meningiomas was also a cause of concern, and the rate of recurrence was very high: approximately a third of the surviving patients suffered recurrences. However, it was considered that, if earlier diagnosis could be achieved, these results might be bettered.

In addition to these general reports, there have been numerous papers dealing with particular aspects of the management of meningiomas. The parasagittal meningiomas have especially attracted attention. Against Olivecrona's conservative policies stand the opinions of Jaeger (1942, 1951) who, apparently on rather slender evidence, considers that the superior longitudinal sinus, even if still patent, can be safely resected anywhere save in the actual rolandic (paracentral)

region. Even more extreme is the unqualified statement of Bassett (1955), that in his experience, the sinus can be ligated at any point with impunity. (The latter writer, in a general consideration of meningioma surgery, further claims that intra-osseous meningioma cells can be "eradicated" by the electric cautery, a more confident opinion than is usually given). Other writers, such as Kaplan (1949), have inclined more to Olivecrona's conservative view. White et al. (1960) are so impressed by the risks of sinus resection that they suggest that sinus replacement by vein graft might be justified, though apparently this has not yet been attempted. Lasierra (1958) for the same reason has replaced a section of invaded sinus with a plastic tube.

Other regional groups of meningiomas have recently received special attention as operative problems. The posterior fossa meningiomas have been considered in papers by Markham et al. (1955) De Busscher et al. (1957) and others, as well as by Petit-Dutaillis and Daum (1949 and 1950: quoted above). Petit-Dutaillis has also reported his experiences with meningiomas of the falx (Petit-Dutaillis and Pertuiset, 1955) and of the tentorium (Petit-Dutaillis et al, 1953). The invasive meningiomas of the anterior and middle fossae have been

reported by Bonnal et al.(1961) in a paper quoted earlier: this paper gives valuable illustrations of the meningioma in its clinically most unfavourable forms. Meningiomas of the lateral ventricles have received more attention as diagnostic problems, than in relation to their surgical management, but it is evident from the reports of Tukanowicz and Grant (1958) and Wilson et al. (1961), and to a lesser degree from that of Gassell and Davies (1961), that these tumours continue to cause operative difficulties. Some of the technical problems raised in these papers will be considered in chapter V; but in general terms, these experiences accord with those published in the comprehensive series reviewed earlier.

The residual disabilities following removal of meningiomas have been mentioned by most of the writers quoted above. The particular problem of post-operative epilepsy was discussed as early as 1935, by Groff, and more recently by Penfield and Jasper (1954) and by Flyger (1956). The statistics of post-operative disability reported in the present survey were in part published earlier (Simpson, 1956) with particular reference to their implications in physiotherapy.

Among the possible sequelae of any tumour ablation

recurrent growth must always be considered. For many patients, this threat bulks more formidable than the immediate risks of the operation. It has however been shown that in the years following the publication of Cushing's (1938) monograph, few surgeons expressed much concern over the frequency of recurrent meningioma, and until recently, there have been no special studies published on the subject. In 1955 however Volynkin, of Moscow, wrote an important analysis of the tendency of meningiomas, especially those termed arachnoid-endotheliosarcomas, to recur after operative removal. He emphasized the infiltrative growth of meningiomas, finding invasion of bone in 25-30 percent of cases. The frequency of multiple primary neoplasms was also stressed, though without figures, and reference to minute multiple tumours, "microarachnoid-endotheliomas", was also made. A distinction was drawn between direct recurrences, resulting from residues left at an earlier operation, and indirect recurrences, resulting from undiscovered primary tumours. The prophylaxis of recurrence was discussed, but in dealing with major sinuses reliance was placed on thermal coagulation rather than resection. It was perhaps a deficiency in this paper than statistics of the incidence

of recurrence were not given, nor were the circumstances under which recurrence took place clearly defined. It was however reported that the more benign meningiomas recurred in from two to ten years, the malignant ones in only a few months. This paper was written in the Russian language, and this may perhaps have limited the attention given it. In 1957 the experiences of Sir Hugh Cairns and his pupils were reported, in the paper embodied in this thesis (Simpson, 1957: appendix A). It was suggested that recurrence was a very definite, though usually long delayed hazard, even after seemingly radical operations. Particular emphasis was given to the danger of recurrence in invaded dura, and especially in the dural venous sinuses. These general conclusions were discussed and strongly supported by White et al. (1960) of Boston. These writers, analysing a small but well followed series of parasagittal and falcial meningiomas, reported five recurrences, two of them fatal. They endorsed Fincher's (1954) belief that the first operation gives an opportunity for curative resection that may not be presented again, and concluded that every effort should be made to secure a radical primary excision. The value of hypothermia was discussed in this connection. Support has also come from Wertheimer

et al. (1959). This report is of particular interest, since it represents a change in emphasis from the earlier opinions expressed from the same clinic, quoted above (Dechaume et al., 1949). The Lyons series has risen to 350 cases, and eight recurrences were reported. This may well appear a gratifyingly low incidence, but the writers made it clear that the figure was probably incomplete. They expressed considerable concern over these recurrences, which followed seemingly adequate resections.

Finally, there have been several recent references to the treatment of meningiomas by means other than surgery. Chemotherapy has as yet received little consideration, but the possible utility of radiotherapy has been discussed by a number of authors. If the meningiomas were highly radiosensitive, there would be many applications for this treatment, both as a primary procedure, after incomplete ablations, and as a prophylactic against recurrence. Unfortunately, the experiences of McWhirter and Dott (1946, 1955) seem to show decisively that these tumours show only very little sensitivity, with the reservation that tumours of the angioblastic group may be more amenable. It is extraordinarily

difficult to assess the results of treatment with such slow growing tumours, but several writers (vide Freid and Davidoff, 1951; Jones, 1960) have claimed benefit in certain instances. Holub (1956) considered that at present judgement should be reserved. But the second report of McWhirter and Dott (1955) is very conclusive, and all the more so because it reverses an earlier opinion. Against this must be weighed a few convincing reports of occasional radiosensitivity, notably case 3. in O'Connell's report (1961: this patient is also mentioned by Jones, 1960). In this patient, it is suggested that radiation of an incompletely removed suprasellar meningioma induced a regression from an angioblastic state to an inert psammomatous tumour, whose growth was arrested for nine years. Death ultimately took place from a cellular astrocytoma, which was considered to be unrelated to the radiation therapy. This important case is further considered on page 235.

v. Conclusions.

Since the first successful removals of intracranial meningiomas nearly eighty years ago, knowledge has advanced and the results achieved have been vastly improved. Yet review of the modern literature shows that there are still many divergences of opinion. It is also apparent that the results of treatment leave a good deal to be desired.

Some of the divergences of opinion are more apparent than real. When surgeons such as Grant (1958) refer to the meningiomas as benign tumours, they do so, quite reasonably, because the meningiomas are very much more favourable than the gliomas; it would be pedantic to challenge their use of the term benign to describe tumours which are often invasive and occasionally metastasizing, because it is obviously used in a relative sense. But there are more serious corollaries to the question of innocence, involving real difficulties at operation. How invasive is the meningioma? In a given case, what is its rate of growth? How radically can it be resected, and what risks should be taken to achieve a curative operation? Between the relatively conservative operations advocated by Olivecrona (Hoessly and Olivecrona, 1955)

and by Guillaume et al. (1957), and the radical resections advocated by many contemporary American writers, there lie choices which, in the particular case, can be exceedingly difficult for the surgeon responsible. Similarly, for the histopathologist endeavouring to give a prognosis, the divergences of opinion on the nature and significance of histological appearances are very confusing.

The results of the surgical treatment of intracranial meningiomas are often excellent. Nevertheless the case death rate in large series is usually at least 10%. There is room for improvement here. The postoperative morbidity is also serious. Estimates of the incidence of permanent disability range from about 15% to 40%; there is a good deal of variation in determining what constitutes a serious disability, and the concept of "Arbeitsfähigkeit" does not fully cover the problem. But, however reckoned, it is a real morbidity: motor and sensory paralysis, blindness, epilepsy, and dementia occur in an unfortunate minority of patients. Earlier diagnosis and more refined surgical techniques should make these tragedies rarer, but for some causes of disability these advances do not promise much benefit.

It is finally apparent that the best surgical treatment may occasionally fail to eradicate the disease. Either the etate of the tumour is found to preclude a total ablation, or an ablation which seemed total is ultimately followed by an unforeseen recurrence. The present survey has been particularly concerned with these related problems, which indeed have attracted increasing attention in recent years.

The quotation from Machiavelli, with which this thesis begins, defines a problem in statecraft that is no less relevant in surgery. To what extent are the results of action predetermined? In the present context, how far are these occasional tragedies inevitable, and to what extent, in practice, can they be avoided?

CHAPTER III.

MATERIAL, PROCEDURE AND TERMINOLOGY.

In the present study, use has been made of three series of intracranial meningiomas. The largest, and most valuable, is the Oxford series. Between April, 1938 and December, 1954, 246 patients with intracranial or intraorbital meningiomas were treated in the Department of Neurological Surgery of the Radcliffe Infirmary. In all, the diagnosis was verified either at operation or at autopsy. Histological verification was obtained in all save two, and in these the radiographic and operative diagnosis seems acceptable. The patients came mainly from Oxfordshire and the neighbouring counties, and it is likely that they represent the large majority of intracranial meningiomas presenting during this period from this geographical area. Two qualifications must be made. First, several other patients died of intracranial meningiomas, and came to autopsy in those years, without being referred for neurosurgical opinion. These were cases presenting exceptional diagnostic difficulty; the number is not known precisely, but it is certainly very small. Second, the series includes some twenty patients sent to Oxford from over-seas, and especially

from the Levant. These patients probably do constitute a group selected on economic grounds, and in that more acute presentations may have been excluded. With these provisors, the Oxford series is believed to be comparatively unselected: this is of some importance when comparisons are made with the results reported by neurosurgeons whose patients are in varying ways selected.

The second series, designated here as the London series, comprises ninety-eight patients treated by Sir Hugh Cairns when working in the London Hospital, between 1928 and 1938. It is probable that this series has been in part selected: the proportion of favourable cases, with very slow growing tumours, seems unduly high. Only limited use has been made of this series.

The third series, referred to as the Adelaide series, comprises 46 patients seen by me at the Royal Adelaide Hospital, the Queen Elizabeth Hospital, the Adelaide Childrens Hospital, or in private during the period May 1956 - May 1962. They represent all the surgically verified intracranial meningiomas presenting in Adelaide during this period, with the exception of a small number treated in other institutions. The majority were under the care of Mr. T.A.R. Dinning. There is reason to believe that this series is representative of general

Australian experience. It is however a small material, and the patients have been followed for very short periods. The series has therefore been used chiefly to provide examples illustrating special problems in neuropathological diagnosis and in operative management.

For the present purposes, it was chiefly necessary to analyse the pathology of these tumours, and to correlate the findings of this analysis with the clinical progress of the patients concerned. The nature of the pathological studies, and the methods employed, are discussed in chapter IV. The clinical progress was determined in two surveys, separated by an interval of seven years. In 1955, the cases comprising the Oxford series were fully reviewed. The causes of operative and post-operative death were determined from the records available, and the fates of the patients surviving operation were established as fully as possible. This was a task of unexpected difficulty. Even the English patients proved to have been surprisingly nomadic in their habits. It was still harder to trace those foreign patients who had returned to their own countries. It was however possible, in the end, to obtain a reasonably satisfactory assessment of the condition, at or after Christmas 1953, in every patient in this series. In about 20% of cases, this was

done in a personal interview. In the remainder, information was obtained by letters from the patients' private physicians, or in a few instances from the patients themselves, in response to detailed and specific written enquiries.

When this review was completed, it was realised that the lack of any cases surviving operations for a longer period than seventeen years was a serious handicap. Therefore, a similar study was made of the cases comprising the London series. Here I was much less successful in tracing the patients concerned, partly because of the long lapse of time, and still more because many of them, having lived in East London, had been dispersed during the war, when heavy bombing was suffered in that area. In the event, only 87 of these 98 patients were fully traced in 1955.

The second survey was carried out in 1962, and concerned chiefly the patients in the Oxford series. On this occasion enquiries were made chiefly by letter. Lack of time made it necessary to carry out this second survey somewhat more rapidly, and in a less detailed manner, especially in regard to the assessment of residual post-operative disabilities. The number of patients personally examined was much smaller: almost

all the reviews were made by members of the neurosurgical staff in routine outpatient clinics, or by general practitioners in response to requests. Although the cooperation given was very complete, there were difficulties in tracing a number of patients, and eventually 24 (about 10%) remained untraced. They had all been located in 1955, and it is likely that the Department would have been informed had any suspicion of recurrence arisen. The London series was not formally reviewed at this time, but it was confirmed that none of these patients had been readmitted for recurrence in the last seven years.

Where patients were known to have died, the certified causes of death were obtained from the Registrar General; when an autopsy was done, the findings were obtained wherever possible, and microscopic material was personally reviewed.

Throughout these studies, Cushing's terminology for the regional classification of the meningiomas was employed. The distribution of these regional groups for the three series is given in table II, with for comparison the series reported by Cushing (1938), Olivecrona (1947) and Guillaume et al. (1957). In only two groups were modifications employed. First,

TABLE II. REGIONAL DISTRIBUTION OF MENINGIOMAS.

SITE	LONDON SERIES	OXFORD SERIES	ADELAIDE SERIES	CUSHING (1938)	OLIVECRONA (1947)	GUILLAUME (1957)
Posterior fossa	8	27	5	28	72	30
Subtemporal	1	8	-	18	17	10
Sphenoidal ridge (a) global	14	32	1	37	96	49
(b) en plaque	2	9	-	16	15	
Suprasellar	7	14	10	28	42	21
Olfactory groove	12	14	1	29	46	24
Orbital	1	4	1	1	?	7
Convexity	20	47	10	54	91	74
Parasagittal & Peritorcular	27	81	14	77	143	87
Falx	2	5	3	7	62	33
Intraventricular	2	4	-	4	18	4
Other	2	1	1	6	6	1
Total	98	246	46	295	608	340

the peritorcular meningiomas were so few that they were either considered with the parasagittal meningiomas, or separately identified as falco-tentorial tumours, according to their anatomy. Second, the meningiomas of the posterior fossa were subclassified by the system advocated by Castellano and Ruggiero (1952), rather than that of Cushing. Spinal tumours were wholly excluded from consideration; this is somewhat arbitrary, but to include them would have involved clinical considerations beyond the scope of the two surveys. However, craniospinal tumours are included among the posterior fossa meningiomas. Orbital meningiomas have also been briefly considered.

Last, and most fundamental, remains the definition of what is a meningioma. As stated earlier (page 43), most modern writers avoid rigid histological criteria, and this policy has been adopted here. Tumours have been considered to be meningiomas if they are in gross morphology circumscribed and with meningeal or choroidal attachment, and if their histology is at least compatible with origin from meningeal cells. This definition comprehends tumours composed of endothelial cells, fibroblastic tumours, vasoformative tumours, and also certain undifferentiated tumours whose cytology recalls

the meninges in embryonic development. I have excluded from consideration three interesting malignant tumours of mesoblastic character because their histology did not particularly suggest a meningeal origin. The cerebellar haemangioblastomas have also been excluded: it is probable that they are closely akin to the angioblastic meningiomas, but their clinical peculiarities, if nothing more, entitle them to consideration as a separate entity.

Throughout this thesis, the term recurrence is used, as clinicians generally use it, to mean the re-appearance of symptoms due to tumour growth, after a period of symptomatic freedom. So used, the term has no pathological specificity, and this is a convenience, since it is not always clear whether the condition represents continued growth of an incompletely excised tumour or multifocal neoplastic change. (This question is further discussed in chapter VII). The term primary operation also perhaps requires definition: it here signifies the first definitive operation (sometimes done in several stages) to remove a tumour. Operations done for recurrence are separately considered.

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To avoid duplication of illustrations, some references are made to figures already published in the article submitted as appendix A; they are identified by arabic numerals. Illustrations in the main section are identified by small roman numerals.

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CHAPTER IV.

PATHOLOGY.

Material.

The 246 cases in the Oxford series provided the main source of material for an analysis of the surgical pathology of the meningiomas. The operation notes, always detailed and often very well illustrated, gave full descriptions of the tumours from the surgeon's viewpoint. In fatal cases, these could be supplemented by autopsy reports, and often by personal dissection of the preserved autopsy specimens. In 244 cases, the microscopic preparations, both from biopsies and autopsies, were available and have been reviewed and classified. (see page 107).

Altogether, 54 patients have come to autopsy, not always in consequence of their meningiomas. Seven of these died without surgical exploration; the other 47 had undergone craniotomy at varying times (the longest being seventeen years) before death. The remaining 190 cases provided only biopsy material.

Neither operation nor autopsy is necessarily an exhaustive investigation. The limitations of an assessment made at operation are obvious; when the tumour is

deeply placed and the operation difficult, the surgeon may receive a very misleading impression. It is important to remember also that an autopsy can only be considered a complete examination when it is done by someone informed of the particular problems of the case. This was not always possible, and it is likely that in several instances infiltration of extradural tissues escaped attention. For these reasons, the statistics of infiltration reported here, and the few attempts made by other writers to estimate the invasive tendencies of meningiomas, are probably biased to minimise the frequency of extradural spread. This important limitation of our knowledge is often overlooked.

The 46 patients in the Adelaide series provided biopsy material only in 37 instances; 8 patients came to autopsy at varying times after craniotomy; one patient died without diagnostic operation, of meningitis. This material was studied in the living state, since I assisted at, or less frequently performed, the operations; the tumours were also examined, in the majority of cases, in the routine course of reporting on neuropathological biopsies. It is very regrettable that the operating surgeon and the neuropathologist should be the same person, but the combination of duties has permitted an

unusually intimate study of the surgical pathology of these tumours.

Besides the methods of conventional pathological examination, the analysis of the Oxford material involved review of the radiographs available, and these included 114 cerebral angiograms. The morphology of the larger neoplastic vessels can be studied thus, though detailed correlation of the histological and angiographic appearances requires special staining techniques not employed in the present study (Monckton, 1953).

Many of the findings made in the initial analysis of the Oxford material have been published (Simpson, 1957: Appendix A). They are however here recapitulated, because in the seven years elapsing since the preparation of this publication, a number of the meningiomas studied have recurred or otherwise demanded further attention. The statistics presented in this chapter represent the findings in the Oxford material, as reviewed in 1962, unless it is otherwise stated.

Gross anatomy.

In this, these tumours conformed with accepted descriptions. Eleven were tumours en plaque, and the remainder were more or less globular. There were

transitional forms; and more rarely, the same tumour might be global when first resected, and plaque-like as a recurrence. The global tumours were most commonly smooth-surfaced; an important minority showed considerable nodularity, however, and this well-known nodularity is of surgical importance. Outlying nodules may be detached during an enucleation, and overlooked; this was actually seen to happen in one case, the residual nodule being fortunately noticed at the end of the operation.

Another important pattern of growth is the formation of thin marginal extensions in the subdural space. This was noted in 22 cases (9%). Usually the extension was a thin flat fringe, extending from the periphery of the dural attachment of the tumour (see figure 1, and figure 3, appendix A) for a few millimetres or more, lying on, but not infiltrating, the arachnoid. This fringe could be the cause of a recurrence: fragments of it might adhere to the leptomeninges after the removal of the main tumour mass. Such a detached residual adhesion has been seen during an operation. It cannot be proved that subdural vestiges are of relevance as causes of recurrent growth, but they may well be. Rarely, the subdural growth is more massive: in several cases, it has formed widespread carpetings over the cerebral

hemispheres, and in a recent recurrence, the tumour was deemed inoperable because of such a subdural extension.

These peculiar patterns of expansion show that meningiomas do not always grow by simple concentric enlargement, such as is seen with truly benign tumours like the leiomyoma. The meningiomas have indeed a propensity to burrow along favourable tissue planes, and this entails many surgical hazards. The basal meningiomas, especially those arising near the anterior clinoidal process, are apt to grow around the great vessels of the circle of Willis, which may actually be found embedded in the tumour, as is shown in figure 2, appendix A. The hypothalamus and the cranial nerves may be engulfed in the same way. Under such circumstances, operative injury to the great vessels is very easy. When the tumour is a recurrent growth, reoperation will be especially hazardous, because of the additional difficulties resulting from post-operative adhesions. Similar propensity to envelope vital structures is a notorious characteristic of meningiomas growing in the cerebellopontine angle. It is also seen with some orbital meningiomas, and indeed in other situations; some of the resulting operative problems are discussed in chapter V.

Multifocal growth was seen in five patients at primary operation or at autopsy, and also in eight patients with recurrent tumours. It is certain that the multiple meningiomas are not a homogeneous group. As Cushing (1938), Ectors and Achslogh (1960), and others have observed, one must recognise a number of categories. There is the condition of generalised meningiomatosis, with or without von Recklinghausen's disease. This state must be accepted as ultimately incurable; there were no examples in the three series at present under study, and the condition is certainly rare. More common, and perhaps a little less disastrous, are multiple meningiomas disseminated in different regions. This state is exemplified by an Oxford patient, who was found to have an intraventricular meningioma, successfully removed, and a large contralateral convexity meningioma, only discovered at autopsy. Such widely separated tumours present great problems in clinical and radiological diagnosis, but fortunately they appear relatively uncommon: in the Oxford series, there were only two definite examples, and in the Adelaide series only one - a little girl with bilateral orbital meningiomas and a meningioma in the spinal canal. Thirdly, one must recognise the condition of multiple primary meningiomas

confined to a single region. The presence of one or more small satellite meningiomas, independent from the main growth, may be overlooked. This state was noted at two primary operations in the Oxford series, and once at autopsy. It has been incriminated as a probable cause of post-operative recurrence by Volynkin (1955), and by me (Simpson: 1957); an operative sketch showing such a satellite meningioma is given in figure 17, appendix A. Finally, multiple tumours have been seen in eight cases with recurrent meningiomas (Appendix C: cases 3, 7, 9, 11, 19, 21, 22 & 24). Here, there are no definite reasons to suspect primary neoplastic change at multiple foci: the secondary tumours are more probably implant metastases seeded at operation or by exfoliation into the operative cavity at some later time. That this can occur is attested by the occasional finding of tumour nodules growing extradurally in the operation wound (e.g. case 7 appendix C; see figure xliii). Seedling growth is especially seen with meningiomas of malignant propensity, but may occasionally occur with otherwise benign tumours. Cushing's (1938) case 91 exemplifies this. So does our case 9 (appendix C), since the tumour shows no cytological anaplasia and has not recurred in the last six years. It may at times

be difficult to decide whether, in a given case, the condition represents multifocal growth or implant metastasis, however, and some reservation must be made in several of our cases.

Invasive growth.

The meningiomas increase in bulk by concentric expansion: hence their commonly globular form. They may also expand eccentrically along lines of least resistance: thus, for example, intraventricular meningiomas occasionally form a ventricular cast. These modes of expansive growth have been considered; it remains to analyse the phenomena of invasive growth.

As a generalisation, it can be said that the meningiomas exhibit expansive growth at the expense of neural tissue, and invasive growth with respect to mesodermal tissues. (Figure i). Exceptions can be cited: some meningiomas do invade brain, and in some on the other hand no invasive propensities at all can be demonstrated, even towards the dura mater. But as a broad rule, this curious polarisation of growth is observed, and it must indicate some quite fundamental aspect of the biology of the meningiomas.

With the exception of the four intraventricular meningiomas, all these tumours had dural attachments

of varying dimensions. Usually these attachment areas have been comparatively large, with a diameter half that of the tumour mass, or more; but in some, the surgically favourable finding of a narrow "stalk" has been made. It has long been recognised that this area of attachment is usually infiltrated, at least superficially; it is wise to assume that it always is. In a few biopsies, I have been unable to demonstrate such invasion, but the material has been inadequate for conclusive proof of its absence. The meningioma cells commonly penetrate the dura along venous channels: figure ii shows this. (It may be added that the dura from which this section was taken appeared normal to the naked eye).

Invasion of extradural structures was particularly studied in the Oxford series, and the results have already been published in some detail. Briefly, the chief findings, revised after the 1962 survey, were as follows.

a. Invasion of a major venous sinus was demonstrated in 37 cases (15%): the sinuses so designated were the superior longitudinal, transverse, sigmoid, and cavernous.

b. Invasion across the falx or the tentorium, termed here trans-septal spread, was seen in 28 cases (11%).

c. Invasion of bone was verified histologically in 50 cases (20%). (Figure iii).

d. Invasion of the orbital cavity was seen with seven sphenoidal ridge tumours. (Figure xxviii).

e. Infiltration ~~ion~~ of muscle was demonstrable in seven cases also - chiefly of the temporalis muscle. (Figure vi, b).

f. Invasion of the paranasal air sinuses was seen with five anterior fossa tumours; invasion of the nasal cavity was not seen in the Oxford or Adelaide series, but was a presenting sign in one of the London patients, in whom frontal swelling and a nasal discharge preceded the appearance of neurological signs.

g. The middle ear was invaded in two cases; in one of these, the external meatus was also ultimately involved. (Figure vi, a).

These findings were given prominence in my earlier report (Simpson, 1957: appendix A) as causes of post-operative recurrence. More recent study has confirmed their importance in this context. The invasive behaviour of the meningiomas also explains many incomplete surgical removals, some post-operative deaths, and many post-operative disabilities.

It must be reiterated that these figures represent the minimum incidence of invasive behaviour, because they are largely based on surgical assessments. Invasion of the superior longitudinal sinus was established in about 45% of the parasagittal tumours: it may well have occurred in a greater number. Invasion of the sigmoid sinus was confirmed in only two of the posterior fossa meningiomas, but very probably occurred in several others. Invasion of the cavernous sinus by subtemporal and sphenoidal ridge tumours can also be missed at operation. Similarly, the estimates of spread across falx and tentorium may be too low. Radiographic studies sometimes give reliable evidence of invasive growth, but negative findings carry little weight: even good quality angiograms fail to demonstrate limited trans-septal spread or incomplete sinus invasion, and osseous invasion is not always apparent in radiographs. Indeed, the assessment of the incidence of osseous infiltration presents particular difficulties. Hyperostoses were present in at least 69 of the Oxford cases, and an osteolytic change was seen in 21: there were therefore gross bony changes in ninety cases (37%). This incidence is very close to the findings in radiological material recently published by Traub (1961: see

page 52*). However, histological studies do not always demonstrate meningioma cells in hyperostotic bone. Russell and Rubinstein (1959: p.48), and earlier writers, notably Rowbotham (1939), believe that hyperostoses are formed in reaction to the separation of the dura, and not necessarily to neoplastic permeation. My own material supports this interpretation: several hyperostoses contained no demonstrable tumour. It may be therefore accepted that the smaller hyperostoses are sometimes free of tumour, but nothing short of serial sections will establish this, and the operating surgeon will be prudent to assume that all hyperostoses and all eroded bone may contain neoplasm. In at least one Oxford case, bony thickening which was regarded as "only reactive" gave rise to a recurrence. Probably the true incidence of bone infiltration in the Oxford series is in the vicinity of 25%. (cf. Volynkin, 1955).

When the meningioma has penetrated bone, it may infiltrate any contiguous structure: only arteries seem immune. Even peripheral nerves and their ganglia may be invaded by extracranial meningiomas: figure iv shows invasion of the ciliary ganglion by an orbital meningioma (Adelaide series). Curiously, the pituitary gland is rarely invaded, and symptoms of hypopituitarism are

* In this thesis

rare with basal meningiomas; however, an example has been seen (figure v).

This invasive growth isnnot the property of any particular histological type of meningioma, nor can it be correlated with the cytological appearances of malignancy. Many of the most invasive meningiomas are very well differentiated and show neither mitotic figures nor other nuclear abnormalities. (Figures 4 and 5, in appendix A, show this very clearly).

Invasion of brain, it has been said, is atypical. The diversity of opinions on this fundamental question have been mentioned: they range from Globus' (1937) belief that penetration of the brain tissue was present in the majority of meningiomas, to the statement by Russell and Rubinstein (1959: p.56) that it is never exhibited by benign meningiomas, and constitutes prima facie proof of malignancy.

Invasion of brain was in fact seen in thirteen cases (5%). Figures vii & viii, and figure 10 in Appendix A, show typical examples. It is extremely hard to know what significance to attach to these findings. The infiltration does not penetrate deeply. It is sometimes detected in surgical specimens where a shell of brain adheres to the excised stumdurn; this was the case

in two of the tumours figured. One of the patients concerned died following operation, and multiple sections of the tumour bed showed that the removal had been complete.

It can therefore be said that such marginal infiltration does not necessarily preclude total ablation: the little digital extensions of the tumour may be sufficiently tough to come out with the main mass. But certainly such digital processes could be detached, and they are probably one cause of delayed recurrence. Whether cerebral invasion of this kind is proof of malignancy is a harder question, and to some extent one of semantics. In the present series, cerebral infiltration was recorded with three tumours which could be considered malignant, in that they were anaplastic, with cytological evidences of rapid growth, and had recurred. It was however also recorded with several tumours showing no unusual cytology, and no special clinical evidences of malignant behaviour. One, indeed, had a history of seventeen years duration (figure viii). Marginal cerebral invasion is certainly an unfavourable finding, and an indication that recurrence is more than ordinarily possible; but in my opinion it is not incompatible with successful surgical cure. If therefore

such tumours are to be called malignant, some qualification is needed.

Metastasis.

Invasive growth is therefore seen to be common, and of extreme importance. Metastasis, however, though given much prominence in recent reports, is certainly very rare, and usually occurs as a late development. There were three examples of remote metastasis in this series. All were in patients with parasagittal tumours, which had recurred after seemingly radical operative excision. One had had such a tumour excised in Toronto, by Dr. K. McKenzie; a local recurrence was removed at Oxford four years later, but the patient died two years after this second operation with a small local recurrence and generalised visceral metastases, in lungs, liver, kidneys and elsewhere. (Case 17, appendix C). The second underwent radical resection of a frontal tumour, together with the attached falx: the tumour recurred rapidly, and at autopsy two small pulmonary metastases were found (Case 6, appendix C). These two cases were reported earlier (Simpson 1957). The third patient was at the time of the 1955 survey in robust health, after excision of a large frontal meningioma; it later

recurred repeatedly, and at autopsy a single very small pulmonary deposit was found (case 7 appendix C: see figures ix - xi). In all three cases the possibility that the metastases might represent some second neoplastic process, independent of the meningiomas, or that the diagnosis of meningioma was itself erroneous, have been considered. It is felt that the histological similarities, as well as the clinical course of the disease, make these interpretations highly unlikely. For the present purposes it is not necessary to labour the point. It may be accepted, from the numerous reports in the literature as well as from these three experiences, that many anaplastic meningiomas with local malignant propensities may ultimately exhibit frank malignancy in the sense that they metastasize. Metastasis by a well differentiated meningioma, such as Jurow (1941) reported, has not been seen in this series, and must be inordinately rate. Neither has there been any example of lymphatic metastasis, the rarity of which is surprising, in view of the presence of lymphatic channels in the dura mater (Millen & Woollam, 1962: p. 134).

Microscopic appearances.

Since the inception of these studies eight years

ago, it has been my hope that the behaviour of the meningiomas could be correlated with their microscopic appearances. With this aim in mind, the meningiomas in the Oxford series were reviewed and classified in 1955. In almost all cases, haematoxylin - eosin and Van Gieson's stains were used; reticulin stains were employed on a large number; in a few, special stains for fat, mucin, and glycogen were employed. Some of the early biopsies had been stained by del Rio-Hortega himself, and his beautiful metallic impregnations were available. More recently, the meningiomas of the Adelaide series were similarly studied, chief use being made of haematoxylin-eosin and Van Gieson - haematoxylin stains. Finally, in 1962, biopsies from patients still alive in 1955 were reviewed, and correlated with later biopsy and autopsy material, and with the clinical progress of the patients concerned.

A descriptive classification, based on the tissue differentiation of the tumour has been employed. (Table I). As has been reported earlier (Simpson, 1957) this is a simple system, derived from the well known classification of Bland and Russell (1938). Five types are recognised.

1. Endotheliomatous: formed of alveolar masses or sheets of cells, with or without whorl formation, and

often syncitial. In this type collagen and reticulin are found only in trabeculae or around blood vessels. (Figure xii).

2. Fibroblastic: formed of spindle cells laying down reticulin and usually collagen fibres in intimate relation to the cell bodies (Figure xiii, a).

3. Fibroendotheliomatous: tumours exhibiting in different areas both endotheliomatous and fibroblastic appearances. (Figures ix & xiv; figure xiv shows an island of endotheliomatous cells embedded incongruously in a fibroblastic area).

4. Angioblastic: identified by their rich network of vascular channels, especially capillaries; these vessels are lined by endothelial cells, with much delicate reticulin formation. (Figure xv). Similar cells lie between the vessels. This type could be subdivided, if it were desired, because some tumours appeared purely capillary in character, closely resembling the cerebellar haemangioblastomas, whereas others showed also many mature vessels and could be termed angiomatoid. (cf. Willis, 1960: p. 729). Transitional forms were noted.

5. Undifferentiated: very cellular, and lacking any organisation; composed of fusiform or multangular cells,

sometimes forming a loose reticular structure, but with relatively little cytoplasm. (Figure xv; see also figure 16 a, b, & c in appendix A). These tumours contain very little collagen, but reticulin is uniformly present, and there are many small blood vessels. Mitoses are present, and often numerous, in all the tumours classified in this group.

No merit other than convenience is claimed for this system. It conforms with those of many other writers, as is seen in table 1, at least as far as the first three types are concerned: these correspond respectively with Courville's (1945) syncitial transitional and fibroblastic types. No special status has been given to the meningiomas with lipoblastic*, myxomatous or osteoblastic tendencies, nor to the very rare melanoblastic meningiomas (figure xvii). The status of the angioblastic meningiomas has been much disputed, but the criteria used here accord with those given more recently by Russell and Rubinstein (1959: p.52). It is only at the recognition of the type termed by me "undifferentiated meningiomas" that some criticism has been directed.

This small but clinically important tumour group is defined partly on negative grounds: the tumours lack the specific features of the other four types. It may

* Xanthomatous change is seen in figure xiii, b.

therefore be argued that they only represent malignant degeneration in a more differentiated tumour, and many pathologists would term them malignant angioblastic meningiomas, or lump them in the general category of sarcomas. Certainly, these tumours, as will be shown, are malignant. However, they bear very little resemblance to the ordinary angioblastic meningiomas, and they do, on the other hand, as Globus (1937) stressed, show some general similarity in their structure to the embryonic meninges. (My own limited studies of foetal material partially support this interpretation). Their characteristics have therefore seemed definite enough to justify special recognition, and the designation given is sufficiently non-committal, even for those who do not regard Globus' phylogenetic analysis with favour. It may be observed that their macroscopic anatomy was in no way remarkable: to the operating surgeon they appeared ordinary, rather vascular meningiomas. Two were studied angiographically; there was in each a rich tumour circulation, with rather irregular appearances in the venous phase (Figure xlviii).

In the Oxford series, this histological classification gave the following distribution of types.

1. Endotheliomatous : 135 tumours : 59%.

2. Fibroblastic : 38 tumours : 16.5%.
3. Fibro-endotheliomatous : 39 tumours : 17%.
4. Angioblastic : 12 tumours : 5.1%.
5. Undifferentiated : 5 tumours : 2.4%.

Unclassified (chiefly because of unsufficient material : this was especially in some of the early biopsies) : 17 tumours : 7.5%.

No very great importance pertains to these figures. As is shown in Chapter VII (see table XIV), no one histological type has a monopoly of the recurrences; though the fibroblastic and angioblastic tumours appear rather more favourable, this may be an artefact of classification, because their peculiar features are less easily identified in anaplastic forms. Furthermore, the criteria are somewhat arbitrary, and the transitional forms are so numerous, that reclassification by another observer might give somewhat different statistics. It is probably significant that in the Adelaide series, classified by the same observer but at a later date, the diagnosis of purely fibroblastic meningioma was made much less frequently, and fibroendotheliomatous tumours appeared more common.

It seems indeed that classification by histological types, to which so much time has been devoted by

pathologists, has relatively little practical value. Only the small group of undifferentiated meningiomas has shown consistently predictable behaviour: all five have recurred, three after operations which appeared radical removals, one very rapidly after an extensive but subtotal resection, and one after palliative decompression and radiation. In the other, larger groups, the histodifferentiation of the tumours has appeared much less relevant than the cytological evidences of their rates of growth.

In each of these groups, there were many tumours of very innocent appearances; a few with the cytological features of rapid cellular growth; and a large intermediate group of fairly well differentiated tumours in which careful examination would reveal only rare mitoses and inconstant cellular pleomorphism. For the endotheliomatous tumours, one can illustrate a continuous spectrum, from such indolent growths as that shown in figure xii to the final extremity of malignancy. Similarly, the fibroblastic tumours exhibit all grades of activity from the fibromatous appearances seen in figure xiii to the highly anaplastic state seen in figure 13, appendix A, which could well be called a fibrosarcoma.

Variations in activity are seen also with the other types. The fibroendotheliomatous type furnishes an unusual example of the biologically interesting process of dedifferentiation. Over a period of four years, three biopsies were taken and finally an autopsy was obtained. The successive sections show a progressive worsening in appearances, from the original state seen in figure ix, to a final state of frank malignancy. (Figure x).

On general pathological principles, one would suppose that these microscopic reflections of cellular activity would give an index of the behaviour of the tumours. There are of course many fallacies in deductions made on biopsies which give only a single picture of what is after all a continuous process: at another time, or in another part of the tumour, the dynamics of growth may be very different. Nevertheless, as a group, the meningiomas are comparatively homogeneous, at least when compared with gliomas, and their growth characteristics are often very constant. Changes such as are illustrated in figures ix & x are exceptional: far oftener, one meets meningiomas which show identical appearances even after the lapse of many years. The tumour shown in figure xviii, a recurrent endotheliomatous

tumour composed of cuboidal cells somewhat resembling liver tissue, retained its interesting and characteristic appearance in three separate biopsies taken over a period of fourteen years. (Case 9, appendix C).

In practice most neuropathologists do attempt to predict the behaviour of meningiomas from their cytology, often identifying those with appearances of rapid growth as 'malignant meningiomas', 'meningosarcomas', or 'meningoblastomas'. The divergences of opinion on the value of such predictions have been discussed on pages 36 and 48 . Malignancy is a clinical concept, and as such cannot be exactly equated with the findings of microscopy, but it is reasonable to expect some correlation.

In the original classification of the Oxford tumours, and in subsequent work at Adelaide, an attempt was made routinely to assess the growth rate of the tumour. Numerous mitoses, high cellular density, nuclear pleomorphism, and lack of cellular orientation were taken to indicate rapid growth. Of these, the presence of mitotic figures was thought to be the most significant: more than two mitoses in a single section of standard size was considered evidence of high cellular activity. The other abnormalities were also taken into assessment,

but nuclear pleomorphism, and even the formation of monstrous nuclei have been seen in tumours whose history suggests quite slow growth. (The tumour shown in figure xix was removed nine years ago, and has not recurred as yet). The absence of these features, and especially of mitoses, together with the formation of well differentiated alveoli whorls or laminae, or of numerous psammoma bodies and mature hyalinised vessels, was taken to indicate slow growth. Figures vii & viii and figures 5, 14 & 15 in appendix A, are examples. Where, as in the majority, the appearances were intermediate in character, the tumour was said to be of average growth rate. (Figures xii, xv & xviii). Although the results of this cytological grading are not easy to express in statistical form, the following comments can be made.

i. About 16% of meningiomas were considered to show unduly high cellular activity. Recurrences in this group were numerous; more than half of the tumours so graded have recurred. Recurrences as a rule tended to appear relatively early, although two occurred after an interval of ten years. Two of these tumours have metastasized.

ii. About 17% were considered to show low cellular

activity. Recurrences in this group were rare; long survival, for upwards of twenty years, was seen even after incomplete removal. When recurrence did occur, it was usually after a long interval of freedom; there was however at least one exception to this (case 22 in appendix C).

iii. The remainder (67%) were considered to be of average growth rate; no special comments can be made on this group. One tumour so classified eventually metastasized (Case 7, appendix C), but only after a change in the cytology, which in serial biopsies suggested an increasing cellular activity.

Infiltrative behaviour was seen in all groups, as noted earlier, but cerebral infiltration certainly did appear somewhat commoner with the rapidly growing tumours.

Such a rough grading is of course very subjective. Nevertheless, it has appeared to be of definite value, not only in identifying unfavourable tumours, but also, conversely, in predicting those likely to prove highly innocent. It has permitted some prognostic ventures after incomplete resections, though many other factors must be considered also, notably the size of the tumour residue, and its neuroanatomical relations.

To some extent, this cytological appreciation - like most published studies of the histopathology of meningiomas - is vitiated by being retrospective. It is easy to see significance in the cytology when the clinical course of events is known. However, in some 160 cases, this criticism can be partially rebutted, because the biopsies were assessed, and the growth rates evaluated, as a prospective study. This was done in 1954 and 1955, when the patients concerned were in good health, without clinical suspicion of recurrence. Their subsequent progress has provided a fair test of the value of the assessment. Twenty tumours have recurred. Twelve recurred despite seemingly complete resections, and these are of especial significance. Three of them were regarded as cytologically very active, and recurrence had been predicted. Four others had been noted as showing perhaps somewhat increased cellular activity. Four tumours were considered to be of average growth rate. One had originally only had been classed as of very low growth rate, and as the recurrence came seventeen years after the original resection, which was not a very radical one, the clinico-pathological correlation seems good. Thus, in general, the value of these cytological assessments has been borne out, though

clearly their significance should not be overstated. Recurrence is not explicable solely in terms of microscopic pathology: surgical factors are still more important, and these are considered in chapter VII.

Finally, cytological studies of growth rates can to some extent be correlated with anatomical distribution. It is generally considered that in certain anatomical situations, meningiomas tend to be particularly slow-growing. The suprasellar, intraventricular and spinal meningiomas are usually expected to be indolent. Cytological studies have supported this belief, at least in the first two groups: no intraventricular meningiomas, and only one suprasellar meningioma, was considered to show evidences of rapid growth, and the number of tumours graded as slowly growing was above the general average.

The meningiomas as space-occupying lesions.

In this analysis of the pathology of the meningiomas, prominence has been given to their invasive capacities, and the significance of these, in relation to operability and to post-operative recurrence, is further discussed in chapters V and VII. However, pre-eminently, the meningiomas are expanding lesions. They produce most

of their symptoms by local interference with the function of adjacent neural tissue, by mass cerebral displacements, and by disturbance of intracranial pressure and circulation. The clinical and radiological manifestations of these processes determine, to a large degree, the diagnosis of the meningiomas; their interpretation is familiar to neuro-surgeons, and is not relevant in the present context, except in that erroneous interpretations contribute a small but important fraction of the over-all surgical mortality. Of greater relevance is the fact that the secondary effects produced by meningiomas may be irreversible, and so result in post-operative death or disability.

Radiological contrast studies have thrown much light on the mass displacements effected by space occupying lesions in general, and the meningiomas in particular. The Oxford material has been fully analysed from a radiological viewpoint, but the results of this analysis have only confirmed what is common knowledge. Similarly, autopsies done on fatal cases in the Oxford and Adelaide material have shown the significance of tentorial and foraminal herniations, and brainstem haemorrhages, as causes of post-operative death, but have not revealed anything

worthy of special consideration. (See p. 192)

The local effects of cerebral compression by the meningiomas do however demand more attention. This subject has been, surprisingly, little discussed, and least of all by American and English writers. The subject receives no special notice in the monographs of Cushing (1938) and Russell and Rubinstein (1959), though these writers, and also Greenfield (1939), make incidental reference to oedema and other secondary changes in association with the meningiomas. Indeed, some American authors have minimised the effects of the meningionas on the subjacent brain; Weil (1946: p.247), for instance, wrote that the slow growth of these tumours permitted the underlying structures to adapt themselves, and considered that severe degenerative changes were exceptional. However, the French and German literature contains some important observations to the contrary. Scherer (1936) of Antwerp noted that atrophy of the cerebral cortex was common, and severe oedema or even necrosis of the white matter not rare. He attributed these changes to circulatory disturbances. More recently, Noetzel (1951) of Freiburg i. Br. has reported the findings in a series of 33 carefully studied autopsies. He found that in 23 of these the

meningiomas were encapsuled in a lamina of collagenous tissue, considered by him to represent the inner layer of the dura mater. In the remainder, the meningioma was in close relation to the brain, and received most of its vascular supply from the pia. Changes in the subjacent brain, which were found in 21 cases, included intense oedema and necrosis of the white matter, and occasionally marginal cyst formation. He also regarded these degenerative effects as the result of vascular interference. Zülch (1956: p.87) considered that only the smaller meningiomas caused fully reversible changes: with larger extracerebral masses, circulatory disturbances, oedema, and necrosis were the rule.

There can indeed be no real doubt that the meningiomas usually cause some local destruction of brain substance. This is evident in routine surgical practice. When an ordinary globular meningioma is exposed, it is sometimes found to be extra-arachnoid, as in figure xxv(a). More usually, however, the arachnoid is reflected from the cerebral cortex on to the surface of the tumour. When the arachnoid in turn is divided, the tumour extrudes or can be made to extrude, and almost always the subjacent cortex is found to be flattened and in part atrophic. Often, the pia mater is adherent to

the tumour, and the surgical plane of cleavage is found to run through grey or white matter, a film of which may be removed with the tumour. This is especially so where there is limited cerebral invasion, but it may occur even when the pial barrier is intact. When the tumour is removed the tumour bed may be viewed: with smaller tumours, and tumours en plaque, it may consist of compressed but recognisable cerebral or cerebellar cortex, but large tumour cavities are usually excavations in white matter. In a case of my own, the removal of a large falx meningioma revealed a cavity involving the corpus callosum. The callosal fibres had, in an area at least 2 cms. in diameter, disappeared. The two pericallosal arteries, which had been preserved, were in immediate relation to the third ventricle, seen from above through a transparent membrane.

Surgical material is obviously unsatisfactory for microscopic study of the tumour-brain relationship, since it is not often necessary to excise brain, and never desirable. Even when a limited resection of cerebral or cerebellar cortex is unavoidable, the excised tissue is usually traumatised. Autopsy material gives a better impression, but happily meningiomas do not often come to autopsy in the virgin state, except

as a chance finding. Small meningiomas not producing symptoms constituted a considerable portion of Noetzel's material: with such tumours, the associated cerebral lesions are likely to be minimal.

In the large material preserved at Oxford it was possible to find only eleven autopsied cases suitable for study of the effects of intracranial meningiomas on brain tissue. The criteria were that death had resulted from the tumour; that no attempt had been made to remove the neoplasm, nor any irradiation administered; and that the brain, or a sufficient part of it, was available for study. Even in this small group, the virginity of several tumours was compromised, by aspiration biopsy (four cases) or by surgical decompression (two cases).

In every case, the brain tissue compressed by the tumour showed definite changes. In two, structure however was comparatively well preserved. In one of these (figure xx) the cerebellum was excavated, but the folia, though thinned and flattened, were quite recognisable. There was some outfall of Purkinje cells, but the general anatomical structure was well preserved. In the other, there was limited neoplastic infiltration of the cerebellar cortex, and a greater loss of Purkinje

cells, but the cerebellar granule cells and the pontine nuclei were less affected. It is interesting that these should both have been posterior fossa meningiomas. Possibly, in that confined space, death from obstructive hydrocephalus occurred before local atrophic changes could become well established. It has been my impression however that the leptomeninges in certain areas, especially in the cerebellopontine angle, tend to form a better capsule than is seen, for example, with meningiomas impinging on the cerebral cortex. A meningioma arising from the region of the sigmoid sinus, in the Adelaide series, illustrated this: when it had been removed, one could not identify the lower cranial nerves, or even the pons, because the inner pole of tumour was enveloped in grey, thickened arachnoid (see page 176).

In the remaining nine cases, there was evidence of grosser degenerative cerebral change, ranging in degree from a thinning of the cortex to severe necrosis and widespread oedema. Figure xxi shows an example of the former: although the cortex is diminished, the individual neurons are recognisable and there is only slight reactive gliosis. These appearances suggest localised pressure atrophy. Figure xxii shows more severe cortical

changes: there is marginal necrosis, with many foci of microglial cells, on the periphery of the tumour. There is also some demyelination in the white matter. Such degenerative changes have led to misdiagnosis: in four instances, aspiration biopsies were considered to show glioma, and operation was abandoned. In the autopsy material, the glial reaction is not really suggestive of a neoplastic change. However, the biopsies were examined by most capable pathologists, and it is clear that there is a real risk of misdiagnosis when the biopsy is taken from the vicinity of the tumour, and not from the tumour itself. The risk is increased when there is a cyst in relation to the meningioma: both in the Oxford and Adelaide series, small arachnoidal loculations have been seen, and in one Oxford case the cyst was of large (85 ml.) volume.

The severity of these secondary cerebral changes could not be correlated with the character of the vascular supply of the tumour. Noetzel (1951) claimed that tumours in intimate vascular relation with the brain were more apt to cause local ischaemic damage: this is a reasonable hypothesis, but in fact such changes were minimal with two tumours showing marginal cerebral invasion - the most intimate anatomical relationship

possible - and maximal in the case depicted in figure xxiii, where the tumour was well encapsuled by a collagenous lamina. In parenthesis, it has not been possible to confirm Noetzel's views on the significance and frequency of this encapsulation. When present, it is indeed favourable surgically, but it has been detected in only a minority of cases: more commonly, the meningiomas are separated from the brain only by the attentuated pia mater, and even this may be difficult to demonstrate. Further, the collagenous capsule, regarded by Noetzel as the inner lamina of the dura mater, may be present in one area and altogether absent elsewhere. Noetzel's belief that it is of dural origin, and that some - he considers the majority - of meningiomas arise within the dura, is also not supported by the evidence of this study, though it cannot be confidently denied.

As figure xxiii shows, the severity of the associated cerebral oedema and demyelination does not correlate with the size of the tumour, which in this instance was quite small. One may accept Zülch's (1956) general dictum, that larger tumours cause greater irreparable harm locally, but the regional changes, oedema of one lobe or one hemisphere, seem to show no such proportionality.

Probably they represent some more fortuitous result of the presence of the tumour. It has been suggested (Greenfield, 1939) that their explanation may lie in the occlusion of a draining vein, or in the local action of some tumour metabolite. The former explanation is favoured by the observation that small meningiomas causing gross oedema are commonly seen in the Sylvian fissure, or medial thereto, where venous channels are large and important.

It would be wrong to over-emphasize the importance of these cerebral reactions. In most cases, they are not so extensive as to prevent a good functional recovery. The area of brain affected is often small, and though the anatomical changes are irreparable, the neurological deficit may fully recover. However, the material reported here suggests that the secondary cerebral changes, atrophy necrosis and oedema, with consequent gliosis, have a definite if limited significance: a. Local necrosis and gliotic change, and regional cerebral oedema, may lead to fatal diagnostic errors, especially in the interpretation of small biopsies. This question is being studied in Oxford (El-Banhawy and Sheldon, 1962); for the present purposes it is sufficient to note that diagnostic errors contributed significantly

to the gross mortality in the Oxford series.

b. Massive regional oedema can increase operative difficulties; these are not as a rule insuperable, but they can occasion some inconvenience.

c. Irreversible brain damage is presumably the pathological basis of post-operative epilepsy. It also accounts for other post-operative neurological deficits.

d. It is not always easy to assess the importance of this factor in determining the hazards of some surgical procedure. For example, the effects of resecting a major venous sinus may be greatly magnified by pre-existing regional brain damage. This question is further considered on page 156 .

CHAPTER V.

SURGICAL PROCEDURES.

General.

The three series now under study span the years between 1928 and 1962. In this period, there were many changes in operative technique, and still more in anaesthesia and resuscitation. There was some continuity in methods, since the operations were all performed by Professor Sir Hugh Cairns and his pupils in the first and second generations: but, inevitably, there was great diversity as well. Nevertheless, one can see, in reviewing the operation notes, that certain constant principles dictated the nature of the operative procedures.

It is not proposed here to detail the surgical techniques employed, except incidentally in relation to particular cases and particular problems. It is however necessary to analyse the general characters of the operations, because they were by no means a homogeneous series of radical tumour resections. In neurosurgery, as elsewhere, there is commonly an antinomy between what is desirable and what is possible: with the meningiomas, the outcome is determined by the surgical pathology, by the condition of the patient, and by other variables.

In many of these operations, the surgeon responsible considered that he had been able to achieve the ideal of complete removal. In others, small residua were known to have been left behind; in others again, the resections were grossly incomplete, and had to be regarded as only palliative. From the recorded descriptions of the operations, which are admirably detailed and exact, and from the available operation sketches (Oxford series) and photographs (Adelaide series), it is possible to identify five fairly distinct grades of operation.

GRADE I : a macroscopically complete removal of the tumour, with excision of its dural attachments and of any hyperostotic or eroded bone, or other visible extradural extension. Where the tumour arises from the wall of a venous sinus, this procedure entails either a marginal or more usually a complete sinus resection.

GRADE II : a macroscopically complete removal, with thermal coagulation of the dural attachment (fulguration by high-frequency diathermy) and excision of any visibly abnormal bone.

GRADE III : a macroscopically complete removal of the

intradural tumour, without excision or coagulation of its dural attachment, or of known extradural extensions of the tumour, e.g. in bone, or within a venous sinus.
GRADE IV : a macroscopically incomplete removal of the intradural tumour, leaving visible remnants in situ.
GRADE V : a decompression, whether osteoplastic or by craniectomy, with or without biopsy.

Such a subdivision may seem over-elaborate, but it was found convenient when the material was first analysed, and has seemed to accord with realities in my own practice. It is of course evident that the surgeon's assessment is not always correct, especially with the deeper tumours. However, there is no other criterion. In a very few cases, the records leave some doubt as to the operative procedure, and here I have selected the grading most probable in the particular circumstances.

Table III summarises the results of this grading. The figures for the London series are unhappily incomplete, as a number of patients dying immediately after the operation have not been graded, from lack of exact information. Probably many of them would have been placed in grades IV and V. The Oxford and Adelaide series are complete, except that five operations for

Table III. Grades of Operation. (Primary operations and operations for recurrence)

Series	I	II	III	IV	V
London	22	26	5	20	2
Oxford	88	101	23	55	11
Adelaide	14	23	4?	4?	-

orbital tumour, and also several burrhole biopsies, and other minor procedures, have been excluded. Operations for recurrent tumour are included in table III; but operations carried out in more than one stage are graded as single procedures.

From this table, it is seen that in an important minority of cases, the operator has had to accept the impossibility of effecting a complete removal. In the London series, and in many of the earlier Oxford cases, this was often because of the poor condition of the patient. The gratifying rarity of operations of grade IV in the Adelaide series, and in recent Oxford experience, largely represents the ready availability of blood transfusions, the control over cerebral swelling given by hypothermia or intravenous urea, and the general excellence of modern anaesthesia. Nowadays, operations

are abandoned only when the meningioma is found to lie in intimate relation to some vital structure.

It is however interesting to see that there has been no increase in the number of ideal (grade I) resections. It is evident that the operating surgeon still, in a majority of cases, finds it impossible or unnecessary to excise the dural attachment of the tumour. Operations of grade II are often very satisfactory: in the short term view, they are almost invariably so. But clearly, thermal coagulation is an uncertain destructive agent. No doubt it will destroy tumour cells in the immediate vicinity of the treated area, but the depth of its action is limited and unpredictable. Several patients in the Oxford series have come to autopsy, from unrelated causes, after operations of grade II. One, the important case described on page 25 of appendix A, and illustrated in figure xxiv, had had an olfactory groove tumour removed a year earlier. The dural attachment had been fulgurated, and on serial sections, this dura was found free from tumour. But, in the bone immediately beneath, there were nests of viable meningioma cells. Similarly, fulguration of the wall of a venous sinus may be effective locally, but

cannot deal with tumour within the lumen or in the opposite wall. And the presence of such more distant extensions cannot be excluded in a grade II operation.

If it is accepted - and the evidence submitted in the previous chapter seems valid - that the meningioma is always potentially invasive on its dural aspect, then the operative principle involved in grade I resections seems logical. Theoretically, such operations should be curative, save when the meningioma is also invasive on its cerebral aspect, or when the extent of extradural spread is greater than is realised. In practice, recurrences do occur after grade I resections, but they are significantly less frequent than recurrences following grade II resections, as is shown in chapter VII.

Not all writers accept the significance given here to the extradural invasive spread of meningiomas. Guillaume et al. (1957) appear to regard as "exérèse totale" any procedure which removes the visible tumour. However, it is submitted here that resection of the potential dural and transdural infiltrations is of crucial importance. It remains to see why, in practice, it is carried out only in a minority of cases.

Regional considerations.

The radical removal of the meningiomas is largely

governed by their anatomical relations, and particularly their vascular relations. These are traditionally, and very conveniently, considered in the regional groupings suggested by Cushing. (In the following section, the statistics are obtained from the Oxford series. The illustrative cases, except where it is otherwise stated, come from the Adelaide series, and, except where it is otherwise stated, represent patients operated on by me. Tables are given for the operation gradings in the more important regional groups, and these contain figures for operations on recurrent tumours, which are further discussed in chapter VIII, as well as for initial operations, which are of chief interest in the present analysis.)

a. Convexity meningiomas. (table IV).

These tumours arise from the dura covering the convexities of the cerebral hemispheres. By definition, they are not related to any major venous sinus, nor to any great artery, except in the case of those indenting the Sylvian fissure and impinging on branches of the middle cerebral artery. They can therefore be removed with comparative ease, and as they are approached from their dural aspects, there is generally no difficulty

in effecting a grade I resection. Figure xxv shows the removal in its most simple form. Presumably the historic operation performed by Sir George Syms, described in appendix B, was something of this type.

In the Oxford series, this was achieved, as a primary procedure, in 41 patients. The chief dangers were to function rather than to life. When the tumour arises over a vital cortical area, such as the central sulcus, it may have already caused permanent damage, which again may be augmented in the dissection of the tumour. It is not always possible to preserve cortical veins and arteries when they are closely related to the tumour margin. However, as a rule, a very gratifying recovery can be expected, even when, as in the following case, some local brain damage is inflicted.

Case Report.

M.F., aged 67, was admitted to the Royal Adelaide Hospital on July 7th, 1957. Three months earlier she had noticed weakness in the right arm, which fluctuated in severity. Three weeks before her admission, she suffered a focal motor seizure beginning in the right arm and spreading to involve the whole right side; this was followed by a temporary right hemiplegia. She had suffered

several smaller motor seizures since. She had noticed no speech difficulty, though she was right handed. She admitted to occasional mild headaches.

On examination, there was no demonstrable dysphasia. The optic fundi were normal. There was a moderate weakness of the right upper limb, and slight weakness of the right lower limb, but no facial weakness; both plantar reflexes were flexor. There was slight impairment of two point discrimination and joint position sense in the right hand. Plain radiographs of skull showed nothing significant, except pineal shift to the right. A left carotid angiogram showed a mass in the posterior frontal region, with a few tumour vessels, but nothing on which a pathological diagnosis could be made.

At operation (August 16th, 1957) a high lateral osteoplastic craniotomy exposed a small meningioma, only 2 cms. long, which was attached to the dura over the cerebral convexity, quite close to the midline in the posterior frontal region. It had firm circumferential adhesions to the pia-arachnoid, but did not extend to the sinus or falx. It derived most of its blood supply from the brain, and the relationship was quite intimate. The operator was

able to remove the tumour in toto, together with its dural attachment; there was decortication in the tumour bed.

Histologically, this was an endotheliomatous meningioma, with villous projections into cerebral tissue: that is to say, with marginal cerebral infiltration. It appeared of average growth rate. (Figure xii). Motor recovery was rapid and complete, and the patient's subsequent progress has been uneventful. She is now unaware of any motor disability, and as far as is known she has had no fits.

Serious neurological deficit is most likely to occur when the tumour is very large, or when it has been necessary to sacrifice the rolandic or external sylvian vein, or branches of the middle cerebral artery in the Sylvian fissure: even these vascular occlusions are often quite well tolerated. Alarming post-operative hemiplegias and aphasias are common, but usually regress, and in fact only two Oxford cases were left with serious motor disabilities. Epilepsy, however, is very frequent.

Procedures other than grade I resections were performed rarely. Three operations had to be classed in grade II, because abnormal dura was cauterised rather

than excised. One tumour was incompletely resected: at the end of a long emergency resection, a small nodule was left in situ. It took nineteen years to recur! In one case, a biopsy only was performed, and misinterpreted; in another (early in the series), a simple decompression was performed, with unhappy issue. In general, one may say that except in very unusual circumstances, the convexity meningiomas are suitable for maximum, ideal, ablations.

Table IV : Resections of Convexity meningiomas (Oxford series).

Grade	Primary operations	Operations on recurrent tumours
I	41	3
II	3	1
III	-	-
IV	1	-
V	1	-

Table V : Resection of sphenoidal ridge meningiomas (Global type : Oxford series)

	Outer 1/3		Middle 1/3		Inner 1/3	
	Primary ops.	Recurr-ences	Primary ops.	Recurr-ences	Primary ops.	Recurr-ences
I	4	-	1	1	-	-
II	7	-	2	-	2	-
III	1	-	1	-	-	-
IV	2	1	5	1	4	-
V	-	-	-	-	-	-

b. Sphenoid ridge meningiomas - global.(table V).

These are anatomically fronto-temporal tumours, since they straddle the ridge between the middle and anterior fossae. Following Cushing, it is usual to consider them in three groups, according to their loci of origin on the inner, middle or outer thirds of the sphenoidal ridge. They have this in common, that they all elevate the middle cerebral artery, and may be in dangerous relation with it; the deeper the tumour, the more likely this is. (Figure xxix). The tumours of the inner ridge may also be in relation with the internal carotid artery, the cavernous sinus, the optic nerve,

and the hypothalamus; their surgical dangers are notorious. They may also invade the orbit (Figure xxviii).

Approach has usually been by a fronto-temporal flap. Meningiomas of the outer third are comparatively accessible. There were seventeen in the Oxford series, and complete removal was achieved in eleven. Four of these operations came into grade I, the dura being stripped from the middle and anterior fossae: the theoretical benefit of this more radical procedure has been less evident in this group, probably because invasion of bone was not always detected even after dural ablation. These more superficial tumours were exposed as a rule without cortical ablation.

The deeper tumours of the middle third were harder of access, and it was often necessary to resect frontal or temporal cortex to expose them: however, such ablations would only represent the removal of a shell of cortex, such as is seen covering the upper surface of the gigantic tumour shown in figure xxvi. There were in this group one operation of grade I and two of grade II. In another case, a global tumour was removed, but its hyperostosis was left alone, in the belief that it was reactive: later events showed that it was in fact

permeated with active meningioma and orbital and intracranial recurrences took place. In the remaining five, resections were grossly incomplete.

The tumours of the inner ridge are still less accessible. In all save one case in the Oxford series, it was necessary to uncap the tumour by resecting a substantial amount of the frontal lobe. (Figure xxviii). Possibly, with the aid of intravenous urea, it will not always be necessary to do this, but even when a lobectomy can be avoided, the tumour itself will usually have excavated the frontal lobe, as is shown in figure xxvii. It is therefore to be expected that post-operative epilepsy will be common. In only two of the inner third tumours was a total removal of grade II possible, and in one of these, the procedure was lethal.

Thus, in the whole group of global sphenoidal ridge meningiomas, a grossly incomplete resection had to be accepted in twelve cases. The reasons were, in most instances, a too intimate adhesion to the internal carotid or the middle cerebral arteries. (Figure xxix). Less commonly, the operation was abandoned because the cavernous sinus was clearly invaded. Although some prolonged survivals have followed incomplete resections, it is important to note that this has been the case only

when the operation has adequately decompressed the diencephalon. Operations which do not do this - the tumour shown in figure xxvi is an extreme example of an incomplete decompression - have been unsuccessful even in the short term.

One may reasonably hope that grade II or preferably grade I resections will be possible in most tumours of the outer sphenoid(al) ridge. The inner ridge tumours must however frequently be inoperable. The chief surgical problem, with such tumours, is to know when to stop. Angiographic demonstration of the position of the internal carotid artery may guide this decision: if the artery is shown to be wholly enveloped in tumour, a complete resection should not be attempted. In this series, no patient has survived division of the internal carotid artery; the middle cerebral artery has been occluded several times without fatality but of course with the infliction of a severe hemiplegia.

c. Sphenoidal ridge meningiomas en plaque.

Extensive invasion of the base of the skull, with or without hyperostosis, constitutes inoperability. In the Oxford series, all the sphenoidal ridge meningiomas en plaque were associated with diffuse hyperostosis of the

sphenoid bone, and(in many cases)of the frontal temporal and zygomatic bones. Nevertheless, in nine cases, operation was considered justifiable, and the intradural component of the tumour was removed. The hyperostotic bone was rongeured away as far as possible, but a complete resection was not claimed,* and these procedures are considered to be operations of grade III. However, as will be seen in chapter VII, these subtotal resections have been on the whole very satisfactory. Certainly they have not borne out the apprehension expressed by Castellano, Guidetti, and Olivecrona (1952), that intervention might promote more widespread invasive growth by giving access to vulnerable extracranial tissues.

Case report.

E.B.P., a man aged 48, was transferred to the Radcliffe Infirmary from Broadmoor Asylum on 22nd June, 1948. He had been there since 1933, suffering from schizophrenia. He exhibited left proptosis and a swelling in the left temple, which was bony hard. The proptosis had been noted two years before his transfer; in the same period he had complained of headache and pain in the left ear. He was not a very cooperative patient, but as far as could be

*Except in the case described below: see p. 146

determined, his vision was well preserved and he had no anosmia or other neurological abnormality.

Plain skull radiographs (figure xxx,a) showed gross hyperostosis of the left sphenoid bone, extending beyond the pterion to involve the temporal squama, and medially almost to the optic canal. Left carotid angiography showed very little vascular displacement, but it was thought that the osteomatous area was denser in the capillary phase, indicating a rich capillary supply.

At operation on 24th June (Mr. J. Pennybacker), the hyperostotic bone was widely excised by drilling and rongeuring; the sphenoidal ridge and the lateral wall and roof of the orbit were removed, as far medially as the ethmoidal air cells, but the orbital margin and the optic canal were preserved. The dura was then opened, and a red velvety carpet of tumour was seen along the sphenoidal ridge; this was about 7-8 mm. thick, and could be stripped away from the arachnoid of the Sylvian fissure. The tumour and the affected dura were excised and a fascial repair was performed.

Histologically, the dural plaque was an endotheliomatous meningioma; in a limited study, it

showed no evidences of rapid growth, but there was invasion of the bone biopsies and of some fragments of temporal muscle.

This operation was considered by the surgeon to be a total removal, and could therefore have been placed in grade I. However, in the 1955 survey, it was placed in grade III, because post-operative radiographs (figure xxx,b) showed some residual hyperostosis.

Convalescence was smooth. As the patient was a known murderer, he was not reviewed in the out-patient department, but a report from the Superintendant of Broadmoor Asylum indicated that at least until October 1954 his tumour showed no signs of recurrence.

However in reply to enquiries made in the 1962 review, it was stated that he was then exhibiting a local orbital recurrence. Radiographs showed new hyperostotic bone formation in the frontal region, and probably also in the zygoma. (Figure xxx,c).

The implications of this case as an example of the slow growth of intraosseous meningioma are discussed in chapter VII. For the present purposes, it demonstrates how difficult it is to achieve anything better than a

grade III resection with the basal hyperostosing tumours; the osseous infiltration can be wider than the visible limits of the hyperostosis. Possibly operations performed earlier in the evolution of the disease might give curative resections : but the very slow progress of the condition makes most neurosurgeons unwilling to advise intervention until there is a substantial disability.

d. Subtemporal meningiomas.

The meningiomas arising from the dura of the floor of the middle fossa resemble in many respects the more common inner sphenoidal ridge tumours. Their relation to the middle cerebral artery is less intimate, but they have the same propensity to invade the cavernous sinus. They are also apt to invade the petrous bone (figure 1) and to penetrate, by this route or through the incisura, the posterior fossa.

There were eight tumours of this type in the Oxford series. Access, by a lateral craniotomy, was easy. Grade II resections were performed twice, and in the remaining six patients the surgeon accepted an incomplete removal or performed a simple decompression. Various reasons dictated these decisions, but the most

important was invasion of the cavernous sinus. Whether fortuitously, or for some anatomical or biological reason, the tumours treated by grade III or IV resections for this reason have recurred with unusual speed.

e. Suprasellar meningiomas. (Table VI).

Meningiomas arising from the dura over the planum sphenoidale, or posterior thereto from the diaphragma sellae, are well known to be favourable surgically, provided they are detected before they have reached a large size. (Figure xxxi, a). Very large tumours in this situation may be inoperable, by reason of intimate adhesions to the anterior cerebral arteries or to the hypothalamus. (Figure xxxi, b).

In the Oxford series, there were fourteen tumours of this type. Operative approach was by a frontal craniotomy, bifrontal in one case; in six patients, a partial frontal lobectomy was performed. Complete removal was thought to have been achieved in seven patients; in one of these the dural stalk was excised (gradeI) but in the others, grade II resections were performed. The difficulty of stripping the dura in this situation is evident, but it is clear that a truly radical ablation would demand this, and also the excision of the small

hyperostoses commonly present under these suprasellar tumours. (Such hyperostoses were demonstrable in radiographs in 40% of the Oxford cases). Such a bony excision would open the sphenoidal sinus, and risk subsequent infections. The suprasellar meningiomas seem commonly indolent in their growth, and grade II resections have in general been satisfactory.

In the other seven cases, grade IV resections were performed, usually because there was difficulty in freeing the tumour from the anterior cerebral arteries. This prudence has on the whole been justified: several of these incomplete resections have given many years of useful survival.

It was Cushing's hope and prediction that early diagnosis would bring these tumours to surgery when still small enough for easy excision. Experience at Adelaide shows that this expectation has been partially fulfilled. A macroscopically complete removal was effected in eight of ten cases: two of these had to be classed as grade III resections, because there were extradural hyperostoses not comprehended in the resection, but the other six were satisfactory grade II operations. In the remaining two, a grade IV excision was done. In one the residual tumour was a tiny nubbin lying dangerously near the optic

nerve, but in the other the residuum was substantial: it was very vascular, and appeared inoperable on this account. The tumour has rapidly recurred, despite radiotherapy, and is clearly an exception to the general innocence of suprasellar meningiomas.

Disability following these resections usually represents the irreversible effect of the tumour on the optic nerves, and here also earlier diagnosis has improved the results. In general, experience in Adelaide has suggested that ophthalmologists are increasingly aware of the significance of progressive optic atrophy, and cases have recently been presented with involvement of one eye only.

Table VI : Resections of suprasellar meningiomas (Oxford series)

Grade	Primary Operations	Operations on recurrent tumours
I	1	-
II	6	-
III	-	-
IV	7	-
V	-	-

Table VII : Resections of olfactory groove meningiomas (Oxford series)

Grade	Primary operations	Operations on recurrent tumours
I	-	-
II	6	-
III	1	-
IV	7	-
V	-	-

f. Olfactory groove meningiomas. (Table VII).

As is well known, these more anterior subfrontal tumours frequently reach great size, and inflict great damage, before they are diagnosed (Figure xxxii). Surgically, the main relation of danger is to the anterior cerebral arteries, which course over the posterior surface of the tumour in the manner so well seen in angiograms. (Figure xxxiii). The tumours of this group are usually bilateral; only two of those in the Oxford series were unilateral.

It is not surprising that a somewhat conservative policy was pursued with these tumours. No grade I resections were performed, doubtless from fear of

creating fistulae into the ethmoidal air cells or nasopharynx. If the tumour should have already penetrated these cavities, it would doubtless be proper to excise these extensions from the cranial cavity, and to perform an immediate fascial repair, as recommended by Pertuiset and Beciric (1955); the need arose in a recently witnessed operation, in which removal of a basal hyperostosis opened into the ethmoidal sinuses. Except under these circumstances grade II resections, with fulguration of the dura, seem satisfactory and were performed in six of the fourteen Oxford cases. One operation was considered to be in grade III, as there appeared to have been no extirpation of a large hyperostosis. Seven operations were grossly incomplete (grade IV resections).

Access was best obtained by a bifrontal osteoplastic flap, and to expose the tumour it was almost always necessary to ablate frontal cortex. In most cases, the tumours were found to be of great size, and operations were tedious. It was often necessary to divide the anterior extremity of the superior longitudinal sinus and falx before adequate exposure could be obtained. Such elaborate procedures imposed a considerable strain on the

patient and surgeon alike, and it is likely that some of the operations (especially those of twenty years ago) were discontinued because of this. Fear of injuring the anterior cerebral arteries was apparently less significant in dictating inoperability. These arteries are often protected by residues of cerebral tissue, and they are frequently less intimately applied to the tumour than the angiogram would suggest. The main nutrient artery of the olfactory groove meningioma is, indeed, very commonly the anterior ethmoidal artery. So it may be expected that, with contemporary supportive measures, these tumours may be removed completely, except when they exhibit massive basal invasion, as in the "olfacto-sellaire" tumours well described by Bonnal et al. (1961). These authors, who refer to my own earlier publication on this subject, regard basal invasion as the cause of rapid post-operative recurrence with such tumours; as will be seen in chapter VII, this has not been evident with the olfactory groove meningiomas in this series.

With such large lesions, it is not surprising that post-operative disability is often considerable. Six of the thirteen survivors in the Oxford series had severe or total disabilities, and two were moderately disabled.

It does not appear however that the operative procedure itself contributed much to this: the patients had already suffered severe damage to the frontal lobes and the optic nerves, and operative trauma does not seem greatly to have augmented this.

There is no reason to suppose that division of the anterior falx and sinus was in any way detrimental. The cortical ablations necessary in exposing the large subfrontal tumours may play some part in explaining the high incidence of post-operative epilepsy (see page 254), but too much should not be made of this: the tumours themselves, or more exactly the changes produced by them in the orbital cortex, constitute epileptogenic lesions.

g. Parasagittal meningiomas.

With these tumours, the problems of treatment come into sharp focus. Diagnosis is nowadays usually straight forward, and surgical exposure presents no insuperable difficulties. But radical excision is often extremely hazardous, and involves some surgical and pathological considerations which are still in part controversial.

The Oxford series comprises 79 parasagittal meningiomas, of which all save two came to operation. Table VIII shows that radical excision, with removal of the

dural attachment, (which of necessity entails either a partial or a complete excision of the superior longitudinal sinus) was performed in relatively few cases.

Table VIII : Resections of parasagittal meningiomas (Oxford series)

Grade	Primary operations	Operations on recurrent tumours
I	11	17*
II	51	5
III	4	1
IV	10	4
V	1	-

(* Grading doubtful in several cases)

In the small Adelaide series the same preponderance of grade II resections was also evident, there being eleven so graded in thirteen cases.

This conservative policy is of course dictated by the surgical anatomy of the parasagittal meningiomas. (See figures i & xxxv). By definition, they are related more or less intimately to the superior longitudinal sinus; in the Oxford series, this vessel is known to have been invaded in about 45% of cases. They are also,

though less attention has been given to this, commonly related to one or more of the important superior cerebral veins draining into the sinus. Finally, the larger parasagittal meningiomas, like the falcial tumours, may enter into relation with the pericallosal arteries. The cerebral cortex bordering the interhemispheric fissure includes much of the striate cortex, the paracentral lobule, and frontal and cingular cortical areas important in higher mental integration. A parasagittal meningioma will often cause a permanent unilateral lesion involving some part of the medial surface of one hemisphere. There is properly a strong reluctance to make this lesion bilateral by interference with the vascular supply of the opposite hemisphere.

The prime reason for performance of grade II resections in this series, as in other published reports, was reluctance to resect the superior longitudinal sinus. The hazards of this procedure have been much discussed. (Dandy, 1940; Jaeger, 1942 and 1951; Love and Gay, 1947; Kaplan, 1949; Meirowsky, 1953; Hoessly and Olivecrona, 1955; Lasierra, 1958). Unfortunately, it is often difficult to distinguish the effects of sinus resection from those directly resulting from the tumour or from the interruption of lesser venous channels. Further,

there are many variables: the individual venous anatomy, the state of the brain, and the general condition of the patient will all modify the results of sinus resection. This has not always been recognised in published reports (cf. Jaeger, 1951).

It is usual to consider the parsagittal meningiomas in three groups, according to their relation with the frontal, middle, or posterior thirds of the superior longitudinal sinus. In the Oxford series, the frontal and middle or paracentral groups were each about 40% of the whole, the posterior group being much smaller (less than 20%). Resections of portions of the frontal third of the superior longitudinal sinus were performed on ten occasions in the Oxford series, and twice in the Adelaide series. The immediate effects varied, and were sometimes quite alarming, as in the following case from my own practice.

Case Report.

R.J., a 44 year old aboriginal woman, was admitted to the Queen Elizabeth Hospital. She stated that for about nine years, she had been subject to headaches. For about five years, she had suffered occasional epileptic seizures: the description of these was imprecise, but they appeared

to have been grand mal convulsions with no focal signature. Neither she, nor her daughter, was aware of any change in mentality.

On examination, there were no neurological abnormalities save a dubious weakness of the right facial muscles. She was a pleasant, well-educated person, but her performance in mental tests suggested the possibility of some mental deterioration.

Plain radiographs showed a large ovoid mass of calcification in the posterior frontal region. (Figure xxxiv). The bulk lay left of the midline, though there was some of the tumour on the right side also. Bilateral carotid angiograms showed downward displacement of the anterior cerebral arteries, as by a falx tumour; no pathological vessels were demonstrated.

At operation, the tumour was exposed by bifrontal bone flaps. On the left, it was superficial in an area about 3 cms. long in the parasagittal region. The arachnoid adhered to the surface of the tumour, which was hard and nobbly. It proved to have a broad attachment to the falx, and was in contact with the superior longitudinal sinus, but did not appear to take primary origin from it. There was no

visible tumour on the right, but when the right frontal lobe was retracted a transfalcial extension about 2 cms. in diameter was disclosed.

After a tedious piecemeal dissection, the whole tumour, with its falcial attachment and a 3 cm. length of the superior longitudinal sinus, was removed. It was gritty, and too hard to be sucked away. The removal appeared complete, but a small part of the falcial attachment was left, after being heavily fulgurated. It must therefore be classed as a grade II operation, though of a very radical kind. Several frontal cortical veins had to be sacrificed.

Post-operatively the patient was at first well, but on the fourth day she became drowsy and lapsed into stupor. Re-exploration suggested that this was due to cerebral swelling, attributed to the interruption of the venous drainage of the frontal lobes. The bone flaps were removed, and an intravenous infusion of 30% urea was given.

Thereafter, she regained consciousness, but was at first shy and withdrawn. After her discharge she experienced considerably difficulty in obtaining employment, and it is possible that she may have

suffered more mental disturbance than appeared on superficial examination. The bone flaps were later replaced.

Histologically, this tumour appeared to be a very psammomatous endotheliomatous tumour. The falx was invaded, but not the walls of the superior longitudinal sinus, which was patent.

In this case, and in two others, the sinus is known to have been patent; in two more it may have been; in seven it was probably or certainly occluded. In all these frontal sinus resections, it is difficult to point to any permanent ill effects specifically due to the sinus resection. Only one patient in this group failed to recover reasonably completely, and as he was found at autopsy to have a cerebral abscess it is obviously impossible to attribute his post-operative dementia solely to the resection.

Operations involving sinus resection in the paracentral third were performed eight times, usually for recurrent tumours. In seven, the sinus was occluded, and in these the resection was apparently well tolerated. This is not to say that all made good recoveries: three did so, and one suffered only a mild paraparesis, but the other

three exhibited profound sensory and motor disabilities. These crippling residua can however be attributed to local brain damage: they were present before the sinus resection and there is no reason to suppose that they were perpetuated by it. In the eighth case the sinus was patent. This patient had a recurrent paracentral meningioma; his complex story is given as case 9, appendix C. It appears that the sinus resection was in this case detrimental: following it, the disability was greatly augmented and has been permanent, presumably from hemispheric infarction.

Only two resections of the posterior third of the sinus were performed, and in both the sinus was already occluded. The patients survived these procedures, and no special disabilities resulted from them; in particular, there have been no permanent bilateral occipital infarctions, though one patient did suffer a transient cortical blindness.

The implications of this small experience of sinus resection are discussed further in chapter IX. It is relevant here to emphasize that there were no deaths in the three series directly attributable to sinus resections. It is also relevant to note that the severe effects of bilateral paracentral lobule damage are not necessarily

obviated by sparing the sinus. Bilateral parasagittal meningiomas will inflict bilateral cerebral damage, and 25% of the tumours in the Oxford series were, or ultimately became, bilateral. One patient was rendered hemiplegic after a grade II resection on the right side: her tumour recurred on the left, and following a second grade II resection she was virtually triplegic (Case 21, appendix C; see page 237).

The decision to perform a grade II resection, with cauterisation of the attachment to falx and sinus, needs no further elaboration. It will be shown in Chapter VII that this procedure, though often successful, carries a high recurrence rate. Operations which left in situ an obviously invaded sinus, with gross palpable tumour, have been placed in grade III: there were only four, and in one of these the grading may be erroneous. Operations of grades IV and V can be briefly dismissed: most of them were done in the early years of the series, and were performed on patients with very extensive tumours, or under peculiarly unfavourable conditions.

It will be seen that the management of these cases was very largely governed by the patency of the sinus. This was assessed at operation. Radiological aids were little used. The finding, on plain films, of greatly

increased diploic vascular channels, coursing across the vault of the skull, does suggest a collateral circulation from an occluded sinus, as Lindgren (1954) suggested. But this is an unreliable guide. In 18 of the Oxford cases, such increased vascularity was noted, and in four of these the sinus was not involved by the tumour. Contrast sinography was not extensively employed. In the Oxford series, open sinograms (Ray et al., 1951) were not used; in the Adelaide series, one patient was so investigated, but the dye was unfortunately extravasated and caused severe status epilepticus. Demonstration of the sinus in ordinary three-exposure lateral percutaneous carotid angiograms was not found reliable though occasionally a convincing demonstration of an occluded sinus with adequate collateral circulation was given. More recently, in Oxford, the subtraction method of Ziedses des Plantes (1961) has been applied to phlebograms obtained in rapid serial changes of films. (See figure xxxvi). It seems probable that this will increase the reliability of sinography by percutaneous carotid injection, since it permits visualisation of sinuses otherwise obscured by the cranial vault.

h. Falx meningiomas.

These tumours, by Cushing's definition, do not encroach on the superior longitudinal sinus, and it is therefore possible to carry out a grade I resection without involving that sinus. This was in fact achieved in four of the five cases in the Oxford series, and three times in the Adelaide series. Such operations are nevertheless major undertakings. The falx meningiomas often enter into close relation with the pericallosal arteries, and furthermore their usually large size and deep situation add to the surgeon's difficulties. It is often necessary, in exposing them, to ablate the cortex covering the tumour, and to interrupt cortical veins draining into the superior longitudinal sinus. All these technical problems are illustrated by the following distressing case.

Case report.

G.G., a 58 year old hotel manageress, was admitted to the Queen Elizabeth Hospital on 1st Nov. 1960. She complained of lassitude, morning headaches, dysuria, and ataxic gait. The duration of these symptoms was uncertain, but was probably at least eighteen months.

On examination, she appeared euphoric and mildly demented; she had been incontinent of urine, but was not distressed thereby. Her speech was normal, but

she had some difficulty in constructional tests. There was early papilloedema. A suggestion of a lower left quadrantic homonymous field defect was obtained by simultaneous confrontation. There was a mild left spastic hemiparesis, including the face, and a disproportionately severe ataxia of gait. Position sense was impaired in the left great toe, and possibly in the right great toe. Tendon reflexes were all exaggerated, the left more than the right; the left plantar reflex was strongly extensor, the right less definitely so.

Plain radiographs were considered normal, though later examination showed mottled calcification in the right frontal region. A right carotid angiogram showed a mass in the posterior frontal region, with tumour vessels; the anterior cerebral artery was not well seen. A callosal glioma was diagnosed.

On 25th Nov., a right frontal osteoplastic craniotomy was carried out. A firm and lobulated sub-cortical tumour was found, and this was exposed by ablation of a circle of posterior frontal cortex. Partial extirpation was performed. The mass appeared to be bilateral, but further exploration was deferred until the histology was known.

This showed a meningioma, of fibroendotheliomatous type.

A left carotid angiogram was now performed, and this showed marked depression of both pericallosal arteries. (See figure xxxvii). The tumour vascularity was better defined. On 16th Dec,, I re-elevated the right frontal bone flap, and turned also a left frontal bone flap. It was then found that a large mass of tumour remained on the right side, extending lateral to the falx in an anteroposterior distance of 7 cms. or more. On the left side, there was a smaller mass, perhaps 4 cms. in diameter. The tumour attached to the falx over a surprisingly small area, perhaps 2 cms. in diameter; it had greatly depressed the corpus callosum which was indeed largely atrophied, so that at the end of the operation the third ventricle was clearly seen from above.

After a tedious operation, the tumour and its falcial origin were removed (grade I operation). The anterior cerebral arteries were preserved. Unhappily, the procedure proved too much for her. Following it, she was mute and exhibited a left hemiplegia. She slightly improved in the second week after operation, but then worsened, and developed hyper-

pyrexia during a heat wave, dying on 29th Dec.

Autopsy showed no residual tumour. The anterior cerebral arteries were patent.

There is usually no great difficulty in excising the falcial attachment once the tumour is removed, and since the inferior longitudinal sinus can be resected with impunity, there seems little warrant for electing to perform grade II resections. Only one such procedure was recorded in the Oxford series. The post-operative disability will depend on the cerebral damage done by the tumour, as well as on the operative injury to the overlying cortex, cortical veins, and anterior cerebral arteries.

Meningiomas of the falx are apt to become bilateral. Carotid angiography may demonstrate transfalcial spread, as in figure xxxvii. However if the transfalcial component is only a small button of tumour, it will not be evident in angiograms. It is an obvious merit of the grade I resection that such small residua are less likely to escape.

i. Falco-tentorial tumours.

Tumours having an attachment both to the falx and to the tentorium are rare. There were only two in the Oxford series. Surprisingly, Cushing (1938) reported twelve such tumours, designating them peritorcular; he admitted however that several may have been parasagittal. He justly observed that these are most formidable tumours. Guillaume et al.(1957) include them in their discussion of falx tumours, but this seems undesirable, for the surgical problems are different.

The falco-tentorial tumours will usually be adherent to the straight sinus. If they are situated posteriorly, they may involve the superior longitudinal sinus and the torcula; if more anteriorly, they may expand into the supra-pineal region, as was seen in an early Adelaide case (not included in this series), and enter into relation with the great vein of Galen.

With few cases, detailed discussion of surgical principles is impossible. It need only be noted that, in the two Oxford cases, no attempt was made to resect the sinuses. In one, these did not appear invaded; the tumour was completely removed, and its attachment coagulated. In the other, a very large tumour, the initial resection was grossly incomplete, but both the

superior longitudinal and the two transverse sinuses were opened and found to be obliterated with tumour. At a second operation for recurrence it was found that the straight sinus was also compromised. Such tumours must usually be admitted inoperable. The suprapineal meningiomas also present forbidding operative problems (cf. Suzuki et al., 1962) but may be managed by ventriculo-cisternostomy, as a palliative procedure.

j. Transverse sinus meningiomas.

Meningiomas arising from the tentorium, with or without attachment to the transverse sinus, may expand upwards as occipital masses, or downwards into the posterior fossa. In these three series, the latter behaviour was much commoner, and such tumours are given consideration below. There were however two cases, one in the Oxford series and one in the Adelaide series, which were wholly supratentorial, and in which the relation to the transverse sinus governed the surgical management. (See figure lii).

This sinus is usually considered to be resectable (Meirowsky, 1953; Castellano and Ruggiero, 1953). However, in the Adelaide case, a limited sinus resection was followed by catastrophic oedema of the occipital and parietal lobes, from which the patient never fully

recovered; she lived for some months, with gross disabilities, and then died of pneumonia. Autopsy showed severe atrophic changes in the affected region. This case is cited, not to contravene the general belief that the transverse sinus can be resected, but to emphasize that in occasional cases unpredictable venous thromboses may produce disastrous infarctions.

MacCarty (1961) in a brief account of the management of these tumours, has mentioned the very real dangers of a cranio-aural fistula. If the tumour shows evidence of extensive erosion of the petrous bone (as in the Oxford case depicted in figure lii), a grade I resection will be impossible, and it may be wise to spare the dura - or even to perform a dural fascial repair.

k. Posterior fossa meningiomas. (table IX).

This important group of meningiomas has received much attention, both from the diagnostic aspect (see page 56) and as problems in management (page 73). Although the material submitted here is concerned solely with the nature and results of operative treatment, diagnostic considerations cannot wholly be ignored, as in several cases they determined the issue.

The Oxford series comprised 27 tumours in this group.

They have been subdivided according to the method of Castellano and Ruggiero (1953):

1. Meningiomas of the cerebellar convexity : 1 case.
2. Meningiomas of the tentorium : 8 cases.
3. Meningiomas of the posterior surface of the petrous bone : 16 cases.
4. Meningiomas of the clivus : no cases.
5. Meningiomas of the foramen magnum : 2 cases.

The Adelaide series comprises only five cases, one tentorial and four posterior petrosal.

All these tumours came to operation, but one patient, an early Oxford case, was in fatal error explored by supra-tentorial craniotomy, and is excluded from further consideration. The operations are graded in table IX.

Table IX ; Resections of posterior fossa meningiomas (Oxford series).

Grade	Cerebellar convexity		Posterior Petrous		Tentorium		Foramen magnum	
	Primary	Recurrence	Primary	Recurrence	Primary	Recurrence	Primary	Recurrence
I	1	1	-	-	-	-	-	-
II	-	-	4	-	6	1	1	-
III	-	-	3	-	-	-	-	-
IV	-	-	5	5	1	-	1	1
V	-	-	3	-	1	-	-	-

This small series illustrates fairly well the scope and limitations of the surgery of posterior fossa meningiomas. However, in certain respects, the methods employed in these cases are likely to be modified in future operations.

Very little can be said of the single case of cerebellar convexity meningioma, initially treated by grade I resection. Such tumours are rare. The tentorial tumours were usually treated by grade II operations, and on the whole this has proved satisfactory. Evidently, however, the transverse sinuses may be involved, and their resection will then have to be undertaken, as with the supratentorial transverse sinus meningiomas briefly considered on page 169. This has been done with impunity by Olivecrona (Castellano and Ruggiero, 1953), by Le Beau, and by Clovis Vincent (Petit-Dutaillis and Daum, 1950); surprisingly, the problem is not mentioned by Markham et al. (1955) from the Lahey Clinic. With these tentorial tumours, surgical management is easier when there is fore-knowledge of the difficulties. The clinical picture is usually non-specific, and an exact preoperative diagnosis depends on radiography. D'Errico (1950) and Castellano and Ruggiero (1953) have emphasized the significance of an indentation of the vestibule and temporal horn of the lateral ventricle,

from upward displacement of the tentorium by a big subtentorial mass, or from perforation of the tentorium with a supratentorial extension. This should be looked for in ventriculograms of posterior fossa tumours; it is a real objection to myodil ventriculography that it will probably miss a supratentorial mass. In the Oxford series of eight tentorial meningiomas, this ventriculographic sign was evident in five cases, and definitely lacking in two. In the eighth, the supra-tentorial component of the tumour was very massive, and the infratentorial structures were not demonstrated in the ventriculogram. (Case 12, appendix C).

A standard suboccipital craniectomy performed in the prone position gives very inadequate access to a subtentorial meningioma, as was evident in one of my own operations; a second-stage resection in the sitting position, by Mr. T.A.R. Dinning, was infinitely easier. The sitting position was not routinely used in the period of these three series; even if it is, there is still great value in exact pre-operative diagnosis, as these tumours may requite supratentorial exploration. The present series does not contribute to the decision between Olivecrona's preference for staged supratentorial and infratentorial craniotomies (Castellano and Ruggiero, 1953), simultaneous exposure above and below the tentorium, as

suggested by D'Errico (1950) and MacCarty (1961), or trans-tentorial exploration from either above or below. It does show however that failure to perform the full exploration, either from above or below, may be disastrous. The patient mentioned above (Case 12, appendix C) underwent successful grade II resection of a supratentorial meningioma, whose dural attachment appeared innocuous, and was only fulgurated. She later died of an unsuspected subtentorial tumour. This indeed is the main criticism of grade II resections for tentorial tumours: they do not exclude trans-septal spread. (Figures xxxviii & li).

Table IX shows that posterior petrosal meningiomas present a gloomier picture. Figure xxxix shows the reason: intimate relation to the pons and the basilar artery - often very much more intimate than in this illustration. It is evidently impossible to perform radical procedures of grade I with deep tumours in this situation; complete naked eye removals will often be impossible, and it may be necessary to accept a subtotal resection. In the confined space of the cerebellopontine angle however a recurrence will declare itself relatively soon, and the palliation given by such a procedure may be brief. Moreover, as table IX shows, reoperation is still less likely to be successful.

It must however be noted that the superficial posterior petrosal tumours are more readily dealt with, and it is possible that with these a radical excision (with resection of the sigmoid sinus) may sometimes be both desirable and possible. Probably such a procedure should have been attempted in the following case from my own practice: the grade II resection actually performed may well be followed by a recurrence, especially in view of the cytology of the tumour.

Case Report.

D.R., aged 39, was referred privately by Dr. R.H.C. Rischbieth. She gave a poor history, but it appeared that she had had headaches for a very long time. Since the birth of her last child two years ago, these headaches had been more severe, and were especially so after defaecation. She had also become a little unsteady, and had given up such sports as tennis and tap dancing. She had recently complained of right sided tinnitus. She exhibited nystagmus, most marked to the left, but very little ataxy. Caloric tests of vestibular function showed a directional preponderance to the left. There were no other neurological or otological abnormalities.

Plain skull radiographs showed porosis of the dorsum sellae, but nothing else of note.

On April 2nd, 1962 a ventriculogram was performed. This showed internal hydrocephalus, with obstruction, not quite complete, of the aqueduct, which was kinked forward. A little air escaped into the cerebellar vallecula, which was displaced to the left.

A posterior fossa exploration, employing a curved horse shoe incision and bi-occipital craniectomy with atlas laminectomy, was performed. The cerebellar tonsils were displaced into the spinal canal, the right to a greater degree. The right cerebellar hemisphere was obviously swollen; a cortical incision exposed a large circumscribed tumour which was found to extend laterally. Eventually, after a prolonged dissection, it was found to be a typical meningioma of the lateral recess, attached to the dura over the posterior surface of the petrous bone, the sigmoid sinus, and the tentorium, in an area perhaps 3 cms. in diameter. It indented the lateral surface of the cerebellum, and no doubt also the middle cerebellar peduncle, but did not abut on the lower cranial nerves which indeed were not exposed. (See figure xl)

An apparently complete removal was effected, with

these reservations: the arachnoid capsule over the deep surface of the tumour may have contained small residues, and the dural attachment was not excised. The dural attachment was carefully fulgurated however, and it was considered that an operation of grade II had been effected. (Figure xl).

The patient made a smooth convalescence, though somewhat troubled by a right haemotympanum. This resulted from an inadvertent breach into the mastoid air cells: the hole had been closed with a muscle graft, but blood collected in the middle ear nevertheless.

Histologically the tumour was a fibro-endotheliomatous meningioma, with a few mitoses suggesting a relatively rapid growth rate.

The three series contain no clivus meningiomas. Olivecrona's experience suggests that the diagnosis of these terrible tumours is best effected by lumbar encephalography and vertebral arteriography; since they are essentially inoperable, it is very desirable that this should be done, but decompression and biopsy will probably also be needed, as a guide to decision on the propriety of radiation.

Of the foramen magnum meningiomas, there is little to be said. If they lie posteriorly, their dural attachment

can be resected, but in the two Oxford cases, the tumours lay anteriorly, and as MacCarty (1961) has noted, even fulguration (Grade II procedure) may be dangerous here, because of the proximity of the medulla and other vital structures. It is not surprising that the single grade II operation in this series was in fact followed by a recurrence.

Some degree of disability following excision of posterior fossa meningiomas is not rare. Operative damage to the cranial nerves, the cerebellum, and the side of the pons may contribute to this, and ais of course to be avoided as far as possible. But there is not, as there is with parasagittal and sphenoidal ridge meningiomas, a great risk that radical excision will entail survival in a state of severe disability: the risk is rather that the patient will not survive at all.

1. Intraventricular meningiomas.

As noted on page 56, these interesting tumours have received much attention in recent years. The Oxford series contains four lateral ventricle meningiomas, one of which was not explored: there were none in the Adelaide series, but the London series contains two examples, both quite instructive.

In three of these six cases, total removal was

effected by a transcortical approach. These operations could be classed as grade I resections, since the attachment of the tumour - the choroidal plexus - was also excised. The procedure entails an incision in the temporal or parietal cortex, and as all three tumours were on the dominant side, this inflicted, besides a hemianopia, a variable amount of dyslexia and dysphasia. In one patient, a young girl, these recovered, and when reviewed twenty-eight years later she had no disability. In the other two, troublesome focal epilepsy persisted, with some degree of intellectual impairment.

From a desire to avoid or delay these, and in the knowledge that the intraventricular meningiomas are usually very indolent fibroblastic tumours, two patients were treated by simple decompression. One later died after radical operation, from a second, contralateral, unsuspected meningioma. The other died chiefly from unrelieved intracranial pressure. A further criticism of the procedure comes from a later case, not included in these series (figure xli): here decompression was followed by fatal intraventricular bleeding. It seems therefore that the unpleasant effects of the transcortical procedure must be accepted, except perhaps when the tumour is of small size, yet productive of symptoms by intermittent block of the

temporal horn (Pennybacker, 1962).

m. Orbital meningiomas.

Within the orbit, the meningioma is an extremely infiltrative tumour (figure iv). This has been emphasized by Forrest (1949), who depicts invasion of the extra-ocular muscles, the optic nerve, and even the retina. On the other hand the growth of these invasive orbital meningiomas is commonly very slow, as the Oxford material illustrates; one patient underwent an incomplete removal more than seventeen years ago, and still has so little disability, or deformity, that she is able to undertake major parts as a film actress.

Orbital meningiomas may be primary or secondary. The latter represent invasion of the orbit by intracranial meningiomas, chiefly those of the sphenoidal ridge: in the Oxford material, at least seven sphenoidal ridge meningiomas invaded the orbit (see figure xxviii). As Van Buren et al. (1957) note, such secondary intraorbital meningiomas are commoner than meningiomas arising primarily in the orbit whether from the sheath of the optic nerve, or (as postulated by Craig and Gogela, 1949) from ectopic arachnoidal nests in the orbital tissues. However, primary orbital meningiomas are not rare. There were four in the Oxford series. One certainly arose from the

sheath of the optic nerve. The other three apparently did not; they may have arisen from the intracranial dura, but no such connection was found in careful operative explorations and it is possible that they arose from extradural arachnoidal rests. Both the London and the Adelaide series contain single examples of orbital meningiomas, and these probably did arise from the optic nerve itself. The distinction is important, because the tumours directly involving the optic nerve are much more difficult to remove completely, unless of course it is permissible to resect the nerve en bloc. When all vision is lost, such a resection is proper. When visual loss is of less degree, it may be prudent to accept a partial removal. The following tragic case illustrates both the difficulty of removing these tumours completely, and also their well known tendency to bilateral origin (Craig and Gogela 1950).

Case report.

K.C., a little girl then aged 3½, was first admitted to the Adelaide Children's Hospital on October 29th, 1954, because of painless progressive proptosis of the left eye, evident over the previous six months.

Examination showed straight forward left proptosis of about 5 millimetres. The optic disc was obscured by a cataract, and vision could not be tested. Skull radiographs were normal.

At operation (Mr. T.A.R. Dinning), on November 7th, 1954, the left orbit was exposed by a small trans-frontal craniotomy. When the left frontal lobe was elevated, a minute fringe of meningiomatous tissue was seen enveloping the left optic nerve as it emerged from the optic foramen. The bony roof and lateral wall of the orbit were rongeured away, and the optic canal was unroofed. When the orbital periosteum was incised, a firm tumour was found, encircling the globe in its whole intraorbital course, up to a millimetre or so posterior to the globe. It appeared to infiltrate the surrounding orbital tissues. It proved impossible to dissect it from the optic nerve, and it was necessary to excise a portion of the nerve with the tumour.

Histologically, the tumour was a cellular endotheliomatous meningioma, with numerous spherules.

Post-operatively, the child developed panophthalmitis and the left globe was eviscerated. Thereafter, she made a smooth recovery, and remained

well for the next three years. Her story, to this stage, was published by Dinning (1956).

In December, 1958 however she admitted to failing vision in her only eye. By the time this was confirmed, her vision was reduced to counting fingers, and there was definite optic atrophy. Skull radiographs were still unhelpful.

At operation (D.A.S.) on January 8th, 1959, the right optic nerve was exposed, and it was noted that on its right side there was a little fringe of tumour. The right orbit was therefore explored. A hard fibrous tumour was found, adherent to the optic nerve, which was kinked sharply around it. (Figure xlii). The tumour was removed, apparently completely, with preservation of the optic nerve; however there was brisk bleeding during this, probably from the ophthalmic artery.

Histologically, this second, independent tumour closely resembled the first: it was a psammomatous endotheliomatous meningioma with invasive tendencies. Very strikingly, it was seen to be invading a ganglion which can only have been the ciliary ganglion (figure iv).

Post-operatively, the child was quite blind. In other respects, she remained well until very

recently, when she presented with signs of a cervical cord tumour. This was removed, and found to be a meningioma, presumably an independent primary growth. (Mr. T.A.R. Dinning).

In the three series, there were six cases with seven tumours. Apparently complete ablations were performed on five occasions: in four (all optic nerve meningiomas) this entailed total loss of vision in the affected eye, but otherwise the results were satisfactory. In the fifth, the tumour apparently arose in the roof of the orbit, without detectable relation either to the intracranial meninges or to the optic nerve. It has recurred repeatedly, despite two seemingly complete ablations.

On two occasions partial removals were performed, and both patients have remained well, with no overt recurrences, for sixteen and seventeen years.

CHAPTER VI

MORTALITY

The statistics of the frequency and causes of post-operative death in these three series do not reveal anything very unexpected. They require brief consideration however, because they put the results obtained in patients surviving operation in a proper perspective. They are also of value in bringing to light some causes of mortality not always evident in published reports. Thus, McKissock's record of seven post-operative deaths in 120 operations for supra-tentorial meningioma (McKissock and Taylor, 1960) sets a superb standard in surgical and anaesthetic management: it is not, nor does it claim to be, a figure for the whole mortality from meningiomas. Similarly, Guillaume et al. (1957) state that only two deaths in seventy recent cases were directly imputable to operation (3%). They state that this creditable figure expresses the curability of the meningiomas ("Ce chiffre exprime assez les possibilités de guérison actuelle des méningiomes".) In reality, however, six other patients in their series also died for various reasons less directly concerned with their operations, giving a gross mortality of more than 10%.

In the London series, 28 patients died within six months

of primary operations. This gives a case mortality of 29%, in a somewhat selected material. It will be admitted that this was a notable achievement in the decade 1928 - 1938. However, the problems, and the resources, of the neurosurgeon have changed considerably since this series was collected, and in a study of the causes of death it is now only of historical interest.

The Oxford series also, to some extent, includes cases treated under conditions less favourable than those of today. This was especially true during the War years, when diagnosis was often delayed, and treatment occasionally performed in adverse circumstances. However, most of the problems exhibited in this series are still very familiar.

Of the 246 patients with intracranial and orbital tumours in this series, 32 died within six months of initial operation or diagnostic procedure. One patient died of a coronary occlusion four months after operation, and can be excluded; the remaining 31 give a case mortality of about 12%. (The slightly different figures given in appendix A represent the exclusion of seven patients who for various reasons did not undergo surgical treatment of their meningiomas and four patients with orbital tumours). The arbitrary period of six months as a term for post-operative deaths was selected because it happens to comprehend the

survival periods of several patients who lingered in a vegetative state for some time after operation. To exclude these patients would be somewhat unrealistic, especially as one of them died of a wound infection.

The mortality for operations on recurrent tumours was naturally greater. There were 48 procedures of this type, and twelve patients died within six months of such operations: a case mortality for recurrent tumours of 25%.

It was hoped that the Adelaide series would show an improvement on these figures. Unhappily, this is not so. Of 45 patients operated on, six died after the initial procedure, and one after an operation for suspected recurrence: the case mortality, excluding recurrences, is therefore about 13%.

The surgical considerations presented in the previous chapter make it obvious that the mortality rate will vary with the different regional groups. Table X gives the statistics, as percentages, for the Oxford and Adelaide series; regional groups have been combined to give more significant numbers, and small groups have been excluded.

Table X : Operative mortality % in regional groups (Oxford and Adelaide series).

Regional groups	Primary ops.	Ops. for recurrence
Parasagittal (+ falx, falco-tentorial and transverse sinus)	11%	20%
Convexity	11%	(4 cases : no deaths)
Sphenoidal ridge & subtemporal	20%	25%
Suprasellar & Olfactory groove	8%	(1 case : one death)
Posterior fossa	20%	44%

From this table, it is evident that regional factors - especially the arterial relations of basal meningiomas - influence mortality. It is also evident however that general factors are of great importance, as appears from the considerable death rate with convexity tumours, of all meningiomas the most operable.

Many circumstances determine these distressingly high mortality rates. Some are hard to assess : late diagnosis, for example, to which writers such as Tönnis (1953) give great attention, is easier to accuse in particular cases

than to demonstrate in the entire series. Table XI gives the main causes of death in the combined Oxford and Adelaide series, which together give a total of 50 deaths. These figures are given with some hesitation, because in several ways their accuracy is dubious. First, in 7 cases the diagnosis was not verified by autopsy. Second, and more fundamental, it is in some cases exceedingly difficult to know which of several lethal factors was most important. This is chiefly a problem where patients have died of extracranial causes, pulmonary, cardiac, or renal, while still in stupor; it is difficult to know what importance to attach to the complication, and most of these have been listed as deaths from brain damage. This seems proper, because autopsy in such patients has always shown cerebral disturbances, chiefly brainstem haemorrhages and other effects of trans-tentorial herniation. Unrelieved, or irrevocable, internal cerebral displacements were also terminal findings in several other patients whose deaths are attributed to other, more proximate causes in table XI.

Table XI : Post-operative mortality (Adelaide and Oxford series).

	Deaths after :-	
Causes of death	(i) Primary Operations	(ii) Operations on recurrent tumours
Operative haemorrhage	2	1
Post-operative haematoma	2	-
Infection	3	1
Inadequate decompression	5	3
Infarction from ligation of major artery	7	1
Brain damage, cerebral oedema, and complications of coma	10	4
Miscellaneous (cardiac & renal failure, unknown cause etc.)	2	3
Diagnostic error	6	-
DEATHS FROM ALL CAUSES	37	13

The deaths from operative haemorrhage include two from the early phase of the Oxford series; the third was an extremely vascular recurrent meningioma high in the

cerebellopontine angle, and operative blood loss was only a part cause of her death.

The deaths from post-operative bleeding do not represent extradural haematoma formation. Both were intracerebral clots. Extradural haematoma necessitated re-exploration on a number of occasions, but was never a main cause of death.

Post-operative infection is shown to be a serious hazard; furthermore, in addition to the four fatalities, there were at least 13 severe but not fatal post-operative wound infections. These included eight cases of osteitis of the bone flap. Four of these infections took place in the last four years of the Oxford series, and two occurred at Adelaide: wound infection, it needs no emphasis, is still with us.

The deaths listed as due to inadequate decompression occurred mainly in patients presenting in the early years, under very adverse conditions; the group includes also some deep-seated lesions found to be virtually inoperable. The eight deaths due to infarction from ligation of a major artery represent an altogether unsolved problem. These were mostly inner sphenoidal or suprasellar meningiomas involving the internal carotid artery and its main branches; there was also a foramen magnum meningioma involving the

vertebral artery. The pathological basis of these catastrophes has been discussed at length on page 95 ; it must be again emphasized that intimate arterial relations also accounted for many incomplete resections. There is no reason to suppose that hypothermia, as now used, will reduce the effect of these arterial disasters; in fact, it was found not to do so in the experience of McKissock and Taylor (1960), and in the single case in the Adelaide material so treated.

The 14 deaths classed as due to <u>brain damage</u> are a heterogeneous group. Three resulted from brain stem thrombosis or oedema suffered during the removal of posterior fossa meningiomas; the others occurred after the resection of supratentorial tumours, and are not easily classified. They occurred mainly in patients whose initial state was bad or where the operation was especially difficult: the case described on page 164 is an example. One patient was actually admitted in coma. In all, the patients never fully recovered after operation, and died after more or less prolonged periods in hospital, chiefly of the respiratory complications of coma.* It is in this group, presumably, and in the group classed as deaths from inadequate decompression, that earlier diagnosis might have been beneficial. One can imagine

* See page 189.

that, had the tumours been smaller or the patients in better shape, the issues would have been otherwise. The patient whose tumour is shown in figure xxvi had spent several years in a mental hospital, during which period the presence of a space-occupying lesion was repeatedly suggested by a neurologist. It is nevertheless necessary to keep a sense of proportion about early diagnosis: however alert the physician is - and experience in South Australia has shown a flattering, indeed embarrassing, awareness of the value of early surgery - there will always be cases of meningioma arriving in bad shape. One reason is the frequency of this tumour in old age. In these series, three patients presented over the age of seventy. (Two of these survived major operation - a patient with a petrosal meningioma treated by Mr. J.M. Potter in Oxford, and a case of parasagittal meningioma of my own). Another reason is the occasional presentation with a subacute or even apoplectic onset, from regional infarction. Finally it must be remembered that in certain situations, meningiomas may reach a great size before causing any symptoms at all.

The last group, deaths from <u>diagnostic error</u>, are of course pre-eminently the avoidable deaths. All were in the Oxford series, and all occurred in the early years,

before angiography was widely used, and at a time when perhaps the possible errors in diagnosis by aspiration biopsy were less evident than they are today. Four deaths were in fact the result of misinterpretation of biopsies taken from the gliotic or necrotic periphery of the tumour. Nevertheless, recent experience (El-Banhawy and Sheldon, 1962) shows that diagnostic errors of this kind can still occur. As Kepes and Kernohan (1959) have urged, it is also possible to make diagnostic errors when the biopsy actually comes from the meningioma itself; this nearly occurred with a biopsy examined by me in the Adelaide series, because the tumour, an osteolytic meningioma, simulated a metastasis both clinically and histologically.

Those post-operative deaths do not comprehend the whole mortality. In the next chapter, the frequency of recurrence is discussed: many patients die from recurrent tumours. A few also die from other complications, notably epilepsy. Taking all causes of death, it can be stated that of the 246 cases in the Oxford series, at least 65 - 26% - have died of their meningiomas. We are still a long way from Guillaume's (1957) estimate of the curability of this disease.

CHAPTER VII

SURVIVAL AND RECURRENCE

Frequency.

As preliminary review of the literature has shown, the tendency of meningiomas to recur after operation is often ignored, and there is no unanimity on its frequency or causes. Study of these has therefore been a prime motive for the two surveys reported here.

For the analysis of the frequency of delayed recurrence, 266 cases have been found suitable. These are patients who underwent resection of intracranial meningiomas, or rarely decompression, and who survived for periods exceeding six months. The greater number (206) are from the Oxford series; they were reviewed in 1955 and again in 1962 (see chapter III) and the survival periods of those still living range between seven and twenty-three years. The remainder (60) are from the London series, and were fully reviewed in 1955 only; their survival periods are from seventeen to twenty-six years, or until death. In a few cases, however, longer survivals were confirmed in 1962.

The results of the first analysis of this material were reported in 1957, and are submitted here as

appendix A. The conclusions given in this report still seem largely valid. However in the intervening years a number of additional recurrences have declared themselves, and the figures published in the earlier paper require revision. It also appears that several opinions expressed there require modification. (In addition, there are some minor changes in the statistical material. One patient, excluded from the first report because of an inadequate follow-up, can now be included. Four operation gradings have been reclassified, and several alterations have been made in the composition of tables; these are indicated in the text).

For the present purpose, the term recurrence must be used in its clinical sense, to mean the reappearance of symptoms due to the growth of the tumour after a period of freedom. In this sense, there have been 69 recurrences following primary operations; in eleven patients, repeated recurrences took place. Fifty-eight were in the Oxford series and eleven in the London series. Verification at autopsy or operation was obtained in 49 cases. In 20, the diagnosis of recurrence stands on clinical grounds: either the patients have died without autopsy, or they are still living but for diverse reasons have not undergone operation. In the

first circumstance, the opinion of the physician certifying death has been accepted: in most cases, there is corroborative evidence, but in four instances it must be said that the diagnosis is dubious. In the three patients still living, the clinical and radiological diagnosis seems certain in one and rather probable in the other two. To offset these few possibly wrong diagnoses, it seems likely that several other patients certified as dying of intercurrent disease did in fact succumb to recurrent tumours.

Thus, in the combined Oxford and London series, the incidence of recurrence reaches the high figure of 26%, and it will presumably rise a little higher with the further passage of years. However, these recurrences do not all carry an equal significance: by no means all followed seemingly complete ablations.

Applying the system of grading described in chapter V, it is found that nine recurrences developed after primary operations of grade I. There have been six additional recurrences after grade I resections of tumours already recurrent after earlier operations. The combined series provide 105 operations of this grade, in which the surgeon has considered that the entire tumour, with its dural or choroidal attachment and any visible

extensions, has been completely excised. Of these 81 were primary operations and 24 were operations for recurrence. So, after this ideal resection, the incidence of recurrence is 11% for primary operations, and 15% if recurrent tumours are included as separate cases.

Operations of grade II, complete ablations with thermal coagulation of the dural attachment, were performed 110 times as primary procedures, and on nine occasions for recurrence. (All these figures exclude patients dying within six months of operation). After primary operations of this grade, there have been 21 recurrences, three of them unverified; there have also been three examples of repeated recurrence after similar operations performed on recurrent tumours.

The incidence of recurrence after primary operations is thus 19%; with the inclusion of secondary recurrences, it is 20%.

Table XII shows the regional distribution of tumours recurrent after primary operations of grades I and II. Percentages in relation to the total number of patients surviving in each group are also given where the numbers are large enough to have some value. Operations on repeatedly recurrent tumours are not included.

Table XII : Recurrences after primary operations of grades I and II (Oxford and London series).

Regional Groups.	Grade I ops.		Grade II ops.	
	No. recurrences	% incidence	No. recurrences	% incidence
Parasagittal falx falco-tentorial & transverse sinus	2	12½%	16	25%
Convexity	4	7%	0	*
Olfactory groove & suprasellar	0	*	1	6%
Sphenoidal ridge & subtemporal	2	*	2	20%
Posterior fossa	1	*	2	20%
TOTALS	9	11%	21	19%

* In these categories, the number of operations performed was very small.

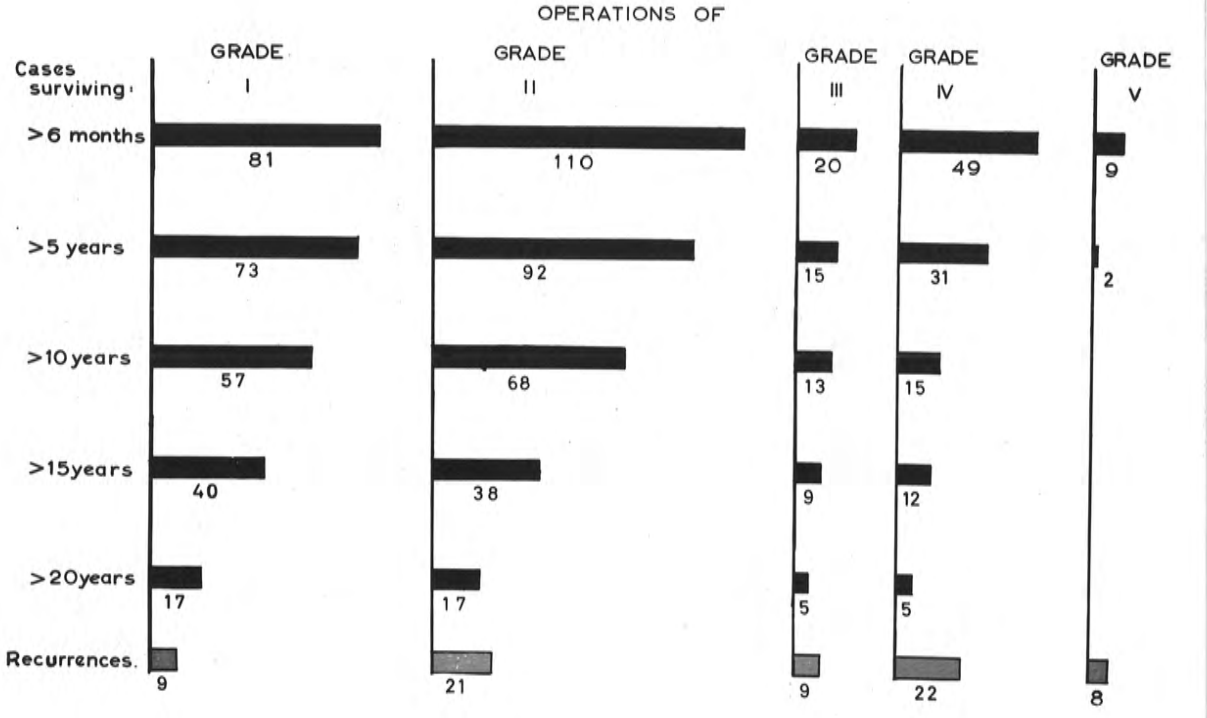
It will be seen that recurrences have occurred in almost every situation; even the convexity tumours, rightly considered the most favourable group, have occasionally recurred. The table shows a relatively high incidence of recurrence by parasagittal tumours, and a relatively

low incidence in the subfrontal situation; reasons for this are discussed below.

These figures indicate a substantial and disconcerting incidence of recurrence after operations which appeared to the surgeon to be complete ablations. The long periods of latency before the recurrence becomes manifest probably explain why some writers (Grant, 1947 and 1954; Peters, 1951; Guillaume et al., 1957) have minimised, or even dismissed, the possibility of ultimate recurrence.

Since such seemingly adequate operations carry this incidence of recurrence, it is to be expected that operations known to be in varying degrees incomplete have a considerably higher recurrence rate. It is however of interest to note that such recurrences are often long delayed: subtotal resections often give very worthwhile palliation. The duration of the palliation is governed by surgical and pathological factors which, as will be shown, can to some extent be estimated for prognostic purposes.

TABLE XIII



Histogram showing survival periods and recurrences according to operative grading (Oxford & London series). This table is not exactly comparable with figure 1 in appendix A, as it does not include operations for recurrence as separate cases. Inclusion of such cases in the histogram originally published was critidsed from a statistical viewpoint, because they had been followed for relatively short periods. Table XIII also of course includes the results of the 1962 survey.

In the combined Oxford and London series, there were 20 patients who had primary operations of grade III, the resections being so categorised because they left in situ, and untreated, some hyperostotic bone, or an obviously invaded dural sinus or other extradural extension. (It is not always easy to tell when this occurred; review of the cases originally placed in grade III suggests that in several the ablation may in fact have been complete, and three have been regraded). There have been at least nine recurrences, six of them verified, in this group (45%). But as table XIII shows, there have also been some very long survivals after operations of this type. These are chiefly patients with hyperostosing meningiomas en plaque, seven of whom have survived ten years or more, despite the known presence of hyperostotic residua. One, indeed, is still alive and regards herself as very well twenty-two years after such a tumour was incompletely excised. The patient described on page 144 illustrates the natural history of such tumours: he has in fact a clinical and radiological recurrence, but it has taken fourteen years to become apparent and is still far from crippling him. Cases such as this rebut the contention that operation accelerates the growth of basal meningiomas (Castellano

et al., 1952).

Where the intradural component of the meningioma was not wholly removed, it is to be expected that a symptomatic recurrence will eventually become manifest. This has indeed occurred after 22 of the 49 operations of grade IV (45%). It is very likely that others would also have developed recurrences had they lived longer: death from intercurrent infection was common in this group. Nevertheless there have been some remarkably long survivals after incomplete resections. As table XIII shows, twelve patients have lived for more than fifteen years after resections known to have been incomplete. One of them developed a recurrence, which was successfully removed, nineteen years after subtotal resection of a large convexity meningioma. Histologically this was of endotheliomatous type, and the cytology suggested a growth rate of average degree. Two others had had basal tumours incompletely excised in 1933. Both died, one by accident in 1951 and one by suicide in 1955. Autopsy in both cases showed the presence of residual tumour, which however in these prolonged periods of latency had not come to demand treatment.

Unfortunately, such happy palliations are not always achieved by grade IV resections. More than half of the

recurrences caused death or necessitated reoperation less than six years after the primary operation, and some of these gave much shorter periods of symptomatic freedom, the patients being profoundly disabled some time before their deaths.

Even the operation of simple decompression (operation of grade V) may under some conditions give a useful palliation. Nine patients survived operations of this kind. All have either died or come to more adequate operations, but it is interesting to find that two of them obtained considerable periods of symptomatic relief, for seven and nine years respectively.

Finally, in any consideration of survival after operative treatment, it is necessary to keep in mind the natural history of the disease untreated. The Oxford series includes eight cases of verified meningioma not treated by any operative procedure likely to be remedial. Six of these died soon after exploratory procedures of various kinds and one two years after a course of radiotherapy. One, however, an old lady with a small sphenoidal ridge meningioma diagnosed by air encephalography twenty-one years ago and by aspiration biopsy ten years ago, is still living, cherished for many years by a butler but latterly by a geriatrician. Moreover, there

is record of four other patients with radiologically visible tumours, two being calcified globular masses within the skull and two hyperostosing tumours of the sphenoidal ridge, who never came to operation. These patients (who of course are not included in the series) probably harboured meningiomas, but they nevertheless survived in fair health for many years and two of them are living yet. Such very indolent lesions are of course unusual, but it must be kept in mind that they do occur. Operation was withheld in these cases because the surgeon was convinced that the radiological appearances betokened very slow growth, and because the symptoms did not include those of raised intracranial pressure. Events have justified this policy.

Causes.

Recurrence can be considered from two view-points. It may be regarded as the expression of an intrinsic malignancy; it may also be seen as the consequence of an insufficient resection. These concepts are of course not mutually exclusive. Even a highly malignant meningioma could presumably be cured by wide resection, unless it had metastasized, and this has been seen to be a very rare event. Conversely, even a highly benign meningioma may ultimately recur if resection has been inadequate. However, in considering the causes of recurrence, it is of great practical importance to determine what proportion of the recurrent tumours are malignant growths incurable by any acceptable surgical ablation, and what proportion represent avoidable failures in the application of standard methods of treatment. For this purpose, the verified recurrences in the Oxford series, and chiefly those recurrent after seemingly complete ablations (grades I and II), have been reviewed.

The inutility of histodifferentiation as a guide to biological behaviour has been discussed on page[111], and is demonstrated in table XIV. It may be reiterated that the angioblastic forms, as here recognised, have not shown the unfavourable character often attributed

to them. On the other hand, the limited but definite prognostic value of cytological studies, emphasized on page 117, is supported by tableXV. (See also p. 216)

Table XIV : Histological type and recurrence (ops. of grades I & II : Oxford series).

Histological type	Number of recurrent tumours
Endotheliomatous	12
Fibroendotheliomatous	6
Fibroblastic	3
Angioblastic	0*
Undifferentiated	3
Unclassifiable	1

* One tumour classed as endotheliomatous had angioblastic tendencies also.

Table XV : Growth rate and recurrence (same material).

Assessment of cellular activity	Number of recurrent tumours
High	9
Average	13
Low	2
Uncertain	1

It would be wrong to place too much weight on these cytological studies. As observed earlier, it is possible that, in a few instances, the knowledge that the tumour had already recurred may have biased the interpretation. It is however important that four of the tumours considered to be of high cellular activity had all the cytological features of malignancy, and several others showed suspicious features. But in more than half the recurrences, the microscopic appearances, even in retrospect, do not show anything very remarkable. This material therefore does not support the belief, explicitly stated by Guillaume et al. (1957: p.147) that one can be assured of the definitive cure of meningiomas unless their histological character is unfavourable.

A different view of recurrence is obtained if one considers the circumstances under which recurrence actually took place. The findings at re-operation or autopsy frequently make it quite clear where and how the recurrence developed.

In the Oxford series, 25 patients suffered verified recurrence of tumours which had appeared completely removed. Nine of these patients suffered repeated recurrence, and counting each separate clinical recurrence,

one can say that the material offers 35 recurrences for analysis (Table XVI).

It will be seen that the largest number of recurrences have arisen from invaded dural structures - the walls of the superior longitudinal sinus, the falx, the tentorium, or the dura over the base of the skull. Either the tumour had infiltrated the dura beyond the limits of a grade I resection, and this probably happened twice, or the tumour recurred because the destructive effect of diathermy coagulation had been inadequate. There were apparently nineteen local recurrences in dura after grade II resections. Evidently, the tumour escaped because it was within the lumen of a great venous sinus, (cf. figure i) or because it had extended across a free dural septum, (cf. figure ii) or because the local effect of thermal coagulation was insufficient even in the immediate vicinity of the tumour. On the whole, the last explanation does not often appear valid; it seems that the diathermy is usually effective when applied to the dural attachment itself. (The most notable failure was in the excision of a foramen magnum meningioma, which recurred after a grade II operation: it is easy to see why in that situation the operator had to limit his use of fulguration. It is however abundantly clear that the

Table XVI : Probable sites of recurrence (Oxford series)

Origin of recurrence (main mass only)	No. recurrences
Invaded dura (including walls of dural sinuses)	21
Invaded bone	2
Orbital recurrence	1
Cerebral and leptomeningeal recurrences (including presumed cerebral implant metastases)	7
Uncertain	3
Extracranial metastasis	1*
TOTAL	35

diathermy will not sterilise even small buds of tumour in the lumen of a venous sinus, or on the further side of a dural septum.

The table also shows how uncommon recurrence from invaded bone is. It does not appear that the incidence

* In two other patients, metastases were found at autopsy, but case 17 (appendix C) is the only instance of fatal metastatic spread.

of recurrence would fall markedly if, for example, bone flaps were routinely removed and boiled, or replaced by prostheses. Invasion of the skull base is often inoperable, and may give rise to recurrence (Figures 1 and liii). Nevertheless, the growth of meningioma in bone is usually most indolent, as experience with grade III resections shows. When osseous recurrence does fungate into the cranial cavity, it can be very troublesome and may be very extensive. Figure viii shows the ultimate consequences of a grade III resection for sphenoidal ridge tumour en plaque: seventeen years later the patient came to autopsy after suicide and was found to have massive basal recurrences extending into the posterior fossa and invading the cerebellum.

Extracranial spread into the orbital, nasal, and tympanic cavities may lead to recurrence. There was in this series only one example of an intraorbital recurrence after seemingly complete ablation (Grade I) : figure liii shows the circumstances under which this took place.* Other intraorbital recurrences followed grade III resections, and an intratympanic recurrence was seen in a patient treated by decompression and radiotherapy.

Since dural and extradural invasion is common even

* Case 2, appendix C.

with the most benign meningiomas, it cannot be said that atypical patterns of growth explain the majority of recurrences. The seven examples of recurrence arising from vestiges in brain or leptomeninges may be considered to represent aberrant, malignant behaviour. However, one was an otherwise benign convexity meningioma, which recurred locally either from cerebral infiltration, a fragment of subdural fringe, or an implant. The recurrence was removed. Seven years later autopsy showed no further recurrence (Case 4, appendix C). It is therefore only in the remaining six cases that one finds behaviour suggesting some degree of malignancy. Case 7 in appendix C illustrates this. A parasagittal meningioma recurred repeatedly (Figures ix & x), at first from an invaded superior longitudinal sinus, next from subcutaneous implants, (Figures xliii), and finally from multiple intracerebral foci, either implants or infiltrative deposits. Cases 3 and 24 (appendix C) also demonstrate multifocal recurrence from either invasion of brain or implant metastases. Implant metastasis in the cerebral wound certainly does occur, either at the time of operation or by delayed exfoliation from residual tumour elsewhere. Such implanted tumours typically

show no dural attachment (figure xlix). It is not surprising that implantation at operation should occasionally lead to recurrence, since piece-meal excision is standard practice, and fragments of tumour may easily be overlooked. Probably many implants fail to remain viable. In one case dying a few days after a seemingly complete removal, serial sections through the tumour bed showed a meningiomatous implant on the ragged surface of the brain; however, the constituent cells were clearly dead. Subcutaneous implants still more rarely appear viable: case 7, shown in figure xliii, is the only example found in this series.

Multifocal primary neoplastic change as a form of recurrence does not figure in Table XVI, but there are several cases in which continued growth of a small satellite meningioma may have been responsible for a recurrence attributed to dural or leptomeningeal spread. The possibility is hard to exclude, but there is no special reason to favour it. There are only two patients in whom multiple tumours are definitely known to have presented at different times. One, described on page 179, died soon after the successful excision of an intra-ventricular tumour, from an unsuspected contralateral

convexity meningioma. The other, a little girl in the Adelaide series, has had three meningiomas presenting at intervals in a period of eight years (p.181).

Time relations.

Recurrences after grade I resections usually declared themselves only after a considerable interval. In verified cases, this averaged eight years from primary operation to confirmation of recurrence. The longest period of latency was sixteen years and the shortest thirteen months.

Recurrences after grade II resections were also commonly delayed: the comparable average period was seven years, the extremes being two and twenty-two years.

Grade III resections are a small and heterogeneous group; the period of symptomatic relief was longest when the residua were osseous, and less prolonged when recurrences arose from a frankly invaded, untreated dural sinus. The period of remission, before recurrence was verified, averaged 6 years: but as has been noted a number of cases so treated are still alive and well.

Recurrences after operations of grade IV tend to declare themselves earlier, but in this group there have also been some notable periods of freedom and again

(table XIII) there are patients still alive after these incomplete resections. The average period before recurrence caused death or necessitated reoperation was about six years, the longest period of freedom being nineteen years. The comparable average period for the patients treated by simple decompression was 3 years.

Many factors govern the length of the latent period before a recurrence becomes evident. They include:-

a. The size of the residuum.

b. Its anatomical situation.

c. The presence of a surgical decompression.

d. The cerebral reaction.

e. The growth rate of the tumour.

The first has been difficult to assess: even when an operation was known to have been incomplete, the surgeon often had an altogether erroneous impression of how much tumour was left. Autopsy in several instances (e.g. figure xxvi) showed residual masses far larger than had been realised. The situation of the tumour has obvious relevance: in the confined space of the foramen magnum (cf. case 13, appendix C) or the cerebello-pontine angle, a recurrence may produce symptoms very speedily. The provision of a surgical decompression may prolong a

symptomatic remission, but this has been apparent only with posterior fossa tumours, as supratentorial decompressions were rarely employed. The unpredictable factors of cerebral oedema or cyst formation in reaction to tumours have been discussed (p.121); at least two recurrent meningiomas were associated with enormous cysts, one being twelve cms. in largest diameter, which doubtless contributed to a rapid recrudescence of symptoms.

However, the most important single factor is the growth rate of the tumour. The cytological assessments of this have given interesting and useful prognostic information. Following ablations of grades I and II, the tumours considered to be of rapid growth rate recurred in an average period of 4¾ years. The comparable period for those of average growth rate was eight years. (There were only two tumours designated as of low growth rate). The same correlation was seen with tumours recurring after grade IV resections: the average period before verification of recurrence was three years where cytology suggested rapid growth, 8½ years for the intermediate group, and eleven years for the tumours of low growth rate.

There were however considerable variations in the latent periods, and caution is needed in giving prognoses

on the cytological evidence alone.

It has been repeatedly noted that meningioma cells in bone proliferate slowly. This seems to be the case even when the tumour is elsewhere of relatively rapid growth rate: in case 5 (appendix C) an undifferentiated meningioma showing cytological appearances of extremely active cellular growth recurred from an invaded bone flap ten years after primary operation. On the other hand, it seems possible that in certain situations some local anatomical factor may promote the growth of recurrent tumours. Although it is not susceptible of proof, one has the impression that meningiomas recurring in the walls of a major venous sinus may grow faster than elsewhere. Certainly, there is an association between growth rate and anatomical situation: the well known indolence of spinal meningiomas and suprasellar meningiomas illustrates this.

CHAPTER VIII

MANAGEMENT OF RECURRENCE

It is evident, from the experiences reported in the previous chapter, that recurrence of surgically treated meningiomas is not rare. Fortunately however the recurrent meningioma is often amenable to further treatment.

In the Oxford series, there have been 58 recurrences after primary operation. Reoperation has been attempted in 37 patients. The immediate operative mortality has been relatively high: nine patients have died within six months of such secondary operations. Repeated recurrence has taken place in eleven patients, and three of these have died after multiple resections recalling Cushing's tragic patients Russell & Donovan (Cushing, 1938). The combined operative mortality for separate recurrences is 25% (see page 187), but other deaths from continued growth must also be considered. In all, 32 patients have died of their recurrent meningiomas, and four others have died of more or less unrelated conditions. There remain 22 patients still living. Among these survivors, grave disabilities are common (see page 249); nevertheless about half are able to work to some extent. Even among those

patients who have died, there are many who received valuable respites from reoperation. There are also several who might have benefited had their recurrences come to operation.

The diagnosis and operative treatment of recurrent meningiomas can therefore be rewarding. There are however certain peculiar difficulties in the management of such cases, and these have received surprisingly little consideration. The subject is discussed by Cushing (1938), but few recent writers have given special attention to the problems involved.

Diagnosis.

The clinical and radiological manifestations of the recurrent tumours in the Oxford series have been reviewed. A detailed report of these would involve considerations beyond the scope of this thesis, but certain observations are relevant.

In the majority, diagnosis was not difficult. Not infrequently the symptoms and signs which had led to the original operation were almost exactly recapitulated, and on occasion the patient himself made the diagnosis. Difficulty arose however when the tumour recurred in a different place. Trans-septal spread by parasagittal meningiomas, giving rise to altogether new motor disabilities,

was usually recognised. But two tumours with supra- and infratentorial components developed recurrences after the excision of the supratentorial components, and these were not at first correctly identified. (Figures 1 and 1i reconstruct the pathology in these patients). In one, delayed diagnosis resulted in death (case 12, appendix C) from unrelieved brainstem compression.

Difficulty also arose where the recurrence presented with epilepsy alone. Post-operative epilepsy was common in this series; it was recorded in at least 87 patients (see page 253). In only 23 were the fits related to continued tumour growth. The diagnostic problem was therefore to determine when epilepsy heralded a recurrence and when it did not. Clinically, a recurrence could be suspected when the epilepsy returned after a period of some years' freedom (as in cases 1, 4, 9, 10, 16, 19, 22 & 23: appendix C). Such a return of fits was found especially sinister when the patient was still taking regular anti-convulsant medication (case 4, appendix C). However, occasionally recurrences took place in patients who had never really been free of fits since their original operations (cases 18 and 26). Furthermore, the contrary had been seen: several patients have been investigated for epilepsy of delayed onset, for which no cause other

than gliosis has been found. One was a woman whose parasagittal meningioma was excised in 1944. Focal epilepsy was first experienced in 1949. Full investigation, including air encephalography and angiography, showed no evidence of a recurrence, and nothing further has occurred in the last thirteen years to alter the diagnosis of gliosis.

Difficulty has also arisen in distinguishing the manifestations of a recurrence from those of atrophic disease. As was emphasized earlier (Simpson, 1957: appendix A), the area of cerebral cortex damaged by a meningioma may constitute a locus minoris resistentiae to any process affecting cortical function. Cerebral arteriosclerosis is especially likely to do this, and apparently caused progressive neurological disorders mimicking recurrence in several patients in this series. This concept has been independently advanced by El-Banhawy and Marguth (1962), who report five such cases, none of them verified either by operation or autopsy. It is of course difficult absolutely to exclude a recurrence under such circumstances, even if neuroradiological studies are negative (see below). The following case is therefore of considerable interest as a verified example of cerebral vascular disease simulating a recurrence.

Case Report.

G.B. (R.I. No. 138462) was admitted to the Radcliffe Infirmary under the care of Mr. J. Pennybacker on 9.3.51. He was then aged 67. He had suffered episodic losses of consciousness for seven years, with grand mal epilepsy and mental deterioration for three months only. He exhibited some dementia and a definite dysphasia, with a mild right hemiparesis. Angiography revealed a left coronal parasagittal meningioma, which was excised (grade II resection) on 20.3.51. Convalescence was reasonably smooth, and speech recovered almost completely.

He remained fairly well until August 1960, when his wife reported that his speech was deteriorating, and that his mental capacity was very poor. By November, he had become very lethargic and confused, and a marked grasp reflex was demonstrable in both hands. A recurrence was suspected, and he was to have been readmitted. While this was being arranged, he became much less responsive; speech was confined to "yes" and "no", and at one period he was reported to be semi-comatose. He was admitted as an emergency to St. Mary's Hospital, Kettering on 11.11.60, where he died three weeks later.

Autopsy showed no local recurrence. A minute nodule of tumour, 7 mms. in diameter, was found adherent to the dura over the right orbit; histologically it was an endotheliomatous meningioma. Presumably this represented an independent primary growth; in any event, it was obviously unrelated to death.

The brain was examined at Oxford. On coronal section, there was evident cortical disruption in the left superior frontal gyrus, with degeneration of the underlying white matter and marked thinning of the corpus callosum. There was also an area of recent infarction in the right rolandic region, with spongy degeneration of the white matter, and a small vascular lesion in the left putamen. Both frontal lobes showed suggestions of cortical atrophy. It is suggested that in this patient, the picture of a progressive frontal lobe syndrome represented the summation of the original frontal damage and a recent arteriosclerotic frontal infarction.

Recurrent meningiomas may or may not exhibit raised intracranial pressure. It had been repeatedly noted that a slack or indrawn craniectomy scar and normal optic

fundi do not exclude massive recurrences. However, when the integrity of the skull has been preserved, the recurrent meningioma can produce the ordinary signs of raised pressure. Indeed, several patients with recurrences exhibited advanced visual failure from secondary atrophy, without much premonitory headache.

Auxiliary diagnostic aids have usually been necessary. Electroencephalography has evident limitations. Nevertheless, a mass large enough to derange cortical function in a wide area may cause characteristic focal slow waves of comparatively high voltage. Figure xliv, taken from case 15 (appendix C), shows typical appearances. In interpreting such records, the effects of recent epileptic discharge, which may also leave residual slow wave abnormalities, must be remembered.

Plain radiographs will be diagnostic when the recurrence is calcified, or when it invades bone and gives the appearances of hyperostosis or bone erosion. The first must be very rare, because psammomatous meningiomas with radiologically demonstrable calcification are usually too indolent to recur. Recurrences with demonstrable hyperostoses are of course comparatively common (cf. figure xxx). It has not been the practice here to outline the tumour bed at operation by silver clips, as

Cushing advocated (1938), to allow review in plain radiographs.

Contrast radiographic studies were employed in the investigation of most of the Oxford patients with real or suspected recurrences, and have permitted, almost always, a correct diagnosis. However, interpretation can be extremely difficult, and the reliance placed by El-Banhawy & Marguth (1962) on such procedures is questionable.

Air studies were employed on eight occasions. There is often, though not invariably, considerable local atrophy after the resection of an intracranial tumour. Consequently, there may be local ventricular dilatation, which can amount to a gross porencephaly. Such ventricular dilatation can, apparently, compensate for an expanding lesion, at least for a time (Figure xlv), and thereby mask a tumour recurrence. For this reason, air studies may not reveal a recurrence, even when it has grown large enough to disturb cortical function. Figure xlvi shows this (case 18, appendix C): at the time of this encephalogram, the patient was suffering not only epilepsy, but also a disabling hemiparesis. It may be urged that air studies will be diagnostic eventually, and that delay may not be of much consequence. In many cases this may

be so, and one may sometimes of set policy defer reoperation until a recurrence is a threat to life. In other cases however delay may be most detrimental, and therefore complete reliance on air studies should be deprecated.

Carotid angiography was employed on some thirty occasions, and vertebral angiography once. A correct diagnosis was almost always given. A recurrent tumour can cause local distortion of cortical arteries in the absence of recognisable ventricular displacement, and thus angiography will be the more sensitive investigation, especially when there is post-operative ventricular dilatation. Nevertheless, the interpretation of such angiograms can be most difficult, for the following reasons:-

a. Cerebral atrophy can also modify displacements in the angiogram though usually to a lesser degree than in the ventriculogram.

b. Recurrences may develope in a new situation - especially recurrences of a parasagittal tumour.

c. When a craniectomy has been performed, the recurrent meningioma may herniate into the defect (Figure xlvii). This, it must be said, is unusual.

d. Recurrent meningiomas are often (though not invariably) less vascular than the primary growth. This may be true

even of such very vascular malignant meningiomas as that shown in figure xlvii; it is still more true of less vascular growths. (Figure xlviii is an interesting exception). It is hard to know just why this should be so; possibly earlier operative interference has eliminated some of the feeding arteries, but other factors may be involved. Whatever the cause, it makes the tumour less readily demonstrable.

e. Changes in the bone texture, due to operation, may partially mask the tumour vessels; the use of the subtraction method overcomes this.

f. Multiple recurrences may make the arterial and venous displacements very difficult to interpret. This is especially so when they are bilateral.

Operative management.

Statistics of the operative procedures performed for recurrent meningiomas are given in tables III - IX.

Technically, the exposure of the recurrent meningioma is tedious rather than dangerous. The re-cutting of an adherent bone flap and the reflection of adherent dura mater present no unfamiliar difficulties. When the tumour is superficial, as were the four recurrent meningiomas of the cerebral convexity and the solitary

superficial cerebellar recurrence, then operation is easy.

It is otherwise with the recurrent basal tumours. The hazards of excising a virgin sphenoidal ridge tumour are greatly augmented when there are adhesions from previous surgery. It was only once possible to perform radical excision under these circumstances. The same is true of recurrent subfrontal tumours; no such operations were performed in the Oxford series, but in two re-explorations for recurrent suprasellar tumours at Adelaide, the difficulties have been extreme. In one, the internal carotid artery was transected in clearing adhesions from the surface of the tumour; in the other, the operation had to be abandoned before the optic nerves had been decompressed. A trans-ethmoidal procedure was then attempted, with only limited benefit. The surgery of recurrent posterior fossa meningiomas is also greatly complicated by previous exploration. If the tumour could not be completely removed at the first resection, it is still more likely to be inoperable as a recurrence, and as table IX shows, no recurrent posterior petrosal tumour has been found removable. In this situation moreover partial removal is unlikely to give a prolonged remission.

The problem with the numerous recurrent parasagittal meningiomas is rather different. Here, it is necessary to decide how radical the resection shall be. There has been, as table VIII shows, a proper readiness to resect the superior longitudinal sinus in such cases, and as a rule, this was fairly well tolerated because the sinus was usually occluded. It cannot however be assumed that this will always be so. In case 23 (appendix C) a recurrent parasagittal meningioma was removed seventeen years after primary resection of a histologically similar mass on the other side of the falx. Presumably the recurrence represented trans-septal invasion, and the falx must have been infiltrated: but the sinus was still patent.

The decision whether to resect the sinus may be aided by preoperative sinography. It will also be helped by knowledge of the tumour biology: cytological evidences of a fast growth rate, and a short latent interval before recurrence, will justify very radical surgery. It is in such cases as these, where sinus resection is essential but hazardous, that the propriety of a sinus repair with autogenous vein graft (as advocated by Gurdjian & Webster, 1958: p.437) may be considered. Such a graft seems more likely to succeed than the plastic tube advocated by Lasierra (1958): the experimental data summarised by

John et al. (1961) suggest that a solid prosthesis will thrombose, and a woven tube may well leak post-operatively.

Dissections of the superior longitudinal sinus in cadavers have shown one grave hazard in this attractive procedure. It is not very difficult to intercalate a length of external jugular or saphenous vein in the superior longitudinal sinus, but to do so a small section of the sinus at each end must be mobilised. To do this may entail sacrifice of superior cerebral veins whose importance may be almost as great as that of the sinus itself. When, as sometimes happens, the sinus is extensively invaded but patent, a graft may however be worth trial, and it is proposed to do this should a suitable case be found.

In general, these resections for recurrent meningiomas have been surprisingly well tolerated. The augmented mortality expresses the various operative hazards indicated above; and the decision to withhold operation in a number of patients represented knowledge of the likely operative risks as well as the general infirmity of the patients. Nevertheless, recurrent meningiomas have often been more easily dealt with than was anticipated; especially in the convexity and parasagittal situations, further surgery should be considered before the only alternative procedure - radiotherapy.

Recurrences, in all situations, may be multifocal. Preoperative angiograms occasionally warn that this is so; more commonly they do not. It is necessary therefore, in all secondary operations, to explore the field very carefully. In two instances (cases 9 & 24), it is likely that sizable masses were overlooked at reoperation. The large mass shown in figure xlix seemed a sufficient cause of symptoms; however, bad postoperative progress soon necessitated another exploration at which a second tumour, evidently missed before, was disclosed.

Radiotherapy.

In the three series, thirtysix patients received radiation therapy of some kind. The reasons dictating this measure varied, but three main indications can be recognised.

(1) Prophylaxis of recurrence after seemingly complete resections (grades I and II).

(2) Supplementary treatment of an incompletely excised tumour (i.e., after operations of grades III-V).

(3) Treatment of a developing recurrence. With this, it is convenient to consider the few cases in which radiotherapy was employed as a primary measure, without

major operative treatment.

The first indication was not often accepted: only five patients received prophylactic radiotherapy after seemingly adequate resections. These were patients in whom recurrence was thought to be especially likely, either because it had already taken place (3 patients) or because of the pathology of the tumour (2 patients).

The results have been disappointing. Two patients have already developed local recurrences, despite irradiation of the tumour area (Cases 7 and 25; appendix C). One of these (case 7) received three courses of radiation for repeated recurrences, totalling 14000 rads; cerebral radiation necrosis was present at autopsy (~~figure xi, C~~) but the tumour itself appeared cytologically very active. A third patient may have developed a recurrence; she died of pneumonia and no autopsy was performed, but the course of events is rather suggestive (Case 11 appendix C). A fourth patient received 4000 r gamma irradiation (2 M.E.V.). She developed bilateral necrosis of both paracentral lobules, presumably as a radiation effect, and was totally disabled when last heard of. The fifth patient was treated very recently. Another patient may be mentioned, though she presented after the terminal date of the Oxford series. Prophylactic

radiation was given after the excision of a rather rapidly growing meningioma. The patient developed massive frontal necrosis and died seventeen months later.

Radiation after an incomplete resection was given on twenty-four occasions. It is very hard to assess the value of radiotherapy under these circumstances, because the operations themselves were palliative resections or decompressions, and long survival after such procedures is well attested (see page 214). But in twelve patients one can say certainly that the value of radiotherapy was at best limited because the patients have died of continued tumour growth. (One of these patients developed scalp necrosis.) Another has required further surgery, and one has died of an unrelated cause. There remain ten who are alive, or were when last traced: the longest survival was twenty years, in a patient from the London Hospital treated with radon implants, but there have been several other prolonged survivals after external irradiation.

Radiation given to meningiomas, recurrent or otherwise, without concomitant remedial surgery, is a little easier to evaluate. It was so employed with seven patients. In five of these, one can confidently say that no useful response was obtained. All patients came

to autopsy or further operation, and histological studies have shown no marked regressive changes in the tumour. Three of these did however show temporary response, in that an external mass shrank somewhat in two, and a reduction in vascularity was demonstrated angiographically in the third. A sixth patient died of cardiac disease. He may have received some benefit from irradiation of his suprasellar tumour, but unfortunately the clinical data are meagre. The seventh patient may be regarded as more encouraging. She had a sphenoidal ridge meningioma en plaque, which was incompletely excised in 1951. Proptosis was apparently increasing in 1953, when radiation was given: since then, she has remained well, and the proptosis has regressed measurably though it is still quite evident.

These patients received radiation therapy in thirteen different centres, and the methods employed were diverse. The dosages have been reviewed, and it is found that in twenty-two tumour irradiation exceeded 4000 r. Smaller dosages were given in the remaining twelve: perhaps coincidentally, these include a number of very long survivals.

It is exceedingly difficult for one not expert in this field to assess the significance of these results.

It does however appear that radiation within the limits of cerebral tolerance was not a reliable therapeutic weapon in these patients; it may have contributed to some prolonged survivals, but equally, it failed to arrest the progress of the disease in a larger number, and was actually deleterious on two occasions. It certainly appeared to reduce the vascularity of several meningiomas, but microscopic evidence of a cellular response has not been obtained. It cannot be said that any one histological type was especially responsive; two angioblastic meningiomas were included in the series, and treatment was ineffective in both. More malignant meningiomas, of which there were four, one of them being of the very vascular undifferentiated type, appeared strikingly resistant. Possibly modern advances in radiobiology and radiotherapeutic techniques may permit more successful treatment of such tumours. It is fair to say that at present the utility of radiation therapy is not established. The published reports, reviewed on page 77, are at best inconclusive.

The report by Jones (1960) of an angioblastic meningioma partly removed and then successfully treated by radiation is perhaps the most impressive in the literature, and even this is debatable. By the kindness of Mr. J.E.A. O'Connell,

I have been permitted to review the biopsy and autopsy sections of this tumour, whichshould not, by the criteria adopted in this paper, be considered angioblastic. Neither the clinical progress of the case, nor the apparent change in the histology of the tumour, is absolute proof of the beneficial effect of radiation. The first could be duplicated in our material by equally good results from similar operations without irradiation, while the change in histology is not beyond the range of variation exhibited by some meningiomas in a single section.

Whatever view is taken of the radiosensitivity of meningiomas there can be no doubt that cerebral radiation has unpredictable risks. Possibly individuals vary in their susceptibility. Possibly too, the chances of misadventure or miscalculation vary in different radiotherapy clinics.

CHAPTER IX.

POST-OPERATIVE DISABILITY

Introduction

The residual disabilities resulting from intracranial meningiomas vary greatly. Many patients enjoy a complete recovery. Several fortunate and phlegmatic patients reviewed recently have expressed surprise, almost amusement, that their well-being should be the subject of a medical survey. Others however have suffered terrible and permanent cerebral mutilation. The recurrent parasagittal meningiomas have been, above all other groups, responsible for severe neurological incapacity. The story of one memorable patient, the victim of such a meningioma, is given to introduce and illustrate an analysis of residual postoperative disability.

Case report. (This is given in summary form as Case 21 in appendix C).

Mrs. Florence D., a housewife aged 41, underwent removal of a right fronto-parietal parasagittal meningioma in the Radcliffe Infirmary on May 21st 1948. Before operation, her chief complaint was transient attacks of hemiplegia, and she had suffered no great disability; indeed, there were no objective neurological abnormalities. Nevertheless, the

tumour was large and the operation (grade II() was not easy.

When she returned to the ward, there was total paralysis of the left leg, with sensory loss, and profound weakness of the left arm. The arm quickly recovered, and movement at the hip also returned within three days. But the left leg and foot remained severely paralysed, and a toe-raising spring and caliper were needed. With this appliance she could walk well within two months of her operation.

She developed a Staph. albus cranial osteitis, and this necessitated removal of the bone flap. Otherwise, her recovery was reasonably smooth, and she resumed a life of normal activity. She could do her housework, including her domestic accounts, and cared for her four children; indeed, two years after the operation, she became unexpectedly pregnant, and was safely delivered of a fifth child. The left leg remained weak, and she preferred not to go out much, but she was able to discard the caliper.

About a year after operation, she began to experience occasional focal epileptic seizures on the right side. Early in 1957, these became more severe, and a spastic weakness of both legs developed. A

recurrence was suspected (see appendix C), and on Sept. 20th.1951, a left-sided parasagittal meningioma, the twin of that removed three years before, was excised (grade II operation).

Immediately after operation, there was an absolute right hemiplegia; recovery began on the fourth day, but when she was discharged there was still a severe motor and sensory loss in the right leg and to a lesser degree in the right arm. The weakness of the left leg was unchanged. The weakness and even more the loss of position sense in the legs were very disabling. Bladder function however was preserved.

Paraplegia is a hard trial of character. On superficial acquaintance, the patient and her husband are not remarkable people. She is a cheerful, placid person from a county town in Norfolk; until her marriage she had been a shop assistant, and her interests were clearly social rather than intellectual. Her husband is a rich shoe-manufacturer, very devoted to her, of similar antecedents, and sharing the same tastes and pleasures. It would be hard to present this couple in heroic terms, but they have impressed everyone with their fortitude and ingenuity. A new

house was purchased, and fitted with numerous appliances to aid the patient to support herself. Hand grips and parallel bars were fitted, and a private nurse was constantly employed. For some eighteen months, the patient attended her county hospital for physiotherapy; the records however suggest that she profited less from this than from the assiduity of her husband, nurse, and local doctor. She never walked independently, but was able to do so between parallel bars. She busied herself with needlework, hemstitching and weaving, despite some residual weakness and stiffness of the right arm.

In 1953 her state again worsened. At first the increasing weakness and stiffness of her legs was attributed to a fall, but when the left arm was also affected, it became evident that she was suffering from a recurrence. On Nov. 26th, a large bilateral parasagittal mass was removed, together with the falx and a 6 cm. length of the superior longitudinal sinus (Grade I operation).

After this, she was profoundly tetraplegic though speech was preserved. Her right arm slowly regained limited function, and she could feed herself with it, though precise movements were impossible. The left arm and both legs were useless. Bladder and bowel

function were preserved.

Now she and her husband had to face the state of triplegia. With perseverance, she regained further function in the right arm, and she lived a surprisingly full life in bed or in a wheel chair, despite frequent focal epileptic fits, until 1958.

She then developed symptoms of raised intracranial pressure, and lost the use of her right arm. There was also unequivocal mental slowing. After some hesitation, it was resolved to re-operate, and on Aug. 21st.1958, a large recurrence was removed.

This time, her recovery was slower, and she exhibited a distressing paranoid delusional state. However, a little power returned to her right arm, and this remained until 1960. She then became totally tetraplegic, and so remains. Speech became slower, but she continues to be able to converse, and takes an evident interest in her family and in visitors. Her psychotic state has resolved, and when last visited, she was stoically resigned to her impending death.

It would be impertinent, in such a study as this, to expand on the circumstances of this tragedy, or to attempt

such a lapidary epitaph as Cushing (1938) gave for his similar patients Donovan & Russell. It is however relevant that this patient, perhaps more than any other, has impressed on those in contact with her the gravity of the problems considered in this thesis. Great surgical skill and devoted domestic care (armed with uncommon wealth) have not saved this woman from neurological disabilities progressing steadily and relentlessly to her present state of absolute incapacity. And, unfortunately, her case is not unique.

Incidence.

Assessments of residual disability from cerebral damage are not easily expressed in quantitative form. When the survey presented here was planned, a percentile rating, comparable with that used by the British Ministry of Pensions, and applied by Russell (1951) in his analysis of brain wounds, was at first considered. It was found however that the data were inadequate for this. The conventional method of grading according to working capacity was therefore used. This rather crude assessment was also used by Tönnis (1953); Horrax & Strain (1952) presumably employed similar criteria in determining their "useful survival statistics".

Five grades of disability have been recognised:

1. None: the original employment has been resumed, or one comparable, and the patient has no troublesome residual symptoms.

2. Slight: this signifies return to original employment, with however some complaint or neurological abnormality not severe enough to impede work.

3. Moderate: the patient has returned to work, but admits a definite limitation in his capacities. This commonly implies a job of lower status, or one less remunerative.

4. Severe: the patient is wholly unable to work, but can care for himself.

5. Total: the patient requires nursing care, either at home or in an institution.

The information needed for this classification was obtained, as stated on page 84, by personal interrogation or more commonly by letter. The letters were specific enquiries into the problems of the particular patient; it was felt that this would be more flexible, and more acceptable to the recipient (physician or patient) than a questionnaire. The grade of disability was as a rule assessed on the patient's best level of achievement; subsequent increase of disability from recurrence or

degenerative disease was separately assessed. Most of the information was obtained in the 1955 survey, and this was the basis of a brief earlier report (Simpson, 1956). However, in the 1962 survey, a few patients were found to have improved in their working capacity, and a few assessments, when reviewed, appeared to have been incorrect; hence the statistics now differ slightly from those given in the earlier report.

Even with this very rough system of assessment, some difficulty was encountered, chiefly with housewives and persons over the age of retirement. Here, the basis had to be the objective neurological abnormalities and the patient's own judgement of her ability to do housework and to engage in social activities. It is in this group that a few erroneous assessments were apparently made at the time of the first survey.

With the exclusion of 32 patients not surviving for more than six months after operation, and of six other patients in whom the data were in various ways unreliable, there were 208 patients whose disabilities could be analysed. The results are set out in table XVII. As in table XII the chief regional groups have been associated, to give larger numbers. The smaller groups are included in the total, but are not considered separately.

Table XVII : Residual Disability (Oxford series).

Regional Groups	Slight	None	Moderate	Severe	Total
Parasagittal, falx, falco-tentorial, transverse sinus (77 cases)	18%	43%	22%	16%	1%
Convexity (42 cases)	43%	43%	14%	-	-
Sphenoidal ridge & subtemporal (37 cases)	24%	32%	24%	8%	11%
Suprasellar & Olfactory groove (26 cases)	4%	42%	19%	27%	8%
Posterior fossa (19 cases)	37%	32%	5%	10%	15%
ALL CASES (208)	25% (52 cases)	40% (83 cases)	19% (40 cases)	11% (23 cases)	5% (10 cases)

The figures for the entire series show, in effect, that about two thirds of the patients surviving the resection of their meningiomas have resumed their original occupations. Some of them have more or less troublesome

sequelae, especially headaches and epilepsy, but they have not suffered any evident economic hardship. In several instances, the return to the original employment was long delayed, and achieved only with considerable exertion.

Of the remaining patients, more than half have resumed some kind of activity. Nevertheless, the patients classified as suffering moderate disability include many with very grave handicaps. This category comprehends about a dozen patients with considerable hemiplegic disabilities, and nine with gross impairment of vision; in many of these, only great fortitude has enabled the patient to escape complete incapacity. On the other hand, this group includes several persons disabled in particular professions by symptoms which might have been trivial in other contexts. A foreman, for example, working in an open hearth furnace, has had a single fit; he has had to resign, and now works as a trainer in metallurgy. A senior professional soldier underwent removal of a suprasellar meningioma; four years later he suffered a bout of status epilepticus, after which he exhibited a permanent amnesic defect, especially affecting recent memory. He had already retired from active duties at the rank of brigadier; when employed at the War Office,

he found himself unable to cope with administrative work, and had to resign after a probationary period. These cases could be classed as slight disabilities, but this would be unrealistic: the patients have in fact been unable to pursue their chosen professions, and have had to abandon reasonable ambitions.

The 23 patients classed as severely disabled, and the ten classed as totally incapacitated, were almost all the victims of very severe organic brain damage. The qualification is made, because there are one or twowhose disabilities, objectively, appear relatively less severe, despite the patient's professed inability to find work; in the large majority, however, the causes of incapacity are gross and obvious. In this group, compound disabilities are common: thus, three patients with posterior fossa tumours were left nearly blind and profoundly ataxic. A considerable number of these severely disabled patients later died, in some cases from the continued growth of their tumours, in others from intercurrent infections.

Regional analysis.

The statistics (table XVII) presenting the disabilities in the several regional groups bear out the views expressed in chapter V. The convexity meningiomas have

justified their reputation as the most favourable group; among the patients who did suffer moderate disability, epilepsy was the commonest problem, and only one patient had a severe permanent hemiplegia. The sphenoidal ridge and subtemporal meningiomas carry a much higher disability rate: and the figures would be still worse were the tumours en plaque excluded. The causes of disability in this group are complex: perhaps commonest was some degree of mental impairment, often compounding some visual or motor disability that might otherwise have been overcome. The relatively low disability rate with the posterior fossa meningiomas is in part due to the converse of this: mental impairment was rare, and usually the patients had determination enough to rehabilitate themselves. The chief exceptions were those with ataxia and secondary optic atrophy, referred to earlier.

The high incidence of disability with the subfrontal meningiomas is disappointing. It is not surprising that this should be so with the large olfactory groove meningiomas, but it is distressing that nearly half the patients with suprasellar meningiomas should be disabled. Late diagnosis, with consequent irreversible visual loss, is the chief cause of this. An important subsidiary cause of disability with the subfrontal meningiomas is epilepsy: it was

a symptoms in more than a third of the survivors, and in several was quite troublesome.

Some of the causes of the high disability rate after excision of parasagittal meningiomas were discussed on page 161, in connection with the problem of sinus resection. In the large majority, motor deficits - hemiplegia or paraplegia - were responsible; in some, there were also significant dysphasic defects. Several of the frontal tumours caused severe and permanent dementia. It may again be emphasized that this incidence of disability represents the outcome of a comparatively conservative policy: sinus resection was not employed in a very high proportion of cases. It is also worth noting that the sufferers from recurrent parasagittal meningiomas exhibited a much higher incidence of post-operative disability. Fifteen patients survived resections of recurrent parasagittal meningiomas, and of these ten exhibited profound and crippling sequelae. These were in part due to the more radical surgical procedures: but it is evident that the destructive effects of the recurrent tumours played a greater role. The patient described at the beginning of this chapter exemplifies this.

General considerations.

If the entire material is considered, it is evident that the residual disabilities fall into four main groups.

First, there are disabilities resulting from impairments in mentality, ranging from gross dementia to psychoneurotic states. (The latter, naturally, have often been in evidence before the onset of the neurological illness, and may express the patient's basic personality.) With the mental defects, one can couple defects in speech and memory. It is difficult to determine the relative importances in patients with multiple disabilities, but it can be said that impaired mentality was the main problem in about a quarter of the graver disabilities (moderate, severe & total). Several of these patients were elderly, and it is likely that senile changes contributed to the mental defect. In such cases, and in those representing bifrontal cerebral damage, psychiatric treatment could offer little or nothing. In a few instances, institutional care was arranged; usually however these patients have been cared for at home, often as a terrible burden on their relatives. A rarer occurrence was the precipitation of an acute psychosis, usually depressive, after operation. This happened several times, and responded well to psychiatric treatment. One such occurred in a young man with a frontal tumour: in his convalescence he developed

a florid paranoid psychosis. This resolved with electric convulsive therapy. He had no previous history of mental illness, and his subsequent progress, over seven years, has been entirely satisfactory.

Second, there are motor disabilities, to which many references have already been made. These were more common as causes of permanent incapacity. It may be noted that in several instances the motor defect was aggravated by painful joint stiffness. To some extent, this is preventable. Especially after the removal of a paracentral meningioma, it is very common for the patient to exhibit a profound initial hemiplegia, which will subsequently recover. Failure to maintain mobility during the period of paralysis may leave a troublesome joint stiffness after the actual weakness has gone. Conversely, in several older patients, the onset of degenerative arthritis has increased motor disabilities from residual cerebral damage. The aggravation of motor disability by coexisting sensory loss is a familiar event, and was evident in several cases with parietal lesions; such patients are occasionally regarded, very incorrectly, as neurotic because the disability is so much greater than the objective weakness. (The lady whose story introduced this chapter was so accused by

a consultant in physical medicine!)

With motor disabilities, skilful rehabilitation has frequently been remarkably successful. The patient whose history is detailed as case 9 in appendix C underwent repeated operations for recurrence and also suffered an attack of meningitis treated by streptomycin. He was left with the appalling and permanent disabilities of dyslexia, total deafness, and a dense right hemiplegia. Lip reading, speech therapy, and physiotherapy have brought him to be able to run a workshop and drive a tractor, and to play a valuable part in the work of his own farm.

Third, visual impairment accounted for about a quarter of the major disabilities. In the majority, these were cases with primary atrophy from parasellar tumours. As has been stated, it may be anticipated that earlier diagnosis will reduce the frequency of this cause of visual disability. The same may be said of blindness from consecutive atrophy. There were eight patients with profound visual loss from this cause, two of them totally blind. Most of them presented during the early years of the survey; it is justifiable to hope that such cases will be very rare in the future. It must however be kept in mind that the manifestations of raised intracranial pressure can be deceptive and insidious. The Adelaide

series includes one tragic case, in which total blindness developed from a parasagittal meningioma occluding the superior longitudinal sinus. The patient never complained of much headache, and the optic fundi, when first seen, were considered to show primary atrophy.

Finally, epilepsy requires special consideration as a cause of inconvenience and disability. In the Oxford series, epilepsy was recorded as a post-operative complaint in 87 patients, and in five others was strongly suspected. This gives an incidence of 41% of all patients surviving 6 months or more; exclusion of orbital and purely infra-tentorial tumours raises the incidence to 45%. The incidence was, as might be expected, higher in patients with preoperative fits, 56% of whom suffered one or more seizures after the removal of the responsible tumour. However, of the 92 patients with supratentorial tumours who did not have preoperative epilepsy, some 32 (35%) have suffered fits after operation.

These figures are in accord, so far as comparison is possible, with the few other studies on the incidence of epilepsy after excision of intracranial meningiomas. Penfield and Jasper (1954: p.298) reported roughly similar findings in a small series. Groff (1935), analysing Cushings material, found a similar incidence

of fits in patients with pre-operative epilepsy, and a lower incidence in patients who had not. Flyger (1956), reporting 313 parasagittal and convexity meningiomas treated at the Serafimerlasarettet, gave an incidence of 41.1% among those patients (78) who had no preoperative fits; unfortunately, the over-all incidence is not given. (The incidence in the Oxford series, for the same limited group, is about 41% also). It is of interest to see that the incidence of epilepsy in Russells (1951) large series of penetratijg brain wounds is almost exactly the same - 45%. One can deduce that the meningioma is neither more nor less epileptogenic than any other localised destructive process involving the cerebral cortex. Whether operative trauma greatly increases the risk of epilepsy is hard to say. In certain circumstances it must do so: the transcortical incisions needed in the removal of intraventricular meningiomas are highly epileptogenic. The frontal lobectomies used in exposing subfrontal tumours are also associated with a higher incidence of fits. It is not wholly certain that this represents the effect of the lobectomy rather than the larger size of the tumours needing such exposure. It will be interesting to see whether the use of urea, which commonly obviates the need for such lobectomies, reduces the incidence of fits.

It would be wrong to overstress the importance of these figures. In compiling them, all patients with known seizures have been included, and the figures therefore comprehend many cases in which post-operative fits were transient and, for the patient, of negligable importance. As with other forms of post-traumatic epilepsy, there has been in many cases a general tendency towards improvement with the passage of years; furthermore, control by anticonvulsants has usually been efficient.

Nevertheless, in a minority, the effects of post-operative epilepsy have been extremely serious. One patient died in status epilepticus; so also did one patient in the Adelaide series. Another patient was killed in a road accident, possibly caused by an epileptic seizure. As has been stated, two patients had to abandon their chosen professions because of epilepsy or its sequelae; another patient (the youngest in the Oxford series, a boy aged thirteen) suffered greatly in education and otherwise from fits which did not subside for about five years. The disability from epilepsy is of course greatest when the fits occur without an adequate aura. The meningiomas involving the sensori-motor cortex are usually, as might be expected, associated with focal

seizures: this was so in 90% of the Oxford cases. With the parieto-occipital tumours, the incidence fell to about 66%, and with frontal convexity and parasagittal tumours to just over 50%: in the remainder, the fits had no focal signature and were in consequence distinctly more dangerous. With the subfrontal tumours (olfactory groove and suprasellar) the incidence of such fits was still higher, and this group also included most of the few cases of status epilepticus.

The prophylaxis of post-operative epilepsy must depend chiefly on medication. Most of these patients received routine phenobarbitone (30 mgms. thrice daily) after operation; the efficiency of this is supported by the number who had their first fit as soon as they stopped the drug. It is probable that this medication should continue indefinitely; at least one patient had her first fit five years after operation. Whether surgery can be modified to diminish the incidence of epilepsy is not clear. Very little is known about the nature of epileptogenic lesions of the cerebral cortex. The intimate relation of brain and tumour, discussed on page , makes it usually impossible to effect removal without some degree of cortical damage. It is significant that Penfield, who has devoted so much thought to the

minimising of cerebral scar formation, has had to report an incidence of post-operative epilepsy much the same as that found in this survey. (Penfield and Jasper, 1954: p.298).

It is expedient to warn patients that successful removal of the tumour does not necessarily guarantee freedom from fits: these can be simply explained as a common and benign consequence of a cerebral scar. Much distress can be avoided if this is done.

CHAPTER X

CONCLUSIONS

The three series of intracranial meningiomas analysed in the previous chapters comprise together 390 cases. This is by no means the largest published collection. It is however so well documented that it provides exceptionally good material for study of the surgical pathology of these tumours, and for a correlated analysis of the results obtained in their treatment. Of particular value is the large number of patients who have been regularly reviewed for many years. Geographical factors have aided this full and intimate follow-up, especially in Oxfordshire and the neighbouring counties. Chiefly however it results from the standard of personal medical care maintained by Sir Hugh Cairns and by those who were influenced by him.

In their pathology, the meningiomas show some of the characteristics of benign tumours: their typical mode of growth is slow concentric expansion, and they are often so well circumscribed from the surrounding brain that their surgical removal is easy. In consequence, some authorities have written of the meningiomas in terms of unqualified optimism. However, limited invasive growth

is very commonly demonstrable. In the studies reported here, invasion of bone was verified in 20% of tumours; invasion of a major venous sinus was found in 15%; infiltration of more remote structures was not rare. These figures exceed those given by some pathologists; nevertheless it is likely that they if anything underestimate the true incidences of external spread by meningiomas. Less commonly, one may find internal spread: the meningioma may to a limited extent invade brain. This was found in 5% of cases in the Oxford series.

Invasion of the dura mater is a potentiality of all meningiomas; it is not a special property of any identifiable variant type of meningioma. Their general tendency to penetrate the walls of venous sinuses suggests some cytotaxic agent, and may reflect the normal relationship of arachnoid villi and venous channels. Invasion of brain is considered by some, most notably Russell and Rubinstein (1959: p.56) to be a specific property of malignant meningiomas. However, the present survey has shown that meningiomas which are in other respects innocent may exhibit marginal cerebral infiltration, with penetration of the pial barrier.

It is necessary to define clearly what is meant by

malignancy in a meningioma. These tumours vary greatly in their biological characteristics. In the material reported here, there are tumours which have grown with extraordinary speed, recurring rapidly, invading contiguous brain, and even (in three instances) metastasizing to the lungs. There are other tumours of such slow growth that even after many years their presence is compatible with comparative well-being. The first are evidently malignant, and the second, as evidently, are benign. But between these extremes there are many tumours which are intermediate in their biological behaviour, and it is hard even retrospectively to establish clear-cut boundaries of innocence and malignancy. A reliable prognostic distinction is still less easily made, either clinically or with the microscope. There is a tendency for surgeons to assume that any meningioma which is highly invasive (cf. Pertuiset et al., 1958), or which recurs after operation (cf. Guillaume et al., 1957: p.147) is histologically malignant. Conversely, pathologists tend to identify unusual histological and cytological features as evidences of malignancy in the clinical sense. Both these views are in part justifiable, but they cannot be made into rigid tenets. It has been repeatedly found in the material analysed

here that typical meningiomas which are of slow growth and which show no other stigmata of malignancy, may be extremely invasive. They may also recur after seemingly complete resection. On the other hand, a few meningiomas whose microscopic appearances would seem to indicate malignancy have been in the event clinically benign. This paradox was noted by Henschen (1955): it has been so clearly apparent in the studies reported in this thesis that a microscopic diagnosis of unequivocal malignancy has been considered proper only when the tumour is frankly anaplastic and obviously of very rapid growth. Thus, the tumours designated as undifferentiated meningiomas have proved uniformly unfavourable. These are identified by their lack of any specific histo-differentiation, by irregular cellular orientation, and by a general resemblance to embryonic tissue (Globus, 1937); they almost always show cytological evidences of very rapid growth. They have apparently gone under various names, and are often termed angioblastic; however, they have not appeared to show much kinship with the well-differentiated angioblastic meningiomas, whose clinical course is as a rule favourable. Highly anaplastic endotheliomatous and fibroblastic meningiomas have also been seen, which have been correctly predicted to recur; in several of these, the tumours could

be termed malignant. In a sense however all meningiomas partake in varying degrees of the biological properties clinically identified as malignancy, and the term must be used in a relative connotation. This blurred distinction between innocence and malignancy is not unfamiliar in general pathology; analogies could be found, for example in the behaviour of bronchial adenomas.

The most valuable contribution of cytological studies has been in the assessing of tumour growth rates, to predict, not whether a tumour will recur, but rather when it is likely to do so if there is any residue. The finding of mitotic figures and a lack of cellular orientation has been regarded as evidence of rapid growth. Contrary to Kernohan and Sayre (1952: p.116), but in accord with Marcos (1954) and Russell and Rubinstein (1959: p.55), nuclear pleomorphism has not appeared of great significance. Conversely, the absence of mitotic figures, and a high degree of histodifferentiation, have been correlated with slow growth. In practice, this simple concept of growth rate has been valuable, though the time of appearance of a recurrence evidently depends to some extent on other factors. Changes in the histology of a given tumour in successive biopsies has been reported by Cushing (1938: the case of Dorothy May Russell) and

more recently by Burmeister and Wendt (1962). This has been seen in very few cases in the material reported here, and it is probably a rare event.

The invasive propensity of the meningiomas has been shown to be a prime cause of therapeutic failure. Invasion of the skull base has made many tumours inoperable. Undetected invasion of dural structures, especially venous sinuses, has been the cause of numerous post-operative recurrences. Recurrence has also arisen from invaded bone, though this is less common; intraosseous meningioma cells seem in general to be very slow growing. Recurrence from invaded brain has also almost certainly taken place, though it is in practice not always possible to distinguish this from an implant metastasis or a leptomeningeal residue. These manifestations of local invasion are well known, but it seems likely that their importance has been under-estimated, especially in the surgical literature.

Another striking and better known feature of the pathology of the meningiomas is their tendency to form dangerously close relationships with major vessels. A great merit of Cushing's (1922, 1938) regional grouping of the meningiomas was his identification of the special vascular relations in each group. Cerebral angiography has confirmed and extended this knowledge. The experiences

summarised in chapter V of this thesis have shown that even with the most skilled operators certain meningiomas are inoperable because of such vascular relations. Cerebral infarction from occlusion of a major artery accounted for 16% of all post-operative deaths in the Oxford and Adelaide series. Other causes of mortality are receding in importance, and in the recent series reported by McKissock and Taylor (1960), such infarctions were the major cause of death. Close adhesion to such vital neural structures as the pons or the hypothalamus is also a cause of occasional disaster.

Even the expansive growth of the meningiomas has more complex effects than some writers have supposed. It is of course a direct threat to life. The dangers of irreversible internal cerebral displacements are too well known to need reiteration. So also is the threat to vision from chronic elevation in intracranial pressure. But it is less well recognised that these tumours may cause profound local neural damage, including regional oedema, necrosis and cyst formation.

The statistics submitted in chapters V - VII and IX have shown that the results obtained in the treatment of this relatively benign tumour are still far from ideal. Death, early or from delayed recurrence, has occurred in

more than a quarter of the patients in the Oxford series. Serious disability was evident in more than a third of those who survived operation; lesser disability was also common. Review of published reports confirms that this experience is not unique. It is significant that those writers with longest acquaintance of the problems write with least optimism. Certainly, the results obtained in recent years (both in the centres from which this report derives its material and in others) show much improvement. Nevertheless, the meningiomas continue to present some unanswered challenges. To some of these, no ready solution offers. But for certain problems, one may venture to suggest lines of approach that may be rewarding.

Analysis of the direct post-operative mortality has shown, a little unexpectedly, that one cause of death is still misdiagnosis. The occasional failure to recognise a meningioma as such will be still rarer if the effects of regional oedema and local necrosis are kept in mind when angiograms or aspiration biopsies are being examined. Other post-operative deaths resulted from the poor state of the patients or the large size of the tumours. These to some extent represent the consequences of delayed diagnosis. Some of the residual post-operative

disabilities might also have been avoided had the tumours been investigated earlier. Policies concerning diagnostic investigation of patients presenting with such symptoms as epilepsy or uniocular visual failure are beyond the scope of this thesis. It is however true to say that operative mortality, inoperability, and residual disability will all be significantly reduced by earlier diagnosis.

The surveys reported here have shown a high incidence of inoperability. In the Oxford series, nearly a third of all tumour resections were macroscopically incomplete. This figure is indeed not representative of contemporary practice; the incidence (at most 18%) in the Adelaide series shows that modern methods of anaesthesia and supportive care permit many previously impossible ablations. There is still however a stubborn residue of meningiomas which with present techniques are inoperable: these are chiefly in the parasellar and cerebellopontine regions. It is possible that the use of microdissection, now under trial in Adelaide and elsewhere, perhaps combined with partial circulatory arrest, may permit the excision of some tumours hitherto inoperable. Such radical methods may be considered as a second-stage procedure where the cytology of an incompletely excised meningioma predicts an early recurrence. The long periods of well-

being often given by subtotal resections indicate the prudence of conservative procedures where the tumour is cytologically of average or slow growth rate.

It has seemed of considerable importance to distinguish between those tumour resections in which the dural attachment is resected, and those in which it is not. Even if the system of grading submitted earlier (Simpson, 1957) is considered too elaborate, this fundamental distinction should nevertheless be made because the less radical procedure carries a much higher recurrence rate. After operations in which the dural attachment and extradural extensions, as well as the tumour itself, were excised, the incidence of recurrence has been about 11%. When the dural attachment was left in situ and treated by the diathermy cautery, the recurrence rate was nearly double (19%). The practise of fulgurating infiltrated dura mater and bone was introduced by Cushing; as he himself said, two decades or more were needed to test the efficiency of this procedure (Cushing, 1938; pp. 449 & 742). The clinical experiences submitted here span that period of time, and they show clearly that the procedure is not reliable. Pathological studies have confirmed this. Tumour cells in the dura actually

treated are killed, but transdural spread escapes. Thermal coagulation is still to be recommended when surgical resection is impossible, but it must be recognised as a less certain method of extirpation. It is hard to say whether radiotherapy, given prophylactically to suspected areas of infiltration after resection, will be more reliable. Schurr (1962) is routinely employing it in this way, especially after sinus-sparing resections of parasagittal meningiomas. The experiences with radiotherapy submitted here are not encouraging. Certainly, radiation has failed to prevent several of the more rapidly growing tumours from recurring; perhaps supervoltage techniques will be more effective, but the dangers of radiation necrosis have not yet been fully explored.

Not all contemporary surgeons accept the importance of the distinction made here between these two grades of ablation. Guillaume et al (1957) for example class both together as exérèse totale, and do not appear to have misgivings about the ultimate likelihood of recurrence. Other authorities, most notably Olivecrona (Hoessly & Olivecrona, 1955), evidently accept the principle of the distinction, but in practice prefer the more conservative procedure whenever the risks of radical surgery are considerable.

These risks must be assessed individually. Each patient presents special problems, and generalisations must be made with reserve. It can however be said that the ultimate risks of conservative resections are not slight. The disabilities caused by recurrent parasagittal meningiomas - the group above all others with which conflicts in operative policy arise - are very terrible and not rare. They give an incentive to extend the application of the more radical procedure. Hoessly & Olivecrona (1955) have advised that a conservative resection should be performed initially, and a more radical procedure when recurrence later takes place. This is often prudent and correct management. But the policy has drawbacks. The recurrent tumour may inflict bilateral cerebral damage, no less severe than would have resulted from a more radical primary resection. Furthermore, it may be much less operable: it may have infiltrated along the falx, or into the brain, and it may have seeded into the operative cavity. In the 1962 survey, it appeared that these dangers are greater than had been thought at first. Finally, even after many years, the venous sinuses adjacent to the tumour may still be patent: resection may be as hazardous as ever.

There is nothing in the material submitted here to

challenge the accepted belief that certain sinus resections are prohibitively dangerous. The posterior two thirds of the superior longitudinal sinus, and the straight sinus, can only be excised if there is an adequate collateral circulation. Those who claim the contrary have yet to prove their case (Jaeger, 1951; Bassett, 1955). Opportunities for the more radical resection offer when these sinuses are occluded. It is suggested that more systematic preoperative determination of sinus patency by angiographic studies (employing the subtraction technique) may be valuable. There is a good deal of variation in venous patterns; more exact knowledge of the significance of this may permit more frequent radical operations. This is true not only of the parasagittal meningiomas, but also of those related to the straight and transverse sinuses. Whether there is a place for sinus replacement by vein graft is hard to say; there appears scope for trial of this where a previous recurrence, or a very active cytology, make radical treatment obligatory. It would probably be best performed as a second-stage procedure.

However, it is necessary to retain a sense of proportion about the desirability of more radical ablation. Of the recurrences verified in this survey,

it seems in retrospect that the majority could theoretically have been prevented by more radical resections of dura and extradural extension. There was however an important minority of recurrences which apparently resulted from invasion of brain. This was especially common with the undifferentiated meningiomas and other more malignant forms. Such recurrences would not be avoided by the more radical procedure, or indeed by anything short of block cerebral resection. Similarly, some "recurrences" doubtless represent the appearance of independent primary tumours. This type of recurrence can only be avoided if the presence of multiple growths is detected by neuro-radiological procedures or at operation. It is considered an important condition by Volynkin (1955) and by French authors, and no doubt it is, though only one patient in the Oxford series is known to have died from this cause. Finally, there are probably recurrences arising from implanted tumour fragments, from overlooked nodules, and from vestiges of the meningiomatous subdural fringe. These may perhaps be prevented by meticulous operative technique, but are certainly not the consequences of an insufficiently radical resection.

Furthermore, serious and distressing as recurrences are, they are often long delayed. When the cytology

indicates a relatively slow growth rate, one can hope for survival at least as long as the average periods of freedom found in this survey. When recurrence does take place, it may often be successfully dealt with. Recurrent meningiomas are sometimes hard to diagnose and often awkward to treat, but in many instances satisfactory secondary resections have been achieved.

It would certainly be wrong to urge operative policies which might seriously increase the risk of post-operative disability. The consequences of infarction in the territory of major cerebral arteries and of bilateral paracentral injury are a strong deterrent: recurrence is the penalty of insufficient surgery, but disability to some extent attends on resections of too radical character.

Admittedly, the statistics relating to disability are not easily fitted into the general pattern. Operative deaths and post-operative recurrences have been shown to express different aspects of the pathology of the meningiomas, some well known and some less familiar. Some residual disabilities can also be interpreted in this light, especially those resulting from the direct local effects of meningiomas. Others represent operative injury, and it is often exceedingly hard to distinguish

the two. Others again entail broader considerations. Post-operative epilepsy for example can be considered as a manifestation of local brain damage. But it has only occurred in 45% of patients, and in these it has varied quite unpredictably in its severity and duration. Almost certainly, some intrinsic constitutional factor is the variable, rather than the pathology of the local lesion. So also various other disabilities can only be understood in the setting of the patient's psychological and physical constitution and his social environment.

In summary, the experiences analysed in this thesis do not point towards any revolutionary change in the management of intracranial meningiomas. These tumours are justly considered to be among the most favourable of intracranial tumours from a surgical viewpoint. The statistics submitted here, and indeed most of the published reports, have shown that the results of treatment still leave considerable room for improvement, but it seems reasonable to hope that this will come in part from the better application of methods now available. It has been suggested that earlier diagnosis will contribute considerably; greater awareness and the widespread use of contrast radiographic investigation appear already to be achieving this, with consequent improvement in the end-

results of treatment. The investigations reported here have however been more concerned with the pathology of the meningiomas and its implications in operative surgery. It has been shown that this is a complex subject, and that the meningiomas exhibit much diversity in their biological properties. There has been hitherto a tendency to view the treatment of the meningiomas as the management of a uniform a disease entity, modified only by factors of gross anatomy. It is suggested that the time is now ripe for more detailed consideration of the problems presented in each individual case. The present survey has emphasized the value of radiographic and cytological examinations in this context. Their utility has been evident even with the standard techniques employed in the past; doubtless, still more will be possible with the methods, both radiological and pathological, now being developed.

CHAPTER XI

SUMMARY

1. Review of the literature suggests that there is still disagreement over certain aspects of the pathology of the meningiomas; the frequency and significance of "malignant" behaviour seem especially controversial.

2. Although some authorities express remarkable optimism concerning the curability of the meningiomas, it is evident that the results of surgical treatment are not always satisfactory, either in terms of survival, or with regard to residual disability.

3. The gross and microscopic pathology of 242 intracranial and 4 intraorbital meningiomas has been analysed. The opinions formed have been partially tested by reviewing the clinical progress of certain of the patients concerned after seven years. They also accord with experience obtained in routine neuropathological examination of an additional series of 46 tumours.

4. It is confirmed that the meningiomas are locally invasive tumours, and especially apt to invade dural venous sinuses. Limited invasion of the brain may

also occur, and extracranial metastasis has been found terminally in three patients.

5. Although the meningiomas are usually considered as a single entity, it has been found that their biological characters vary from malignancy in the fullest sense to extreme innocence. The correlation of clinical behaviour and microscopic appearances is not always close, and it has seemed undesirable to identify a specific category of malignant meningiomas on microscopic evidence. However, a grading of cellular activity, expressed in terms of tumour growth rate, has given useful prognostic information, to some extent on the probability of recurrence, but still more in forecasting its likely chronology.

6. The results of surgical treatment in three series of meningiomas, presenting in the periods 1928-1938, 1938-1954, and 1956-1962, have been determined as fully as possible. These three series comprise together 390 patients, in almost all of whom curative operation was attempted.

7. The mortality after such operations was high: in the most recent series, it was 13%. Reasons for this vary; however, intimate relations of the tumours to

vital arteries and vital parts of the brain were, and remain, of particular importance. Misinterpretation of the secondary cerebral effects of meningiomas has also contributed to the mortality by causing errors in diagnosis.

8. Operations on intracranial meningiomas vary in extent; this is dictated by the regional anatomy as well as by the pathology of the tumour. A system of classification recognising five grades of operation is proposed.

9. Incomplete tumour removals (grades III-V) are becoming rarer: in the most recent series, only 18% of operations were considered to be incomplete ablations. However the majority of complete ablations did not involve excision of the tumour's dural attachment; a distinction is made between those radical operations in which this is done (grade I resection), and those in which the area of attachment is cauterised (grade II resection). Pathological reasons for the superiority of the grade I resection are presented.

10. The incidence of recurrence has been studied in 266 patients who survived operations performed between

1928 and 1954. Recurrences have occurred more frequently than in the published reports; this is attributed chiefly to the length of the periods of observation. After operations of grade I, the ideal of a radical resection, the incidence was 11%; after operations of grade II, it was 19%. Long survival after grossly incomplete resections was encountered.

11. The most important single pathological cause of recurrence was invasion of dural venous sinuses; cerebral infiltration, invasion of bone, implant metastasis, and multifocal neoplastic change also contributed.

12. The diagnosis of recurrent meningiomas presented some interesting problems: these are discussed, together with the differential diagnosis from post-operative cerebral gliosis and cerebral vascular disease. The management of recurrent meningiomas is also discussed, together with the results obtained.

13. Radiotherapy was administered to 36 patients. The results have been extremely disappointing, but there is reason to believe that limited benefit was derived in several patients. Severe radiation necrosis was

seen on two occasions. It is however possible that newer methods now under trial may be more efficient.

14. Review of the operative procedures employed, and the results obtained, suggests that earlier diagnosis might have been beneficial in certain patients. The value of this should however not be over-estimated.

15. No fundamental alteration in surgical policies can be suggested. It is however submitted that a fuller use of pre-operative phlebography might aid in planning radical extirpations. It is also suggested that when the propriety of a radical resection is in doubt, it may be wise to wait until the histology and cytology of the tumour have been studied: the finding of a rapidly growing meningioma, and particularly one of undifferentiated variety, may justify more radical operation as a second stage.

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Papers incorporating some of the material presented in this thesis are mentioned in the text. In addition, observations on the diagnosis of recurrent meningiomas (contained in chapter VIII) were presented at a joint meeting of the Society of British Neurological Surgeons and the Polish Neurosurgical Association, held in Warsaw in September, 1962.

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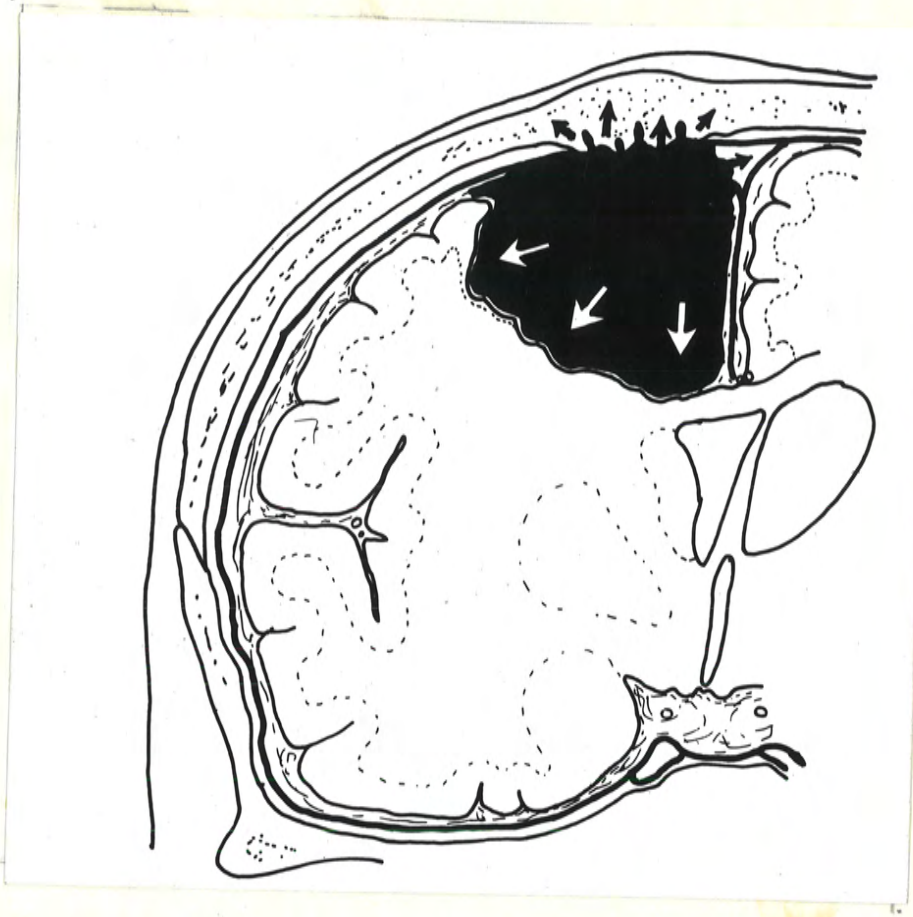
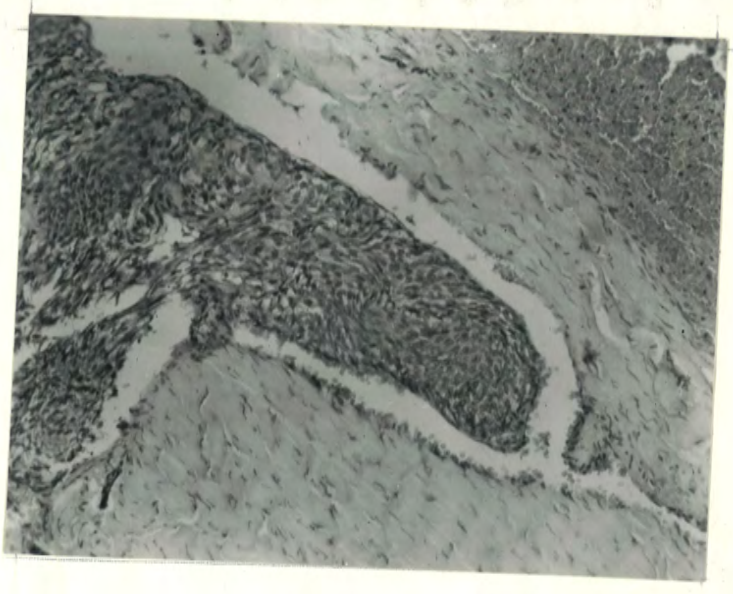
PATHOLOGY.

Figure i. Growth of a parasagittal meningioma (diagrammatic). Invasion of dura, bone, and superior longitudinal sinus is indicated by black arrows; white arrows indicate expansion into the cerebral hemispheres. The leptomeningeal barrier is preserved, but a tongue of tumour expands into the subdural space on the lateral margin of the tumour.

Figure ii. Permeations of dura by meningioma: a mass of tumour is seen in the lumen of a vein (H. & E. X 160; Oxford case).



i

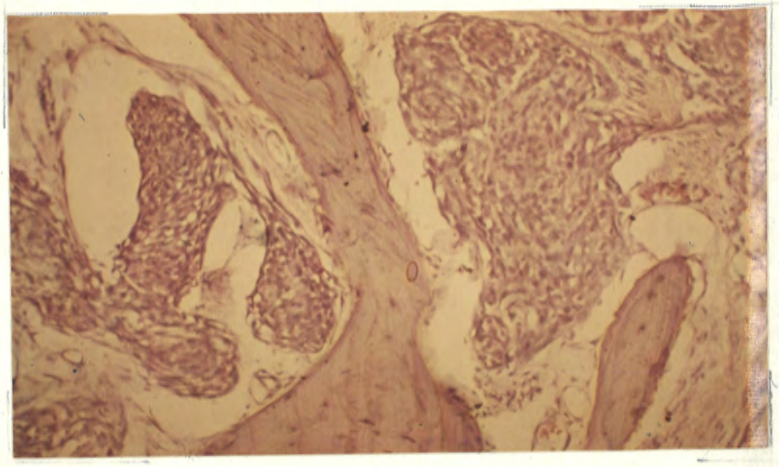


ii

Figure iii. Invasion of bone; in this section, an osteolytic effect is evident and reactive hyperostosis is not prominent. (H. & E. X 150; Adelaide case).

, (a) X 150 (b) X 550

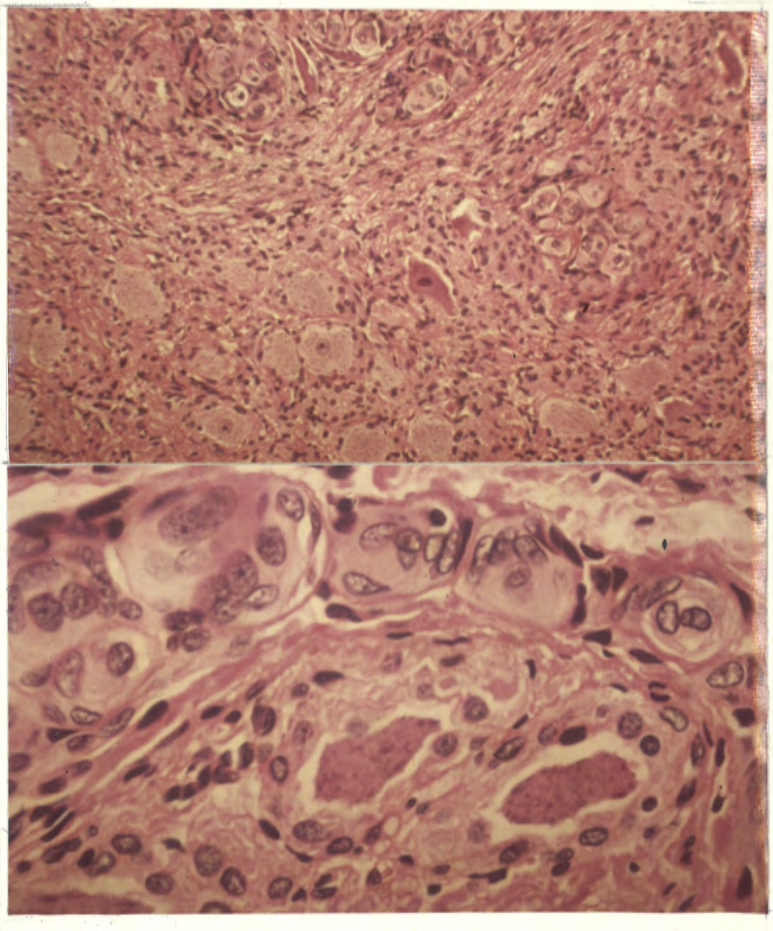
Figure iv. Invasion of ciliary ganglion by an orbital meningioma. The neurons show well marked degenerative changes. (H. & E.; Adelaide case, described on page 181).



iii

a.

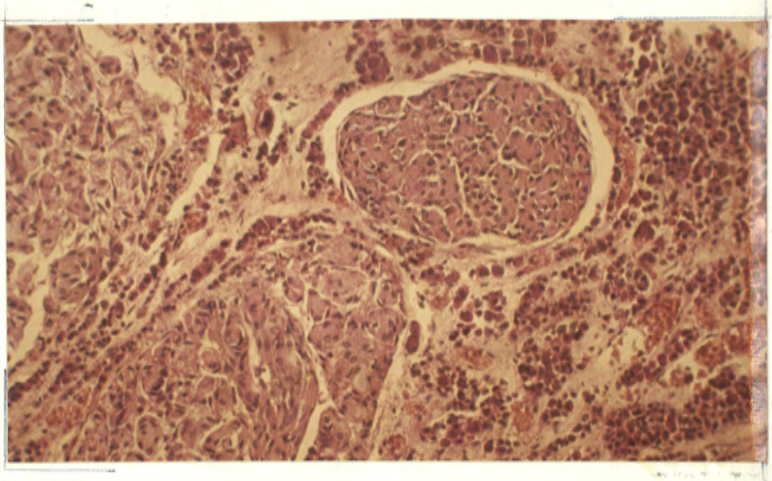
b.



iv

Figure v. Invasion of anterior hypophysis by a recurrent sphenoidal ridge tumour. In this field, the tumour cells form cords in the lumen of a vessel. (case 1, appendix C). H & E; x 150 & 550.

a.



b.

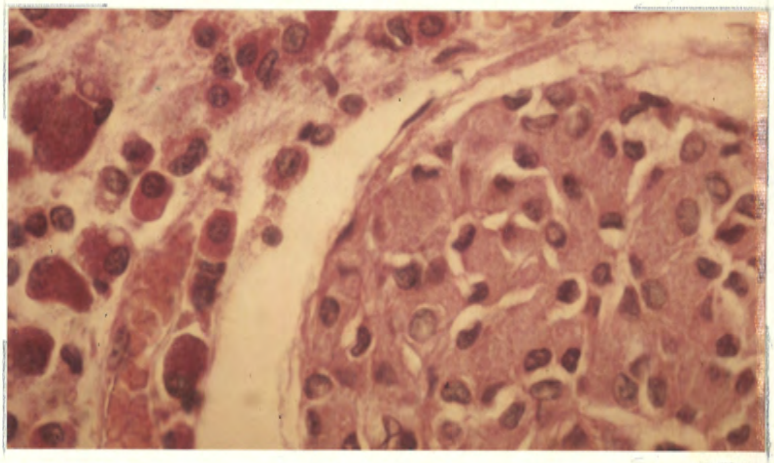
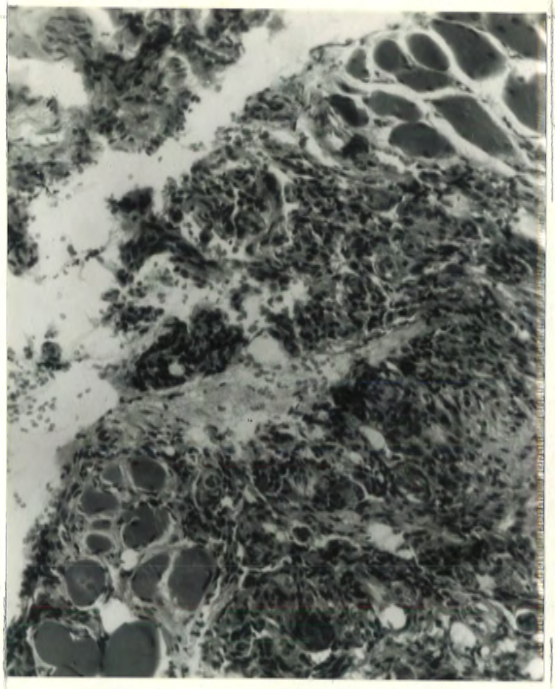


Figure vi. Unusual manifestations of invasive growth:

(a) Submucosal spread in the middle ear, from a petrosal meningioma (H. & E. X 140; Oxford case).
(b) Infiltration of temporalis muscle by a sphenoidal ridge meningioma (H. & E. X 140; Oxford case).

Figure vii. Invasion of brain by a parasagittal meningioma. There is marked hyperaemia around the islands of tumour cells. (H. & E. X 150; Adelaide case - biopsy).



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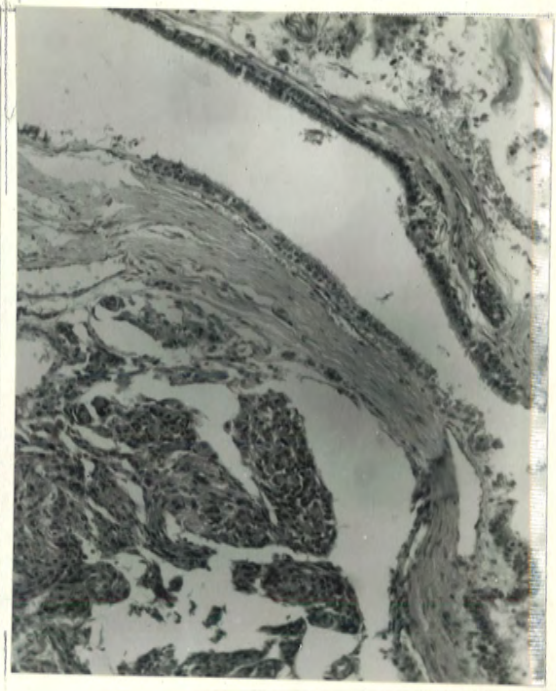
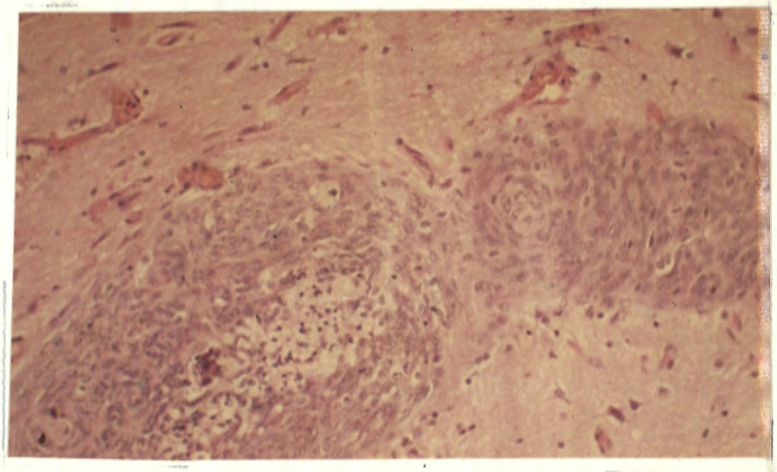


a

vi



vii

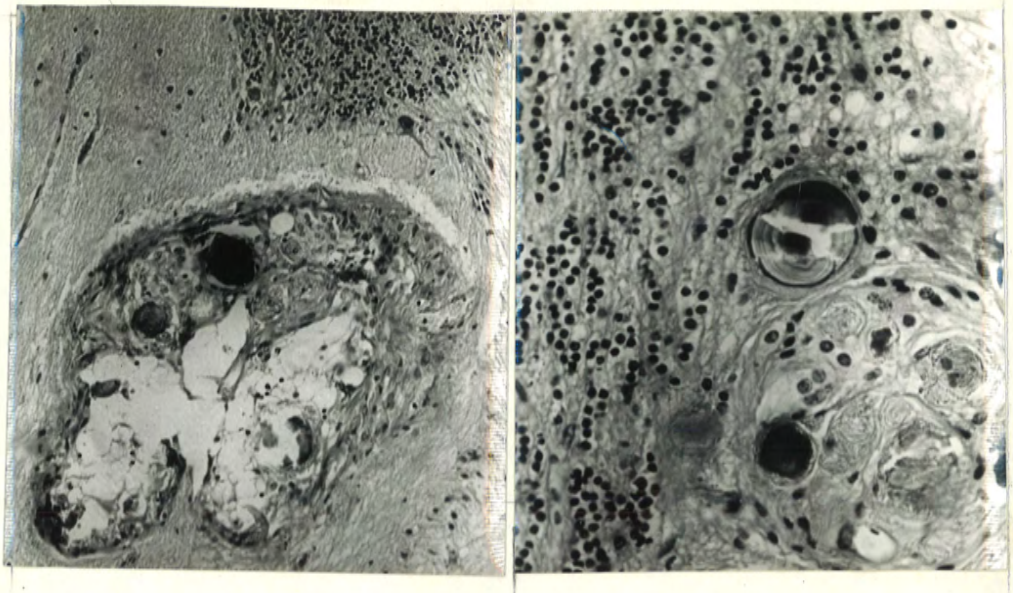
PATHOLOGY.

Figure viii (a) Invasion of cerebellar cortex by a recurrent sphenoidal ridge tumour en plaque. This section was obtained at autopsy seventeen years after the primary tumour resection. (H. & E. X 100; Oxford case).

(b) The same (H. & E. X 250). The absence of cellular reaction to the tumour is well shown, as are the numerous psammoma bodies.

Figure ix. Fibroendotheliomatous meningioma. This section was taken from the first operation on the recurrent parasagittal meningioma described as case 7 in appendix C. (H-van Gieson X 250).

Figure x. The same tumour at the fourth operation. Mitotic figures are numerous (H-van Gieson X 250). This change in cellular activity is unusual: but see Cushing (1938) and Burmeister and Wendt (1962) for comparable cases.



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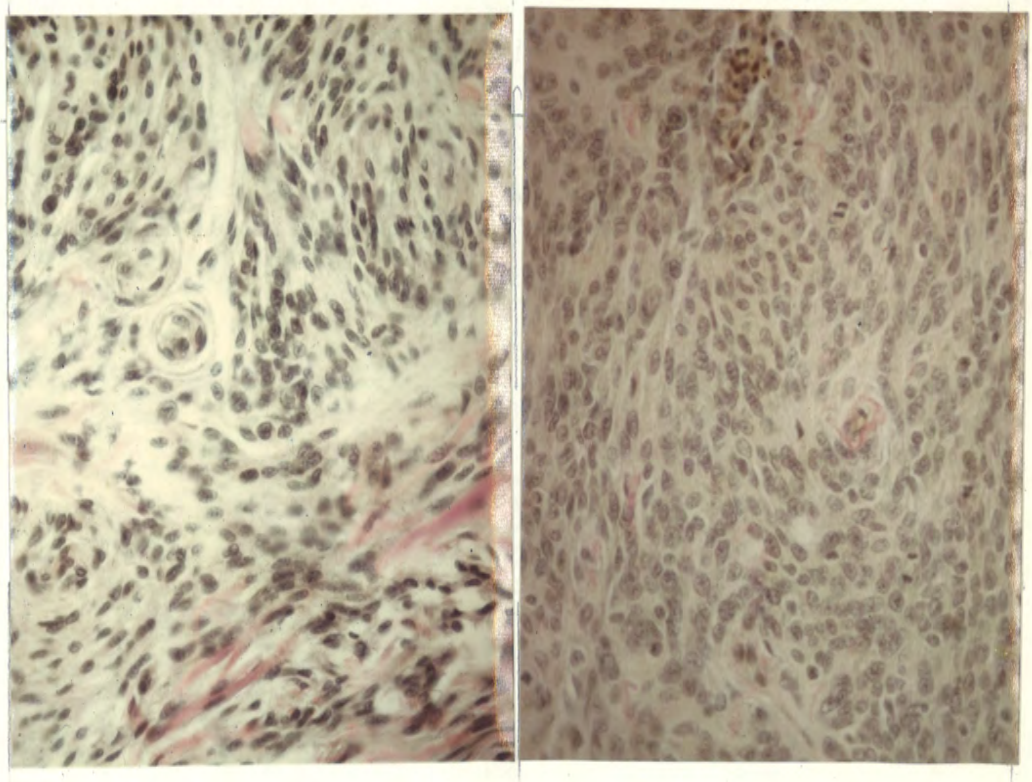
viii



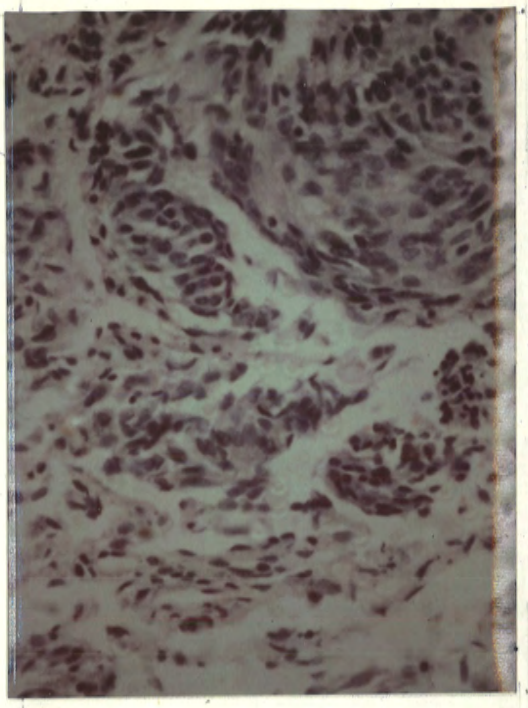
ix x

Figure xi. Pulmonary metastasis from the tumour represented in figure ix & x.

Figure xii. Typical endotheliomatous meningioma, well differentiated into small whorls. (H. & E. X 550; Adelaide case, described on page 136).

Figure xiii.(a) Typical fibroblastic meningioma (H-van Gieson x 250; Oxford case).

(b) Xanthomatous area in the same tumour. Numerous cells with foamy cytoplasm are seen. (H-van Gieson X 250).



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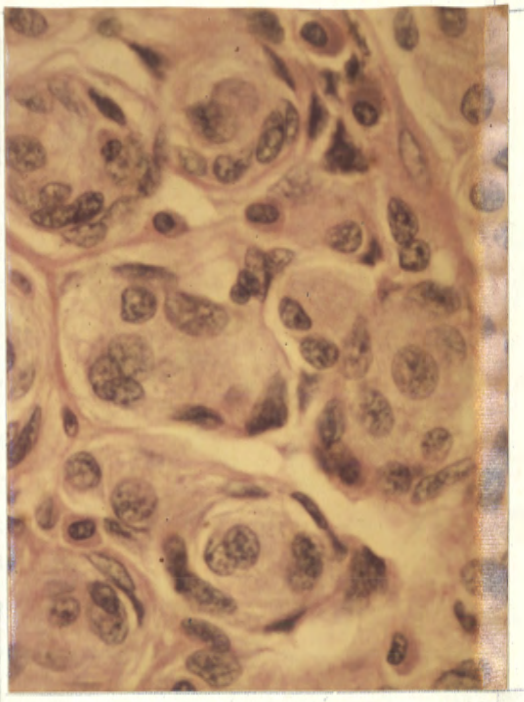
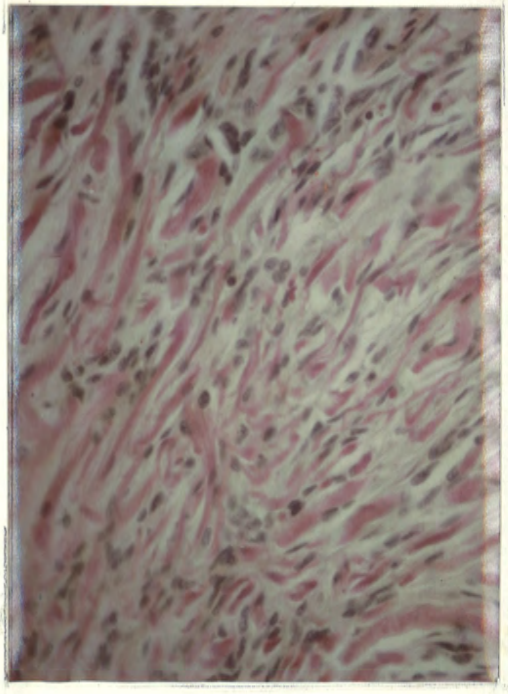
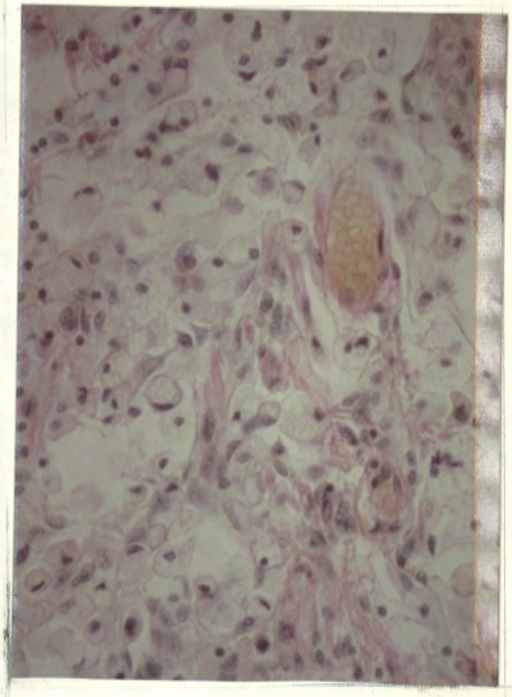


xii



a



b

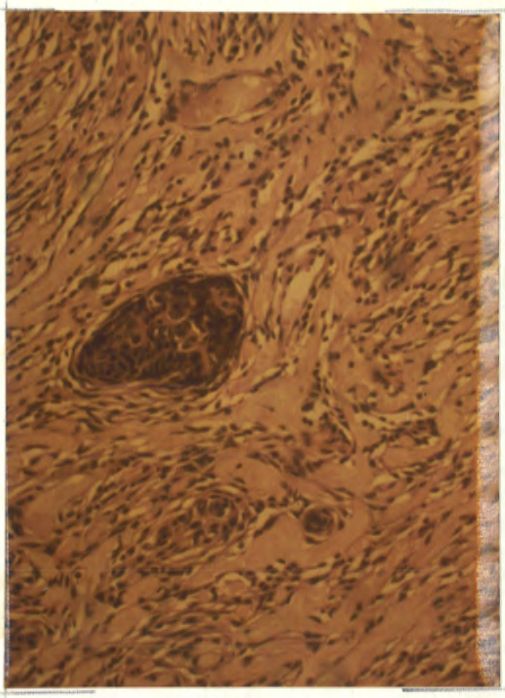
xiii

Figure xiv. Fibroblastic meningioma, with small nodule of endotheliomatous tissue in centre of field. Appearances like this have sometimes been regarded as evidence of metastatic carcinoma deposited in a meningioma. (H-van Gieson X 150; Adelaide case).

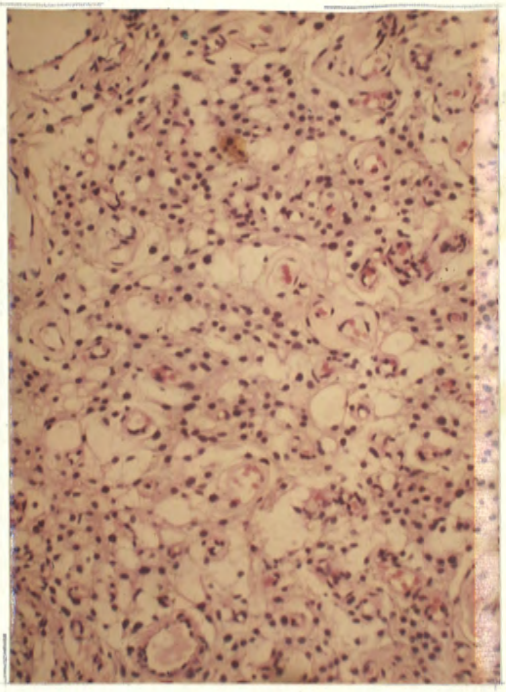
Figure xv. Typical angioblastic meningioma. This type has shown no malignant propensities. Angiography usually shows a dense homogeneous tumour blush (H. & E. X 170; Adelaide case).

Figure xvi. Undifferentiated meningioma. This tumour was in the cerebellopontine angle, and recurred very rapidly after a grade III resection. Special stains showed delicate intercellular reticulin fibrils (H. & E. X 250); Oxford case).

Figure xvii. Melanoblastic meningioma. This case is not included in the present series. The tumour was in the subtemporal situation, and was incompletely removed (grade IV ablation). She remains well, five years later. (H & E X 550; Oxford case).



xiv



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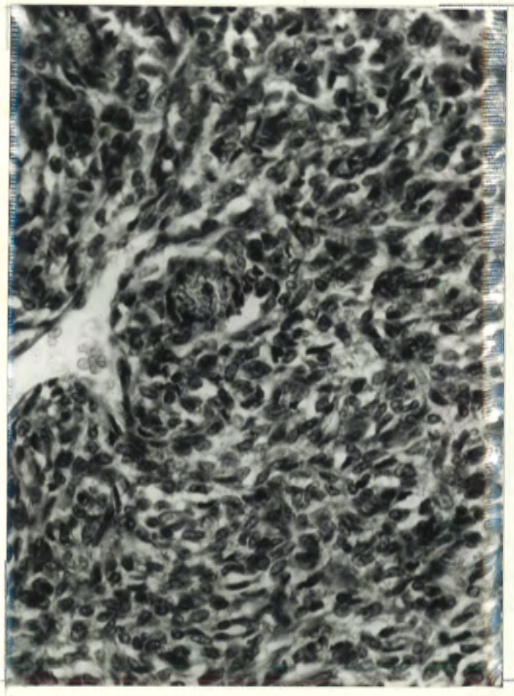
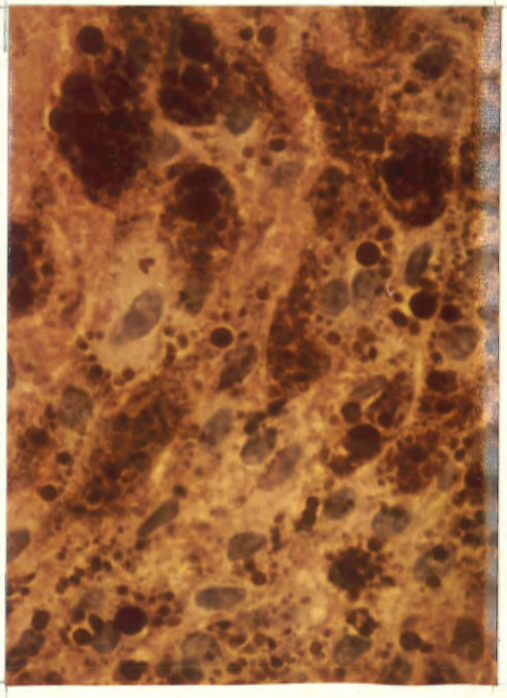


xvi



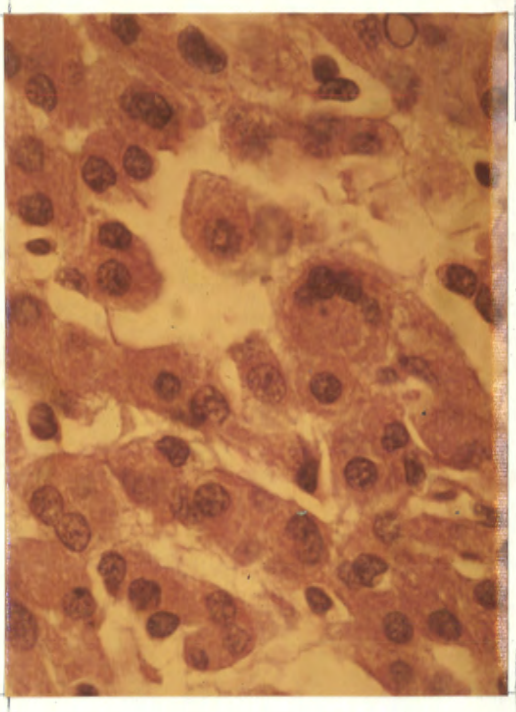
xvii

PATHOLOGY : CEREBRAL REACTIONS

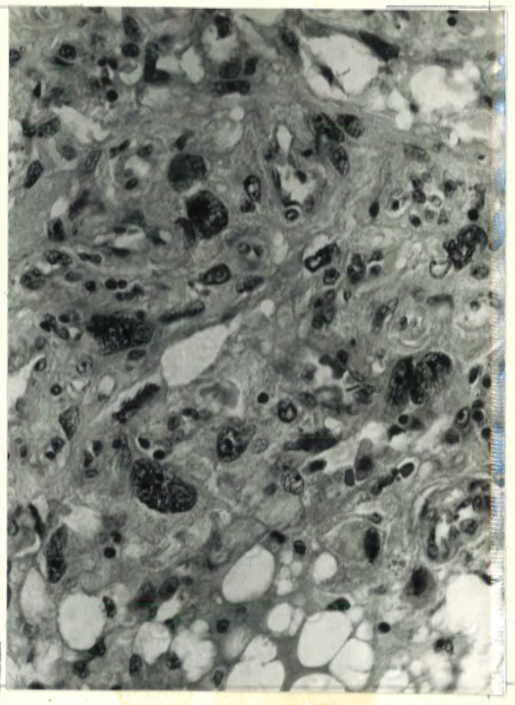
Figure xviii. Endotheliomatous meningioma of unusual histology: the cuboidal cells are arranged in cords rather suggesting liver tissue. This tumour recurred twelve years after a primary grade II resection, and again from independent foci fifteen months later. In all three biopsies, the appearances were indistinguishable. The tumour has not recurred in the last seven years. (H. & E. X 550; Case 9, appendix, C).

Figure xix. Predominantly angioblastic meningioma, with xanthomatous areas. Many cells have giant nuclei, and there is marked pleomorphism. However, there are no mitoses. There has been no recurrence since this tumour was removed by a grade II ablation nine years ago (H. & E. X 250; Oxford case)

Figure xx. Section of cerebellum, indented and compressed by a recurrent tentorial meningioma. The folia on the superior surface are flattened, with loss of cellular constituents, especially Purkinje cells, but the general structure of the folia is recognisable (H. & E. X 2.8; case 12, appendix C).



xviii



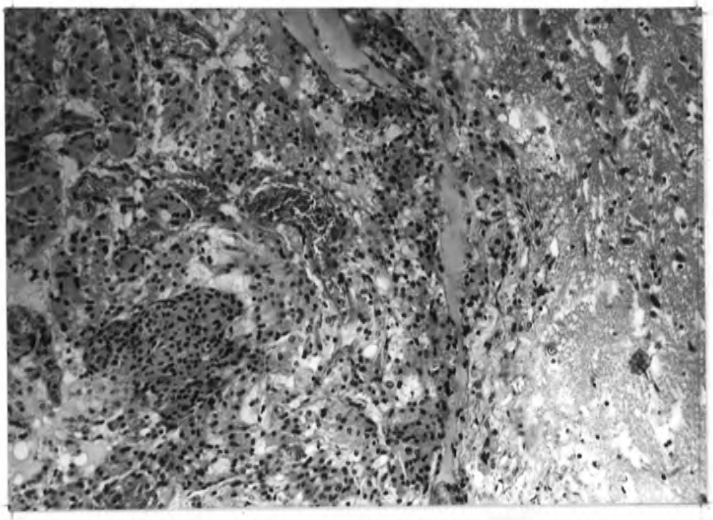
xix

xx

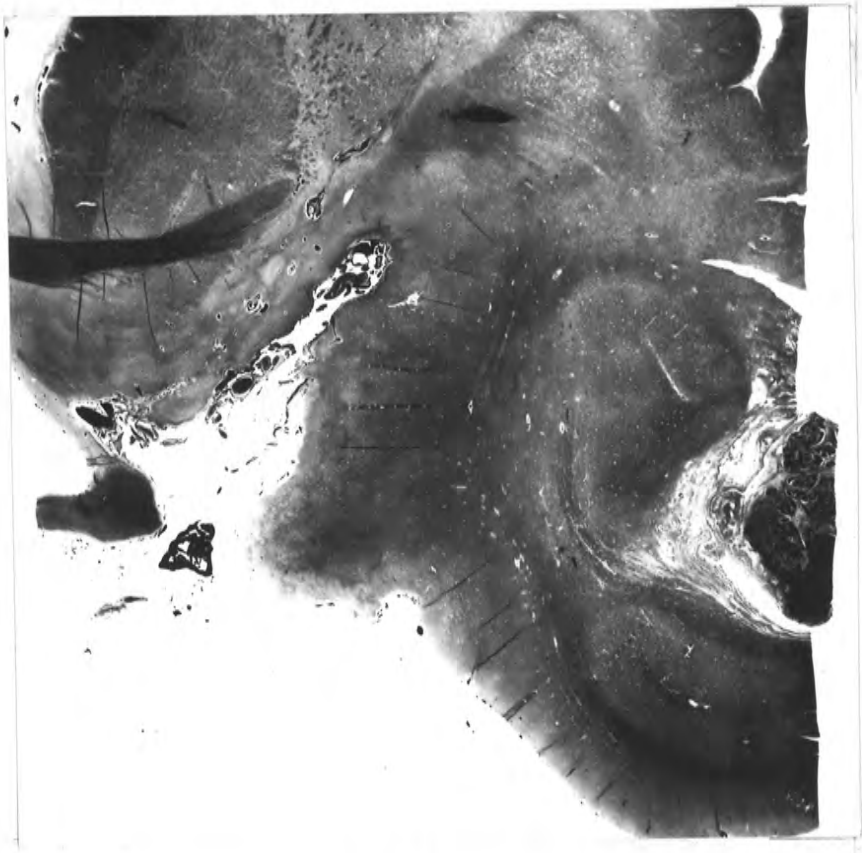
PATHOLOGY : CEREBRAL REACTIONS

Figure xxi. Cerebral cortex, showing effects of compression by large meningioma. Cortical lamination is lost, but isolated neurons are recognisable and there is only a slight increase in glial cells. Large vascular channels are seen in the capsule of the tumour. (H-van Gieson X 100; Oxford case)

Figure xxii. Reactive cerebral changes near the margin of a tumour. On the right, at the point X, is seen a nodule of meningioma, disimpacted from its bed. This bed is seen as a partially necrotic zone, with small cystic formations. There is also some demyelination in the white matter of the temporal lobe (Weil X 2.8; Oxford case)



xxi



←X

xxii

PATHOLOGY : CEREBRAL REACTIONS

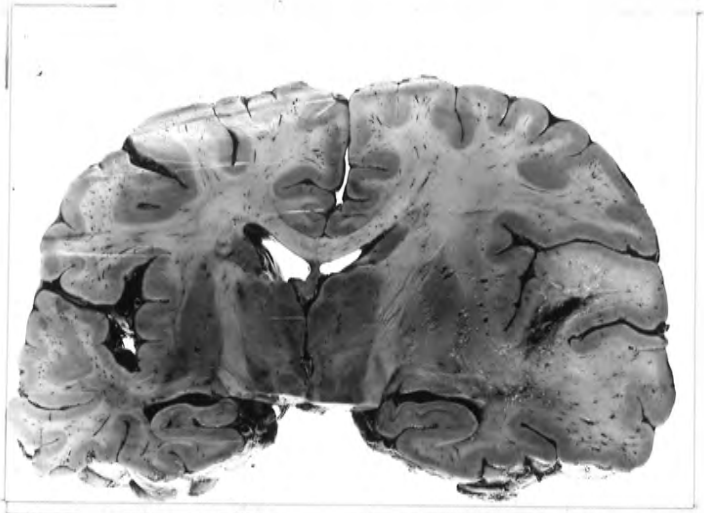
Figure xxiii Massive changes in the temporal lobe, resulting from vascular changes secondary to a relatively small meningioma of the sphenoidal ridge (Autopsy; Oxford case).

(a) Coronal section through mid-temporal region, showing intense oedema and necrosis below the sylvian fissure.

(b) Weil section of same region.

(c) The tumour: a small, very vascular mass behind the sphenoidal ridge. It had a well developed collagenous capsule.

a.



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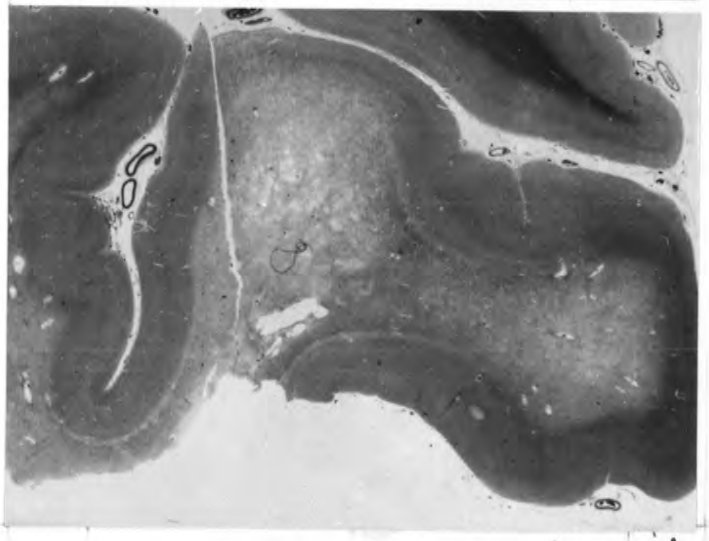
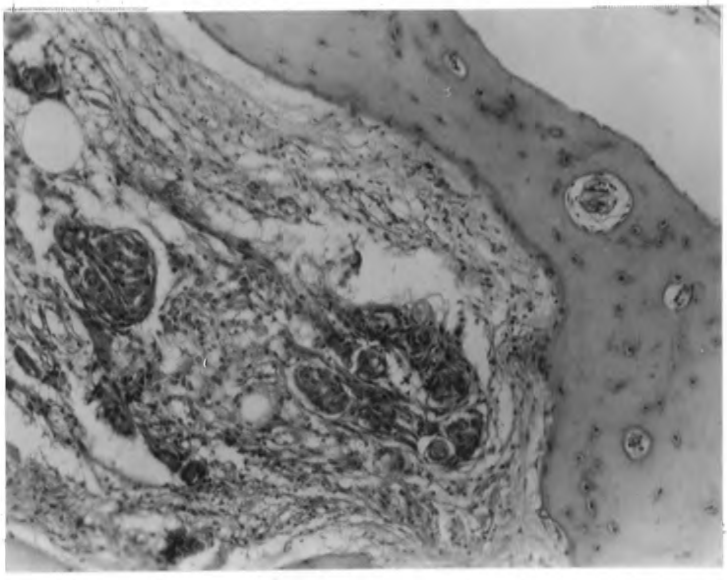


tumour

c.

Figure xxiv. Invasion of the roof of the sphenoid air sinus. In this case, an operation of grade II had been performed. The patient died by accident a year later. Autopsy sections showed no tumour in the dural attachment, but the underlying bone contained nests of meningioma cells. (H. & E. X 160; Oxford case). This case illustrates limitations in the value of fulguration.

Figure xxv. Operative photograph showing removal of a convexity meningioma. In this instance, the tumour is extra-arachnoid, and can be rolled out of its bed with very little decortication. This has not been the usual experience.



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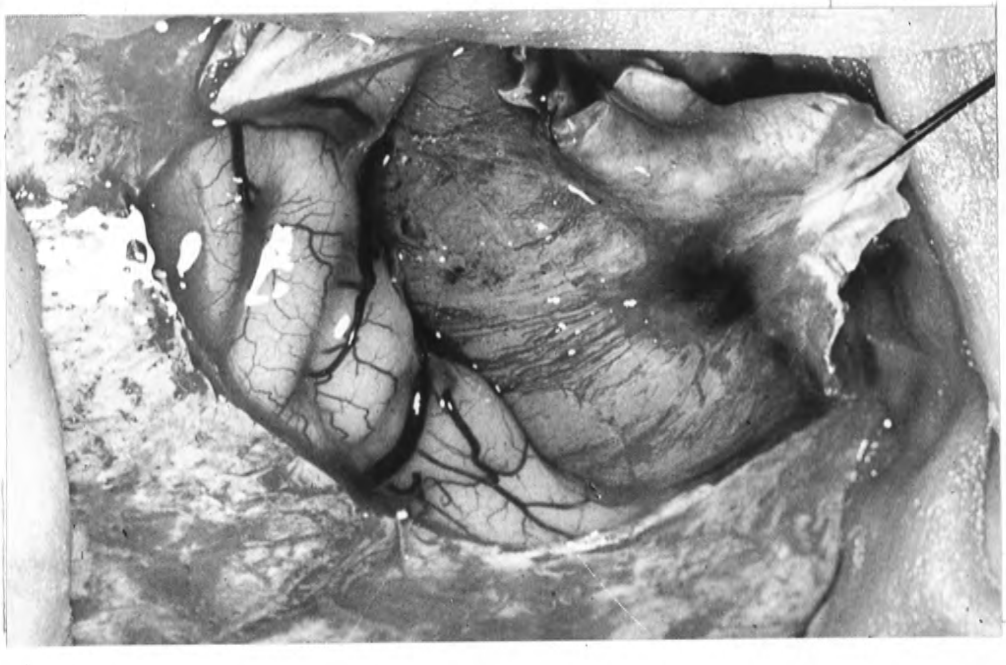


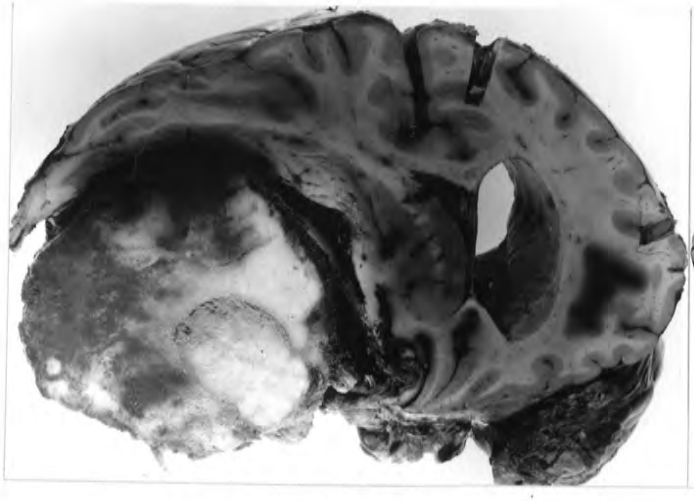
xxv

SURGICAL ANATOMY : SPHENOIDAL RIDGE MENINGIOMAS.

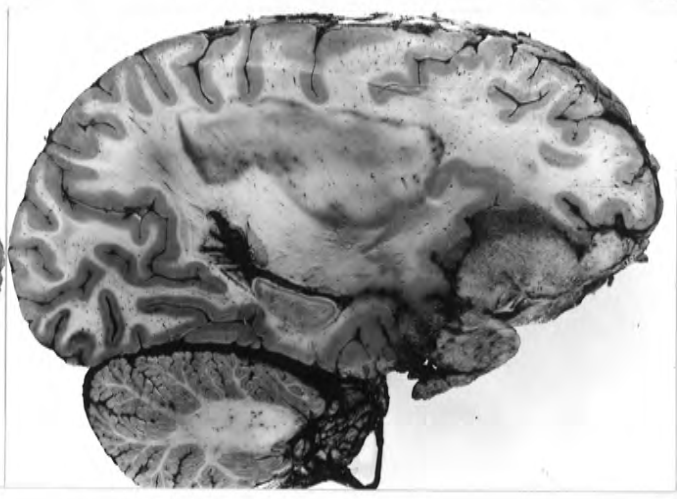
Figure xxvi. Large meningioma of sphenoidal ridge, probably arising initially from the middle third. A partial resection of the temporal component had been carried out shortly before death, and the magnitude of the residual mass was not fully appreciated (Oxford case).

Figure xxvii. Meningioma of inner third of sphenoidal ridge, indenting orbital surface of frontal lobe. (Oxford case).

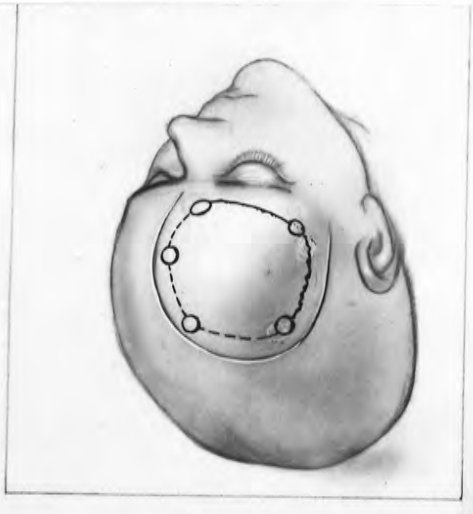
Figure xxviii. Operative exposure of a meningioma of the inner sphenoidal ridge, with suprasellar and intraorbital components. The tumour was completely removed (grade II ablation) and the patient was well when reviewed nineteen years later (London case; reported by Brain & Cairns, 1935).

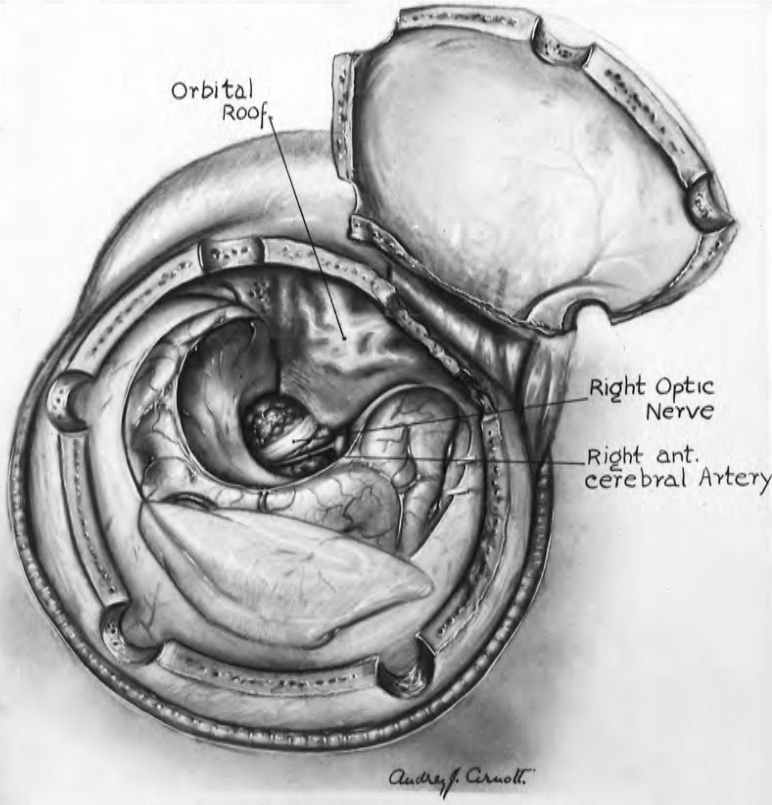


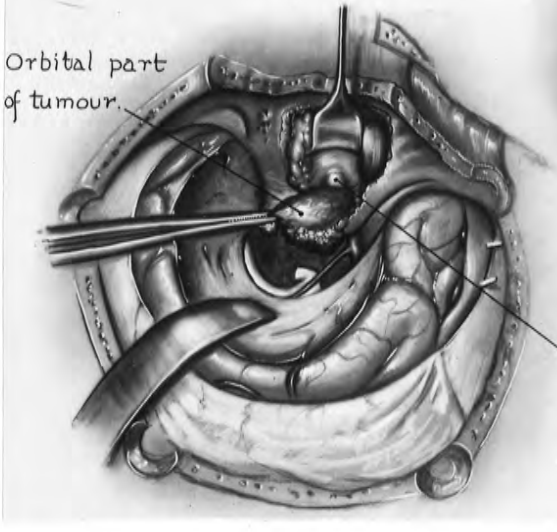
xxvi

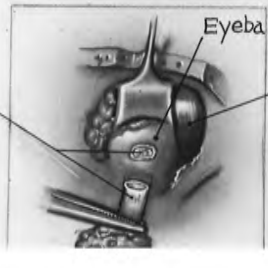


xxvii





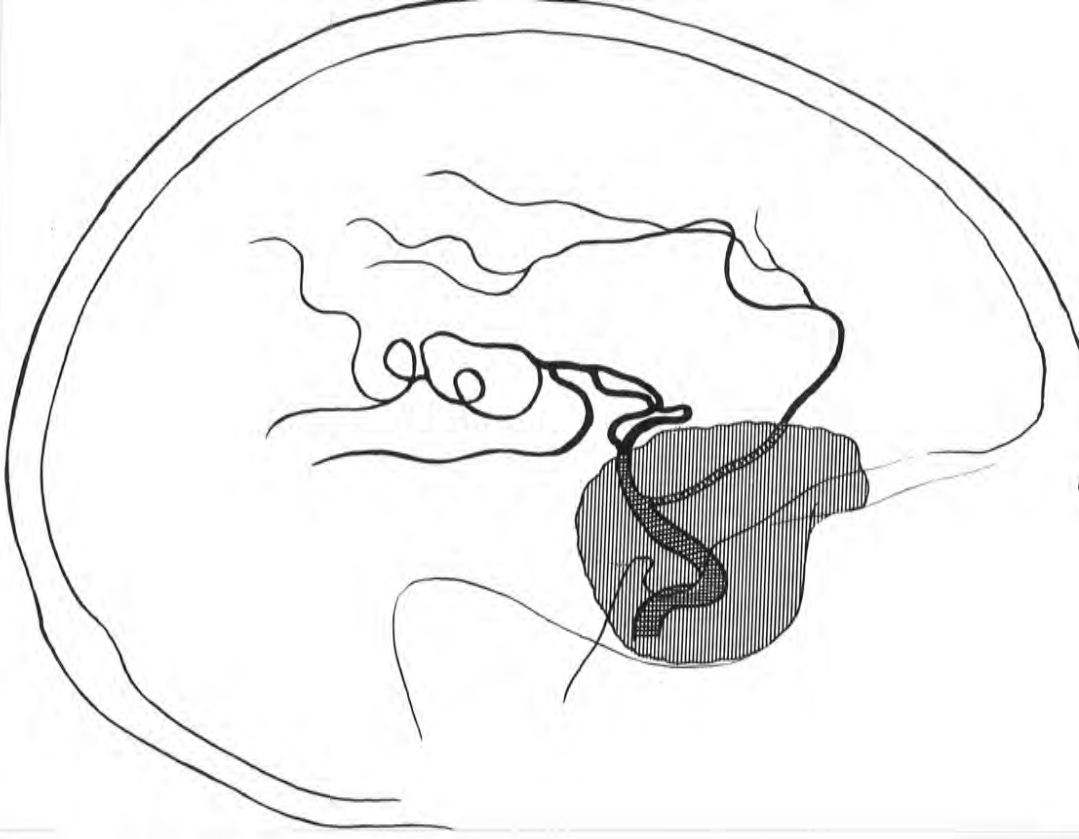




xxviii

SURGICAL ANATOMY : SPHENOIDAL RIDGE MENINGIOMAS.

Figure xxix. Diagram showing arterial relations of large sphenoidal ridge meningioma. The middle cerebral artery is bowed over the tumour. Operative removal is possible, and was achieved in this case, but there is considerable risk of hemiplegia. (From arteriogram, Oxford case).



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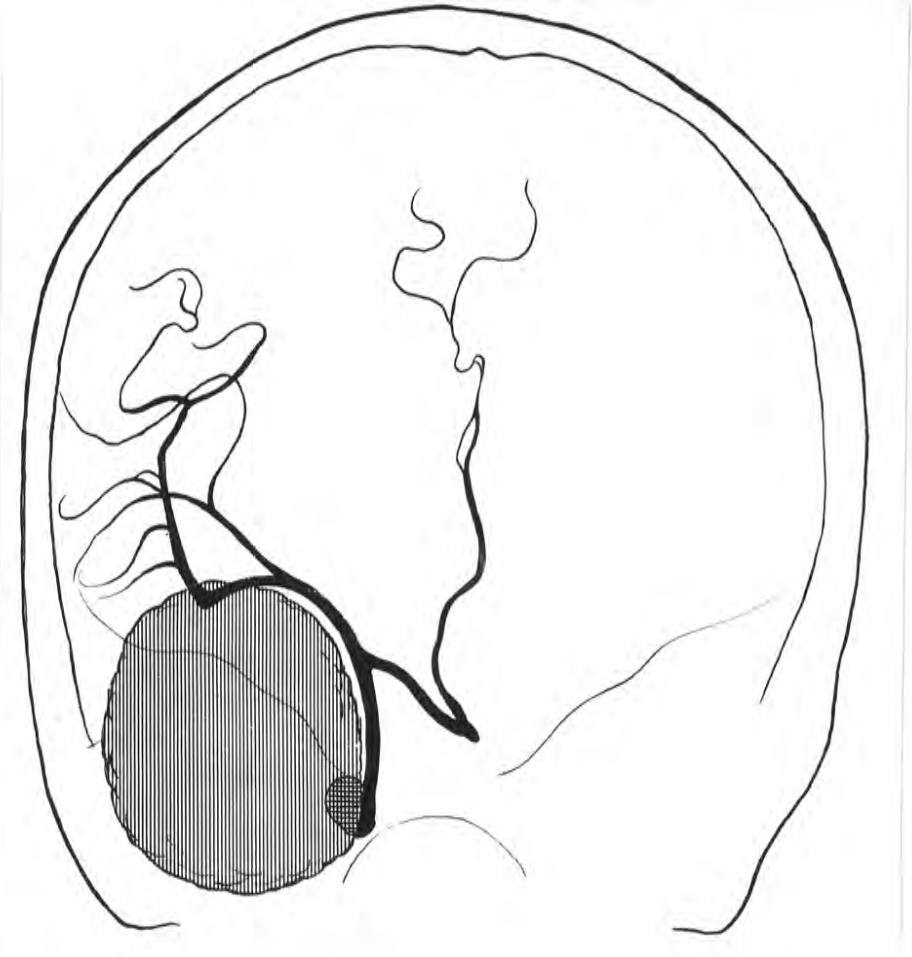


SURGICAL MANAGEMENT : SPHENOIDAL RIDGE

MENINGIOMA EN PLAQUE.

Figure xxx. Radiographs of sphenoidal ridge tumour en plaque, with hyperostosis involving the skull base.

(a) Condition before operation.

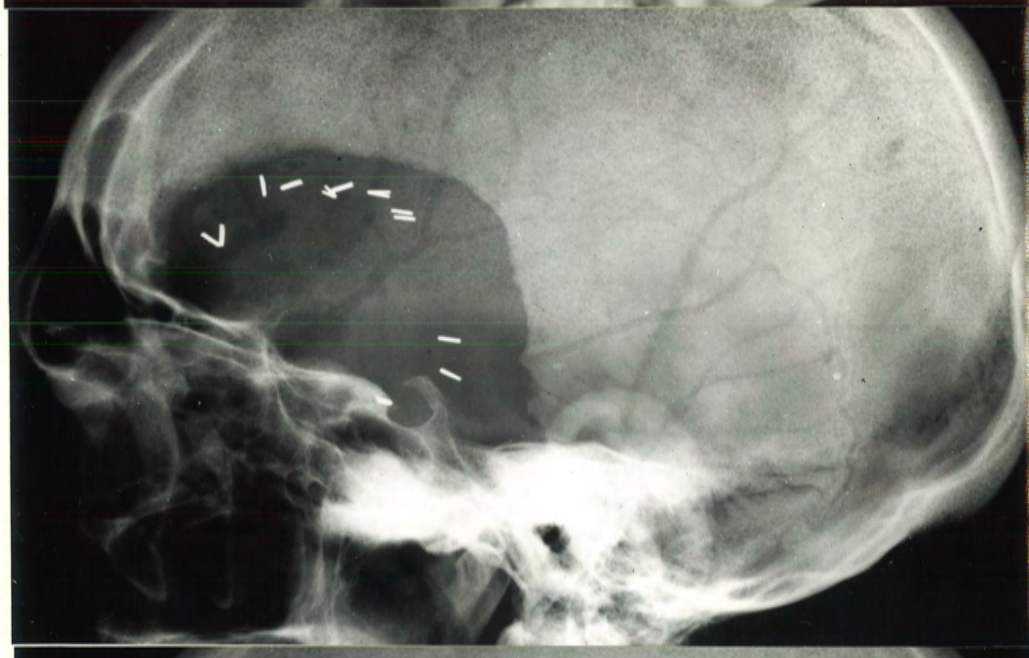
(b) Post-operative radiograph showing extent of resection. There is residual hyperostosis in the sphenoid bone.

(c) Radiograph taken thirteen years later. The sphenoidal hyperostosis has increased in size slightly, and there is massive additional hyperostosis in the roof of the orbit and zygoma. (Oxford case, described on page 144).

xxx

a.

b.



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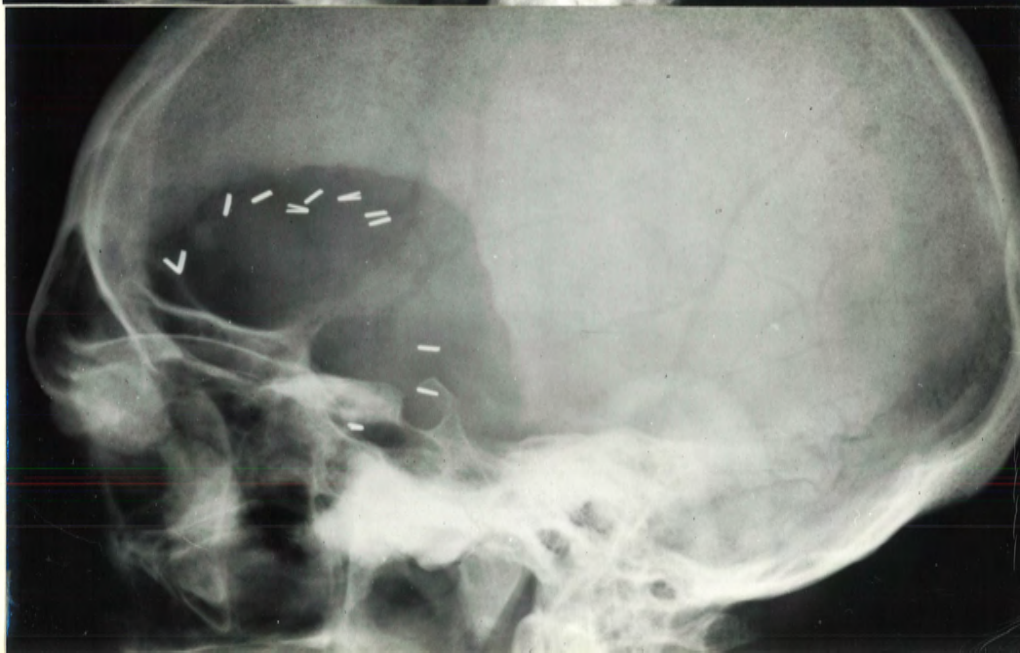


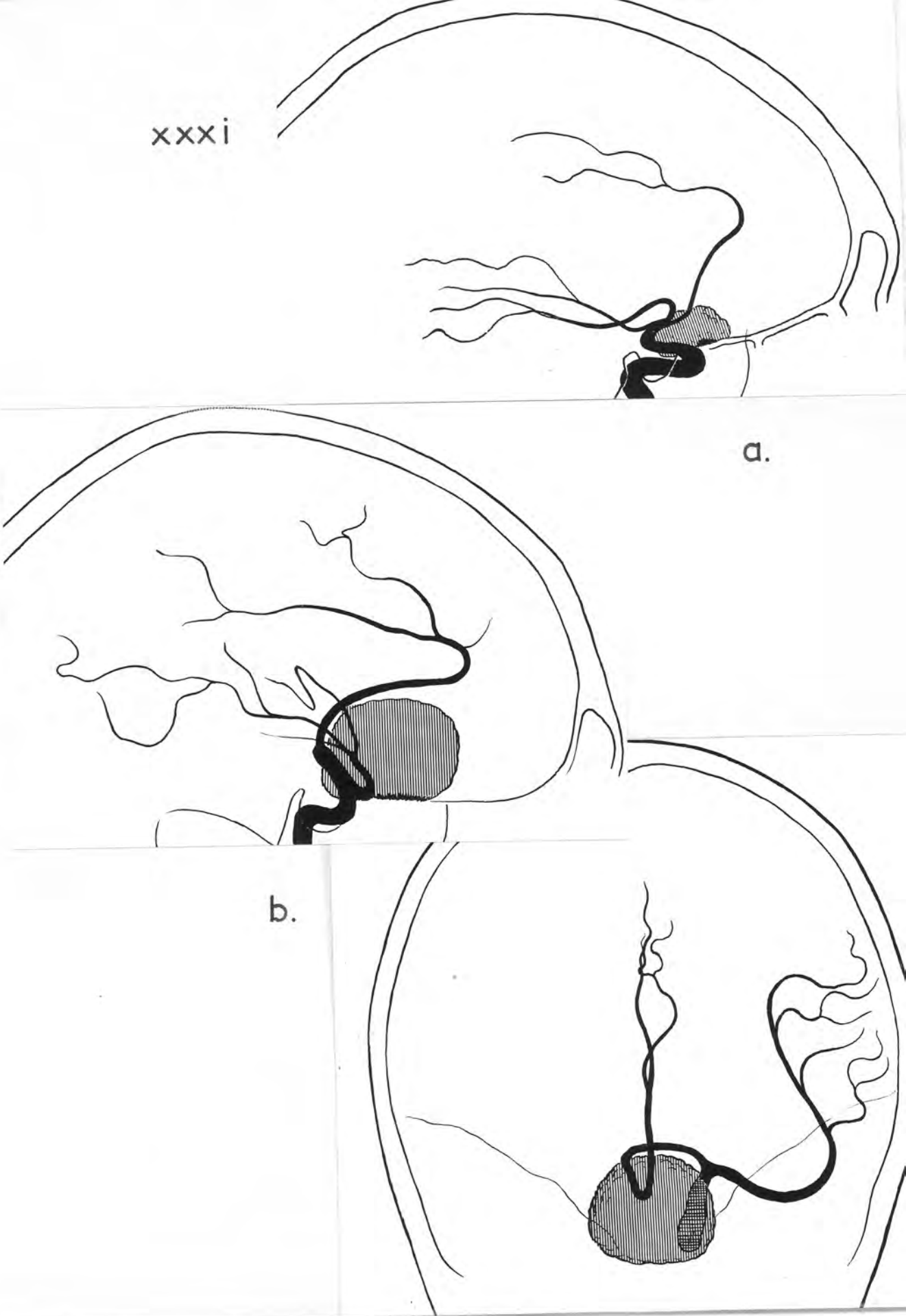
SURGICAL ANATOMY : SUPRASELLAR

MENINGIOMAS.

Figure xxxi. (a) Diagram showing arterial relations of small suprasellar meningioma. The anterior cerebral artery is in contact with the tumour, and slightly elevated by it. Operative removal is usually possible (From angiogram of Oxford case).

(b) Diagram showing arterial relations of larger suprasellar meningioma. The anterior cerebral artery is markedly elevated, and there is a grave risk of injuring it, and also of trauma to the internal carotid artery. In the patient whose angiogram is used in this figure, a complete resection was impossible (Oxford case).

xxxi



SURGICAL ANATOMY : OLFACTORY GROOVE

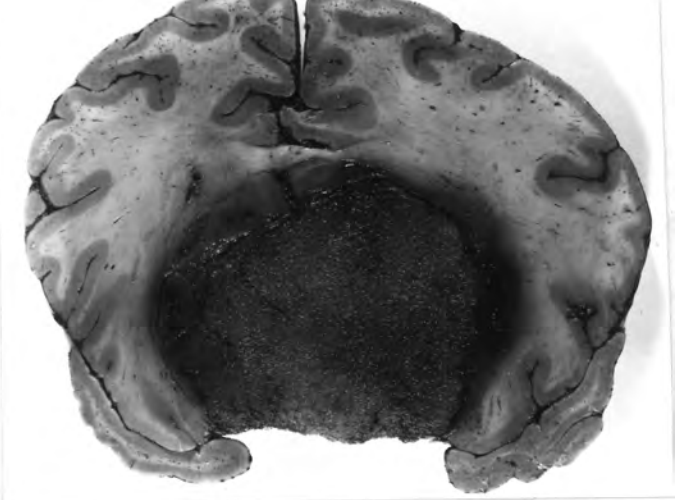
& PARASAGITTAL MENINGIOMAS.

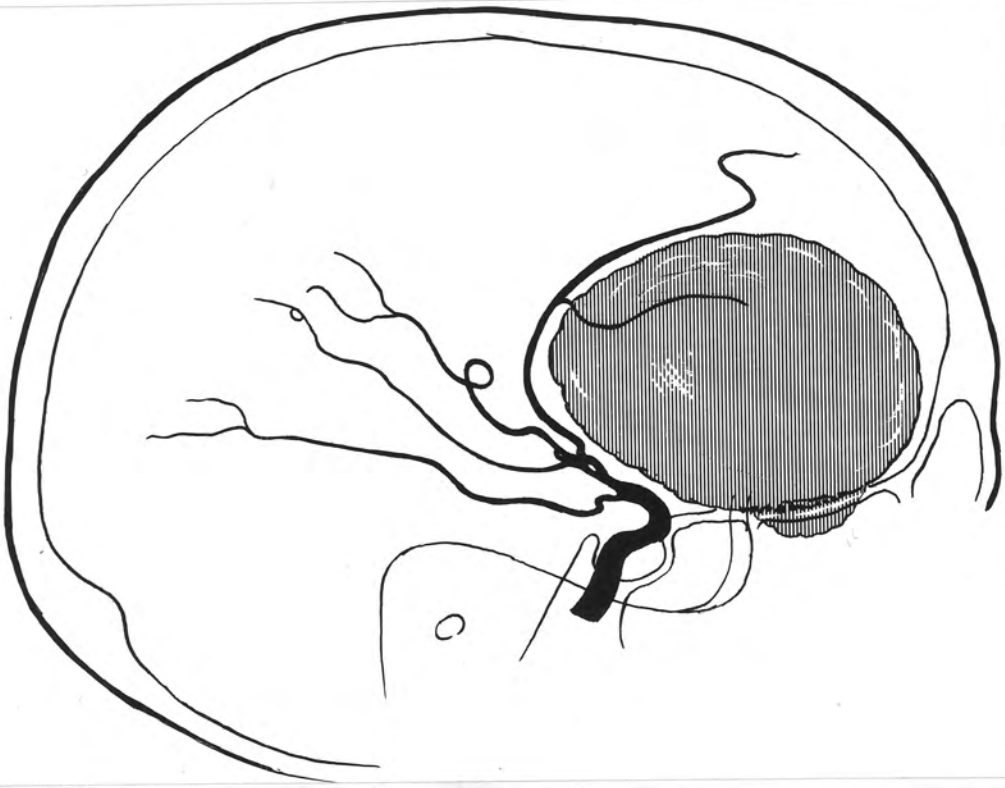
Figure xxxii. Enormous subfrontal meningioma, probably originating in the olfactory groove or anterior sphenoidal regions. Most museums contain similar specimens, commonly obtained from mental hospitals: insidious dementia is the common presentation. (Oxford case).

Figure xxxiii. Diagram showing arterialrelations of olfactory groove meningioma. The relation to the anterior cerebral artery is often less intimate than the angiogram suggests. (From angiogram of Oxford case).

Figure xxxiv. Plain radiograph showing large calcified parasagittal meningioma (Adelaide case, described on page 154.

xxxii





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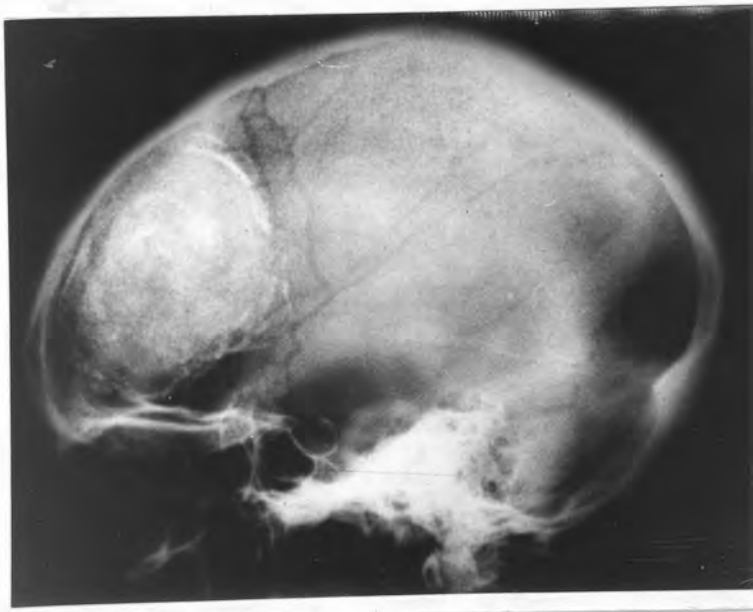
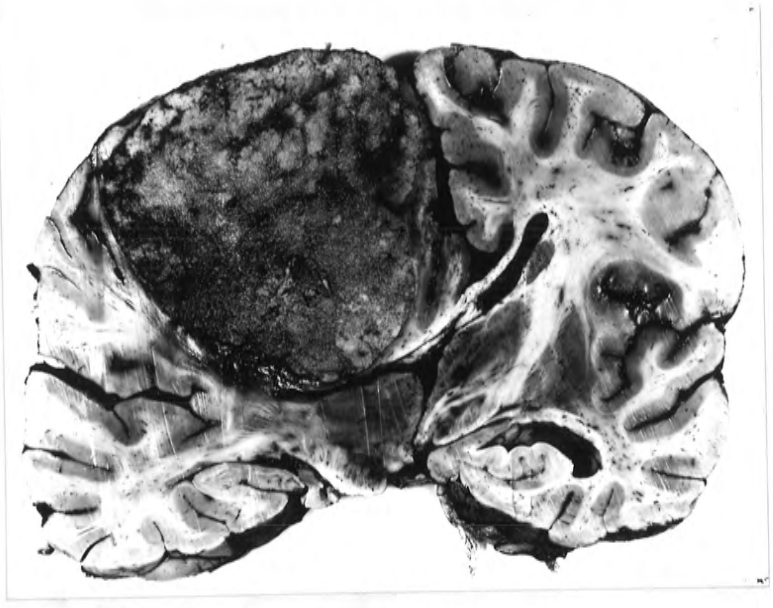


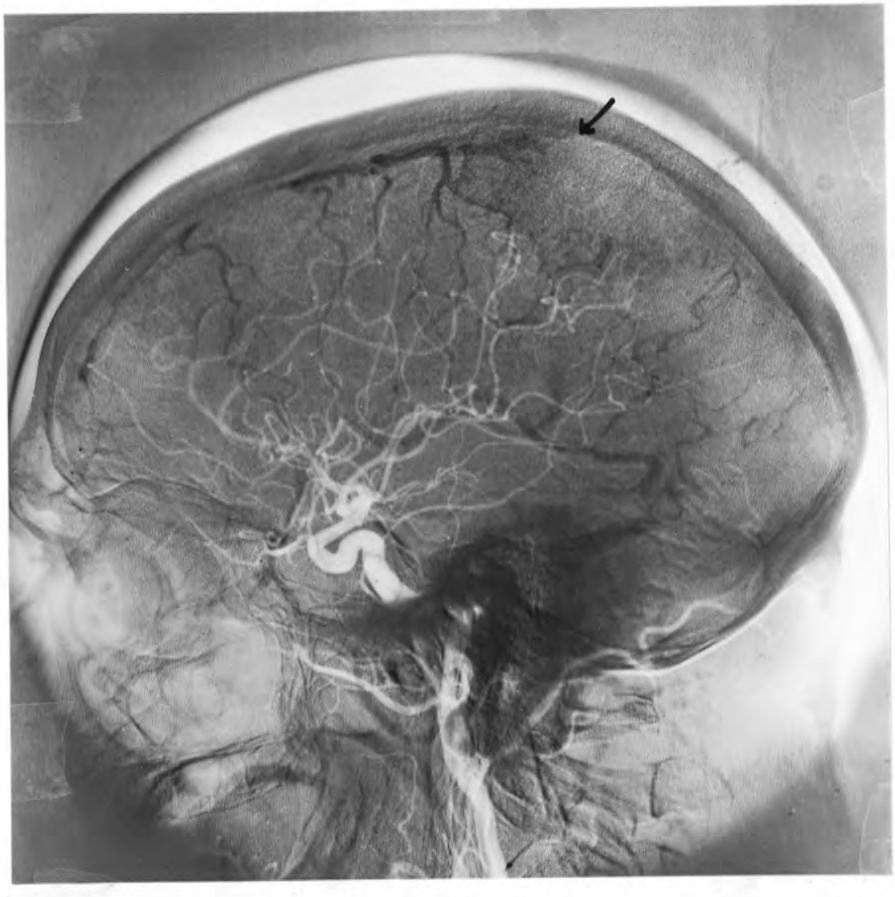
SURGICAL MANAGEMENT : PARASAGITTAL MENINGIOMAS.

Figure xxxv. An enormous parasagittal meningioma. In this section, the tumours abuts on the cerebral convexity, and is separated from the falx by a layer of cortex. More posteriorly, there was a direct relationship with the falx and superior longitudinal sinus, the walls of which were probably invaded. The specimen also shows bilateral temporal grooving as a consequence of transtentorial herniation. (Oxford case).

Figure xxxvi. Phlebogram and arteriogram in a parasagittal meningioma: demonstration of sinus occlusion by subtraction method of Ziedses des Plantes (Oxford case : not in present series). The arrow indicates the point of occlusion. Modification of the photographic process will give even clearer demonstration.



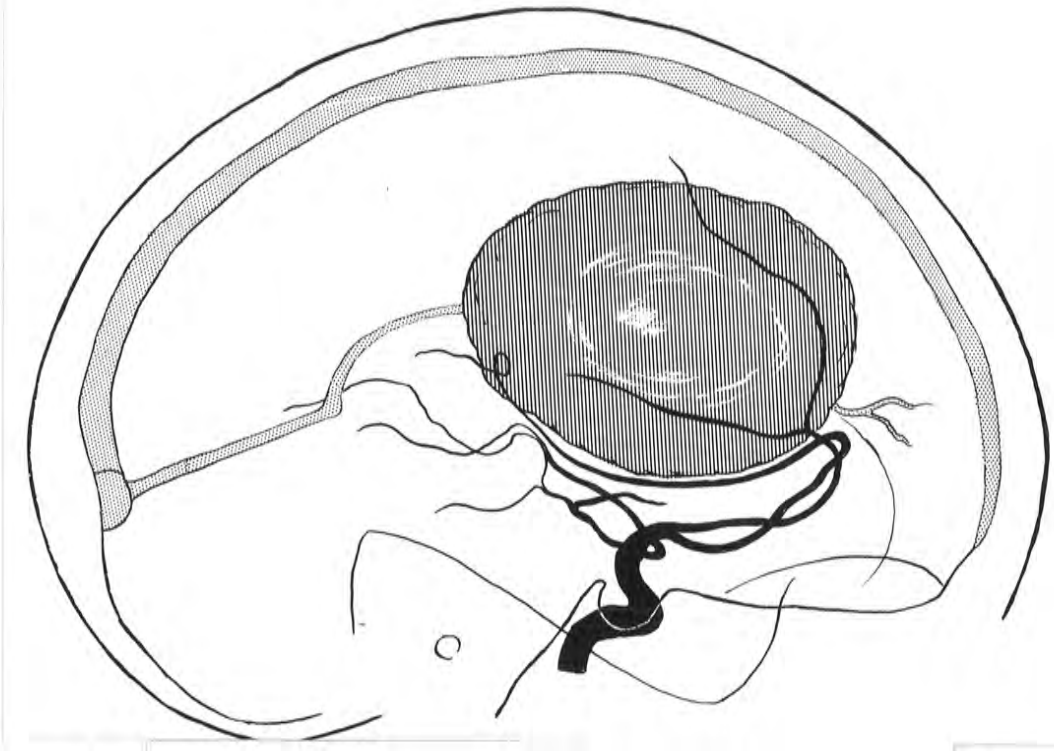
xxxv

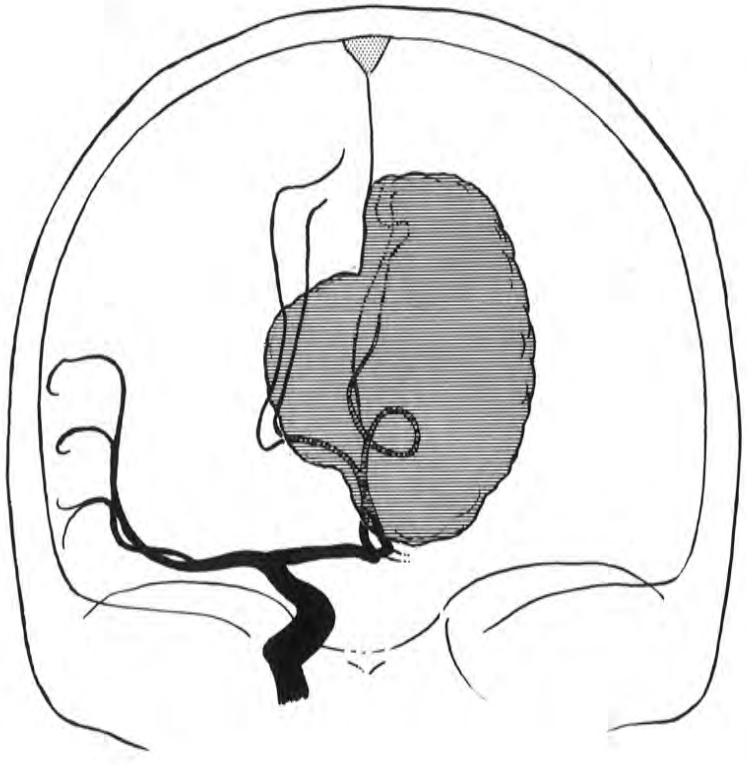


xxxvi

SURGICAL ANATOMY : FALX MENINGIOMAS.

Figure xxxvii. Diagram showing arterial and venous relations of large falx meningioma. The under surface of the tumour is indirect contact with the anterior cerebral arteries; the inferior longitudinal sinus is engulfed, but the superior longitudinal sinus is not involved (from angiogram of Adelaide case described on page 164.





SURGICAL ANATOMY : POSTERIOR FOSSA

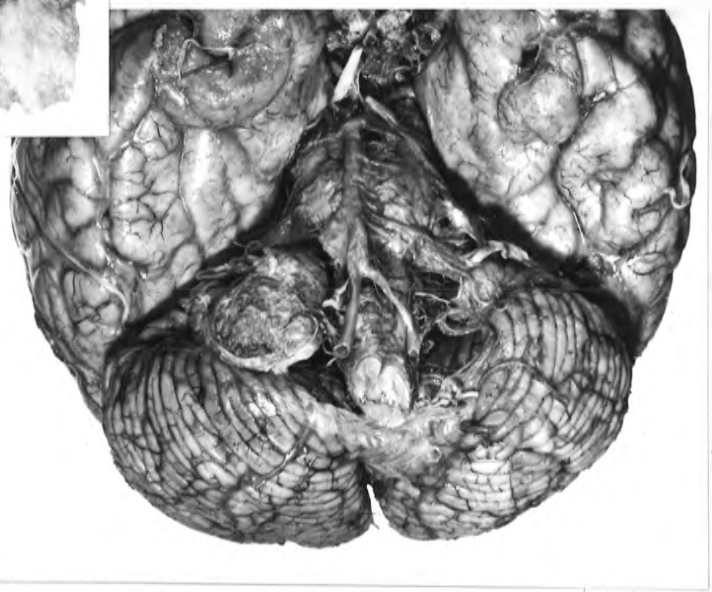
MENINGIOMAS.

Figure xxxviii. Recurrent petrosal meningioma with trans-tentorial extension. Such an extension is one cause of recurrence after grade II resections. In this case the tumour, the undifferentiated meningioma shown in figure xvi, had recurred very rapidly after a grade II resection. Radical ablation of meningiomas in this situation will often be impossible (Oxford case).

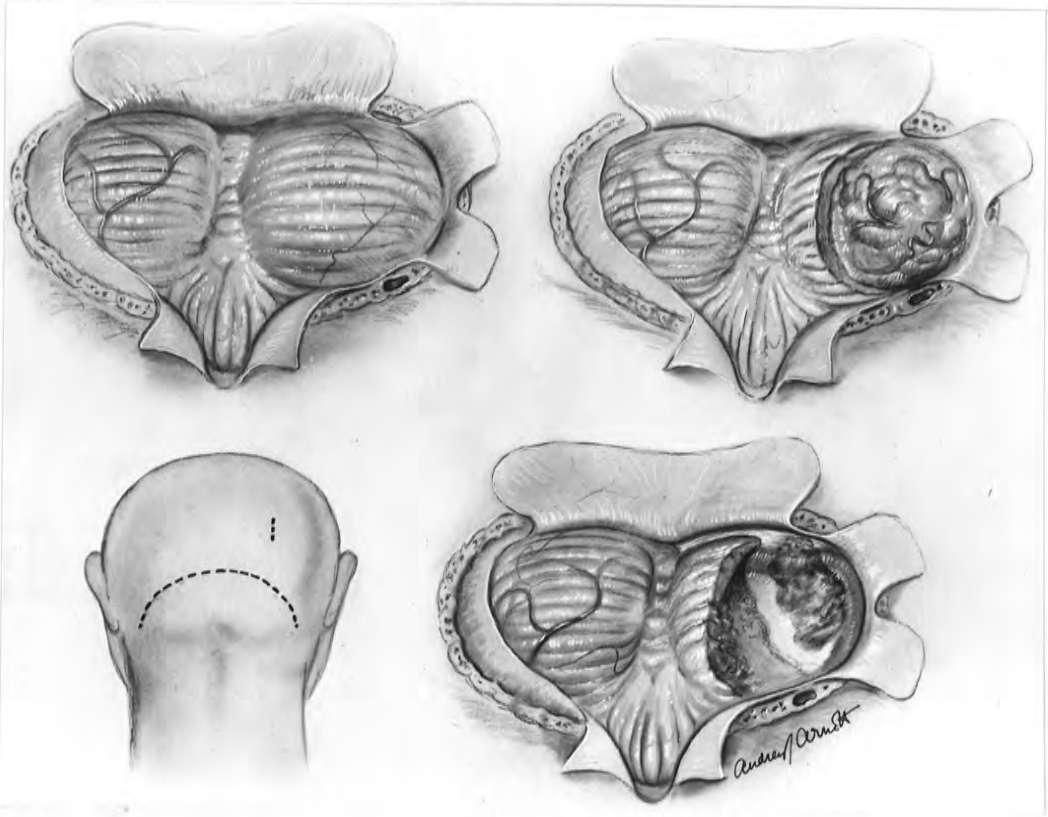
Figure xxxix. A small posterior petrosal meningioma, intimately related to the pons, the lower cranial nerves, and the branches of the vertebral and basilar arteries. Larger tumours in this situation may enter into direct relation with the main vessels. (Oxford case).

Figure xl. Exposure and removal of a posterior petrosal meningioma with area of origin encroaching on transverse sinus. The potentially invaded dura was scraped and coagulated, but not resected: a grade II operation (Adelaide case described on page 170).

xxxviii



xxxix



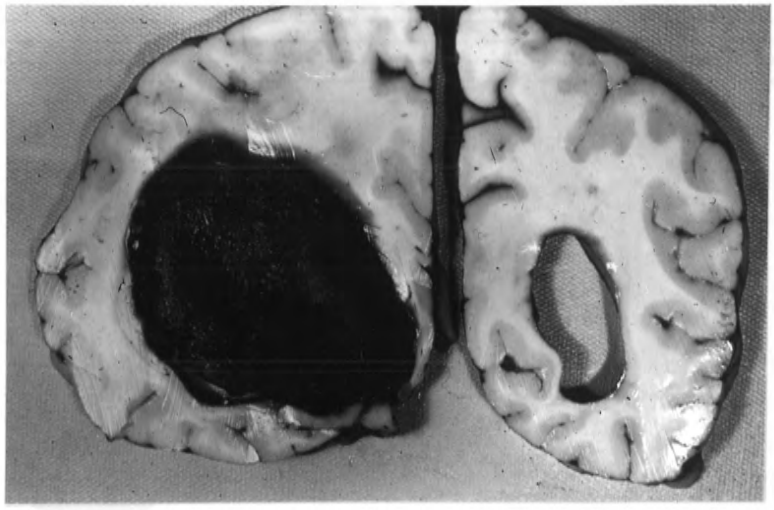
xl

SURGICAL ANATOMY & MANAGEMENTS :

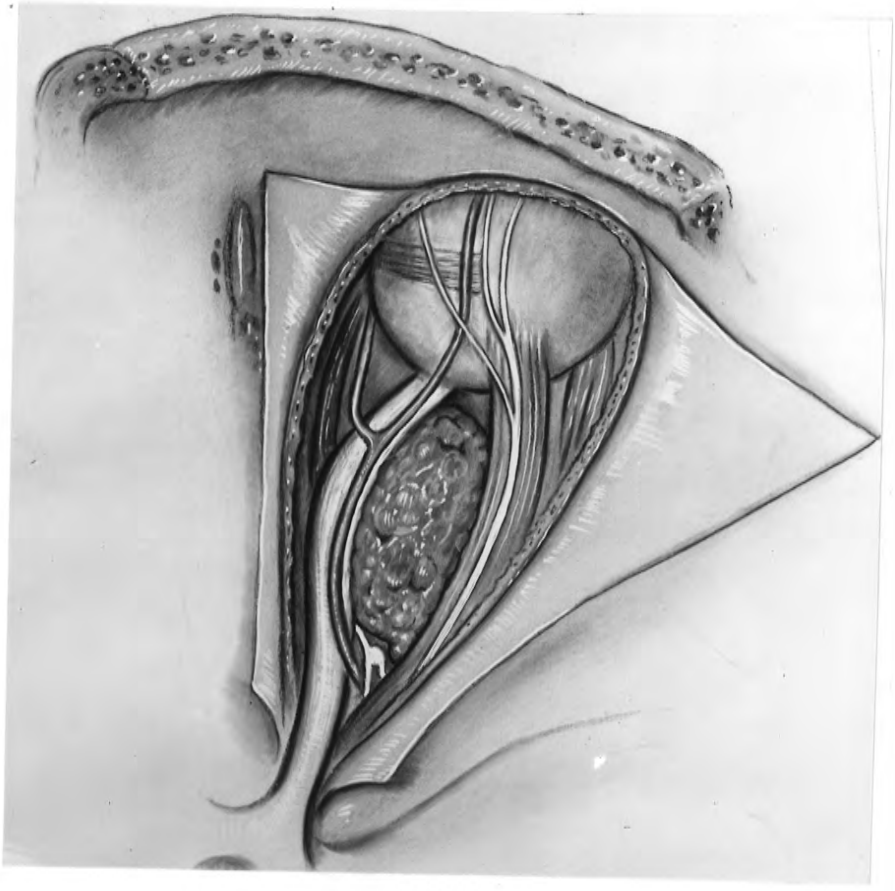
INTRAVENTRICULAR AND ORBITAL MENINGIOMAS.

Figure xli. Fatal bleeding into the lateral ventricle following decompression over a large intraventricular meningioma (Oxford case: not in present series).

Figure xlii. Operative exposure of a meningioma of the optic nerve. The tumour lay lateral to the nerve, which was sharply kinked. It could be dissected away from the sheath of the nerve, but invaded neighbouring muscle and other structures. (Adelaide case, described on page 181).
Figure iv shows the invasive nature of this tumour.



xli



xlii

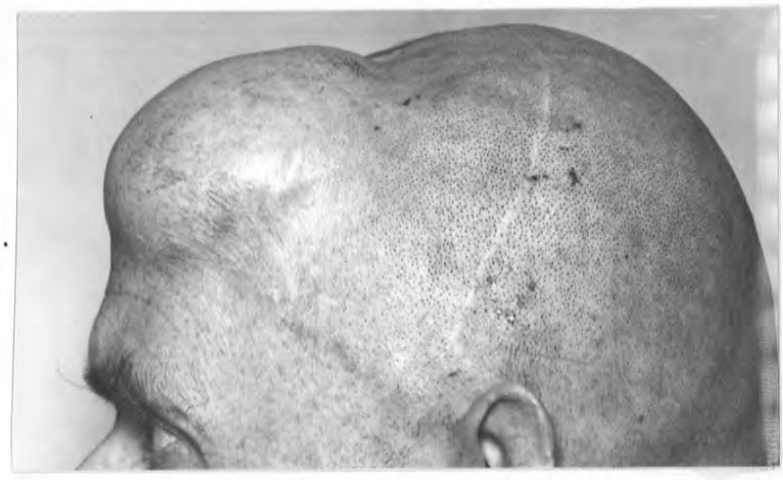
RECURRENCE.

Figure xliii. (a) A subcutaneous recurrence, presumably from an implant deposited at an earlier operation. This tumour was found to be entirely extradural. Later other extradural nodules appeared.

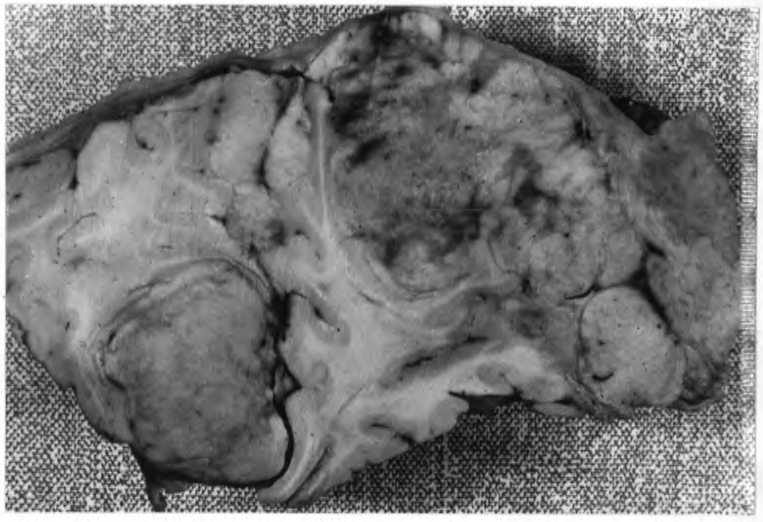
(b) Autopsy on the same patient: two massive nodules in the frontal lobes.

(c) Nodules (? implant metastases) in the dura mater : the same patient. (Case 7, appendix C: histology in figures ix - xi).

a.

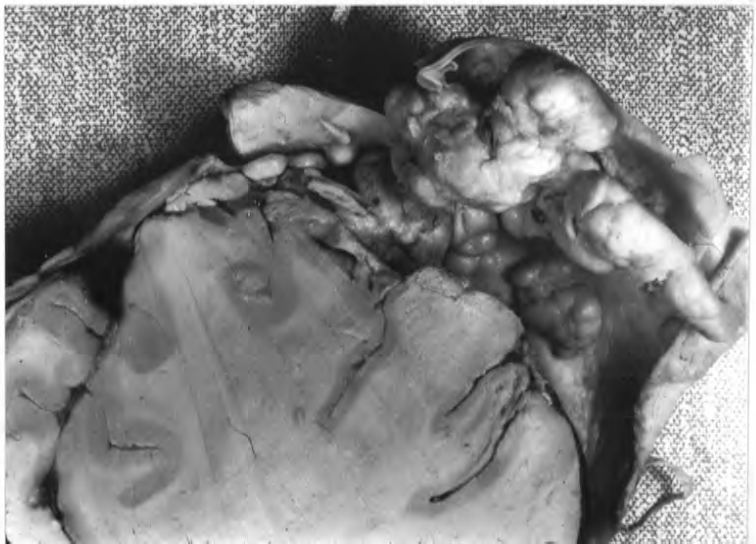


b.



xliii

c.



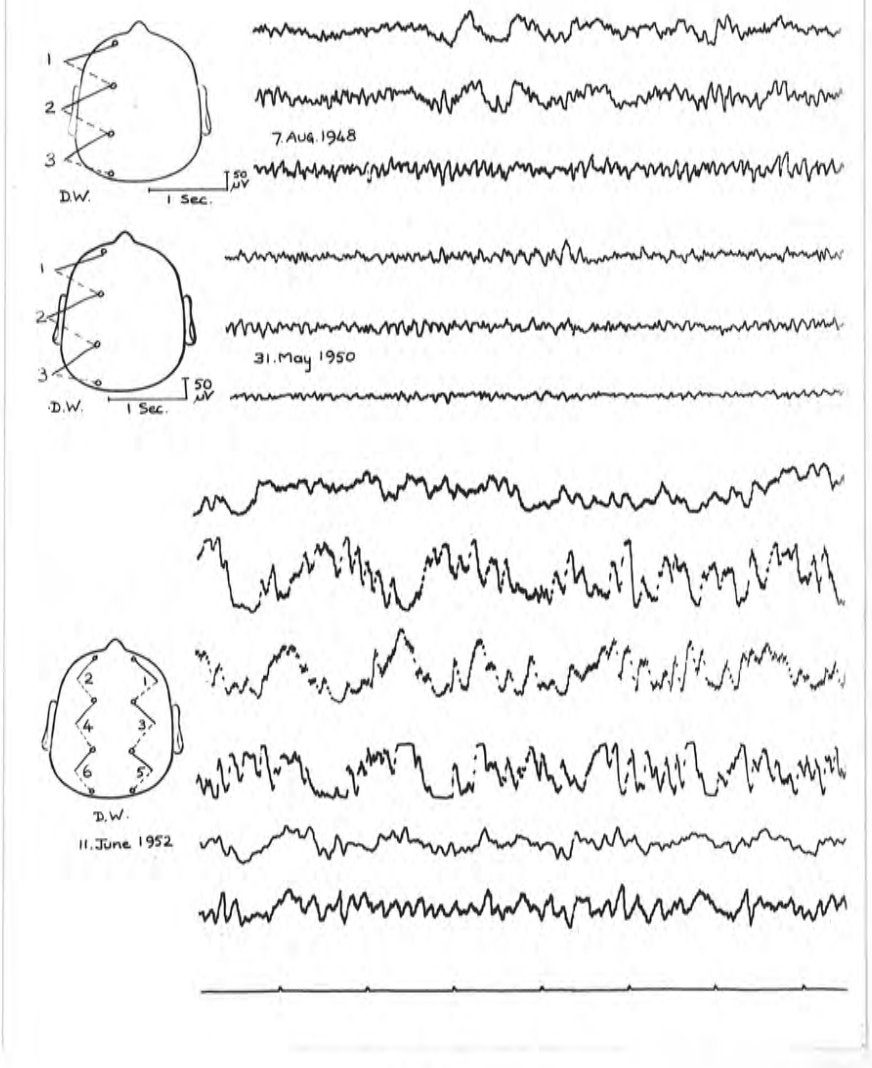
RECURRENCE : ELECTROENCEPHALOGRAPHY.

Figure xliv. Electroencephalograms from case 15 (appendix C).

(a) pre-operative record. 7.Aug. 1948, "episodes of 1-2 c/sec. slow waves in the frontal areas..... showed a focus over the left pre-frontal area". (Miss F.M. Taylor).

(b) progress record 22 months later. 31 May 1950: "bilateral dysrhythmia.... with random spiking: some residual abnormality in the left frontal region" (B.L. Thomas)

(c) record at time of first recurrence. 11 June 1952: "gross high voltage slow waves from ·5 -1 c/s, mainly in the left frontal area but with some spread to the right.....
A tumour recurrence seems more likely than a post-epileptic state". (Miss F.M. Taylor)


a.
1
2
3
D.W.
1 Sec.
50 μV
7. Aug. 1948
b.
1
2
3
D.W.
1 Sec.
50 μV
31. May 1950
c.
2
1
4
3
6
5
D.W.
11. June 1952

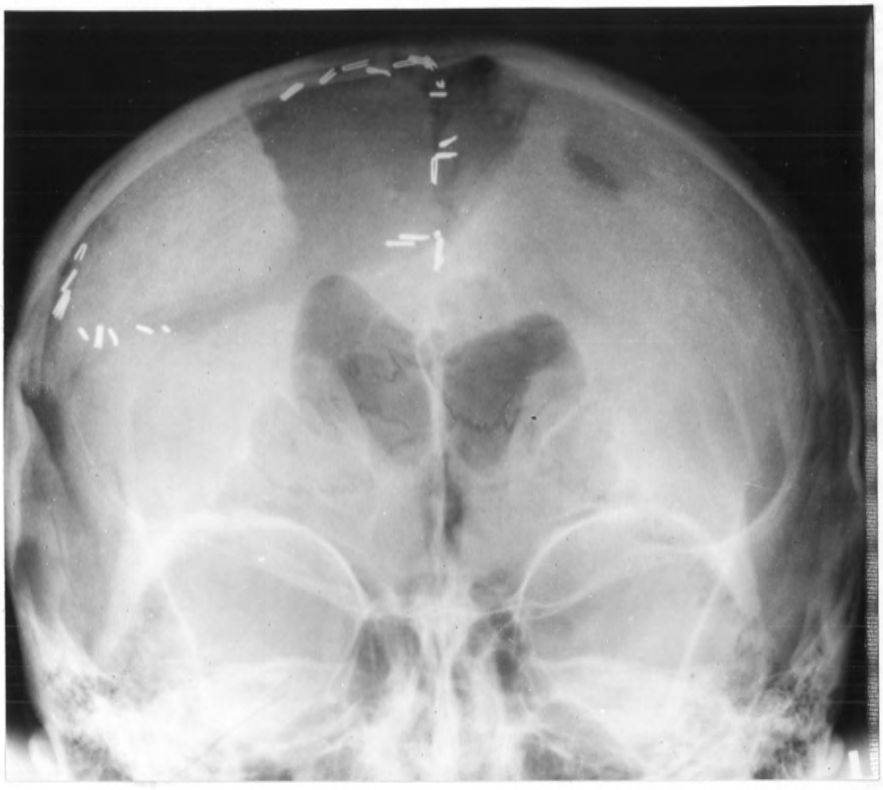
RECURRENCE : RADIOGRAPHIC

DIAGNOSIS.

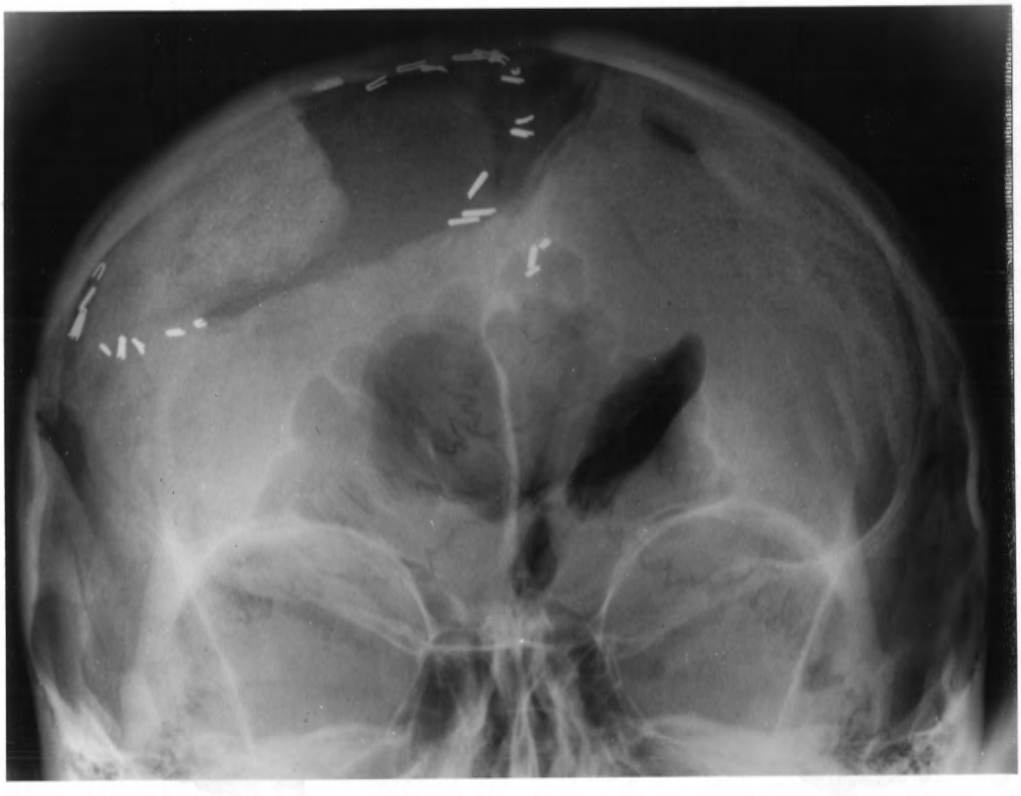
Figure xlv. (a) Air encephalogram performed six months after grade II resection of a frontal parasagittal meningioma. There is slight dilatation and upward distortion of the ipsilateral ventricle. Recurrent tumour had not yet reached sufficient size to effect any ventricular displacement.

(b) Five years later, air encephalography shows a right frontal mass. Before this could become evident, the recurrent tumour was able to reach a very large size, presumably at the expense of the previously dilated ventricle. (Case 26, appendix C).

a.

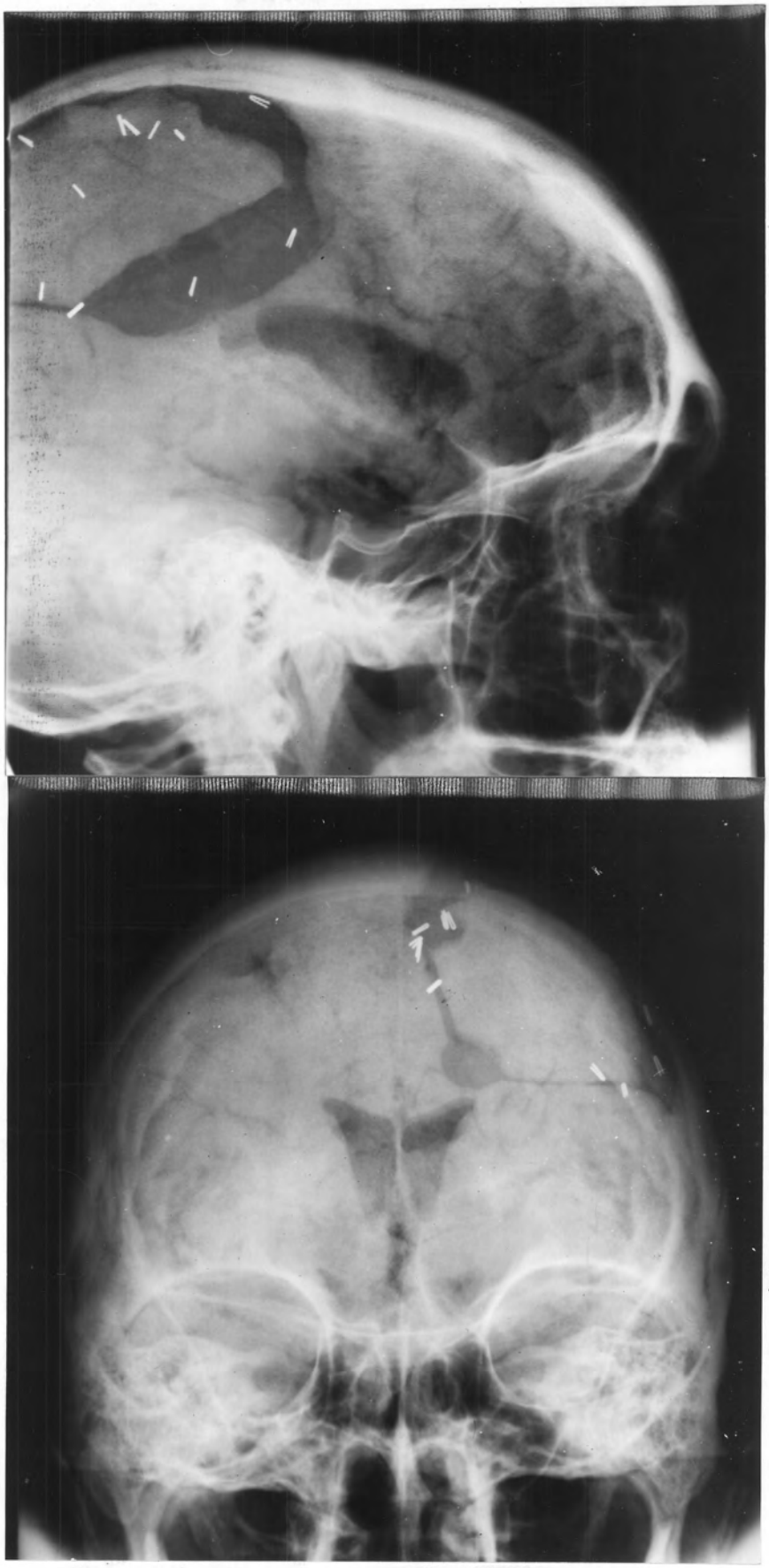


b.



RECURRENCE : RADIOGRAPHIC DIAGNOSIS

Figure xlvi. Air encephalogram performed nearly three years after grade II resection of parasagittal meningioma. At this time, the patient had symptoms and local signs of a recurrence, but the air encephalogram was considered to be normal and he was not explored (Case 18, appendix C).

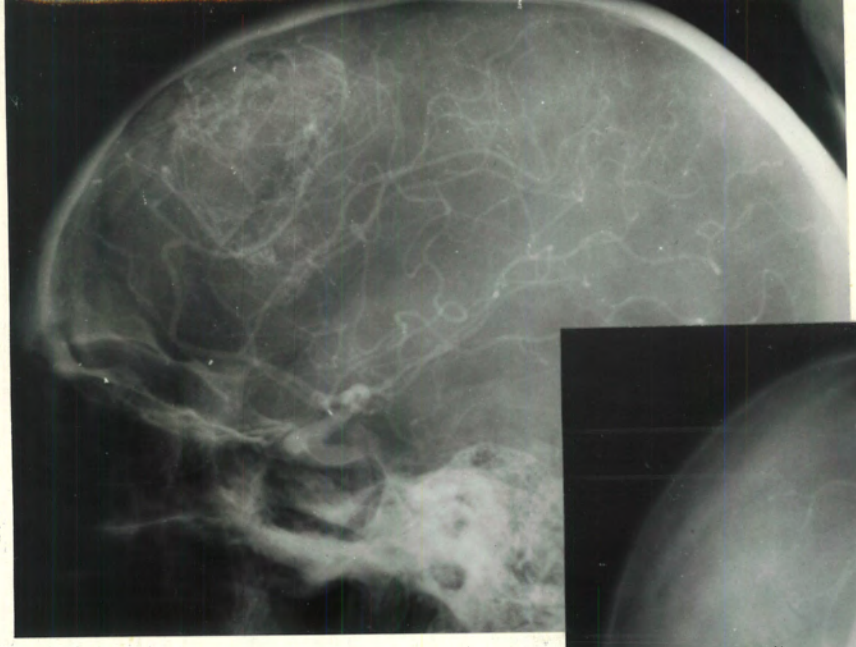


RECURRENCE : RADIOGRAPHIC

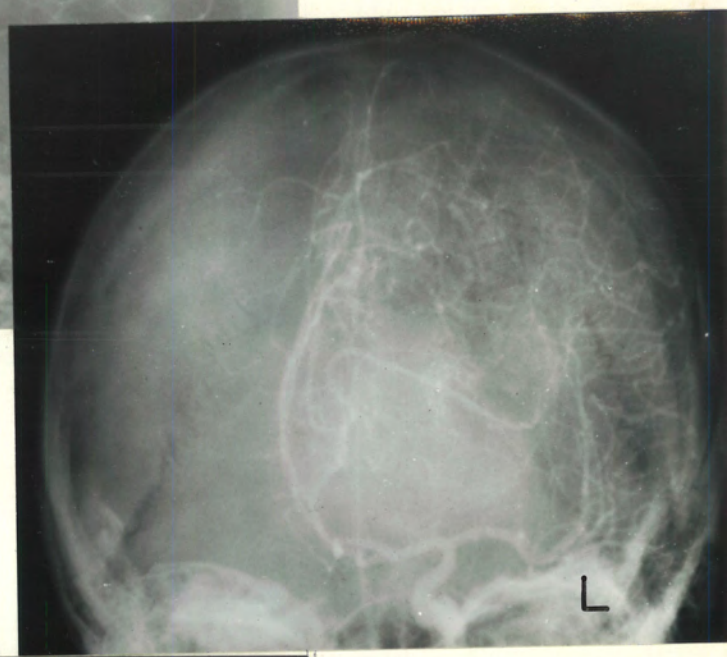
DIAGNOSIS.

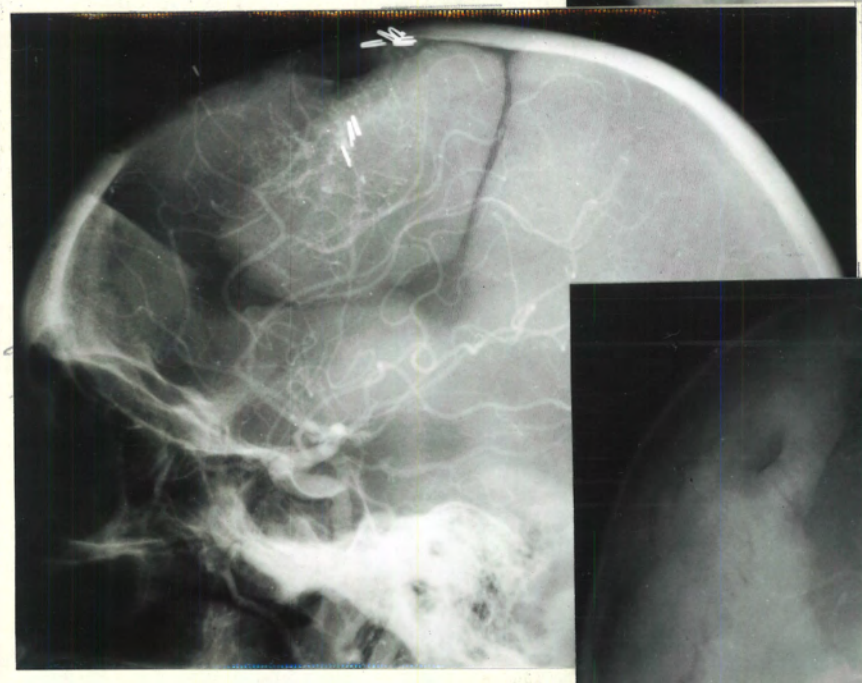
Figure xlvii (a) Frontal parasagittal meningioma, wholly left sided. Grade I resection was performed.

(b) Recurrence of the same tumour, now bifrontal but still predominantly left sided, despite the massive vascular displacement towards the left. (Case 6, appendix C).

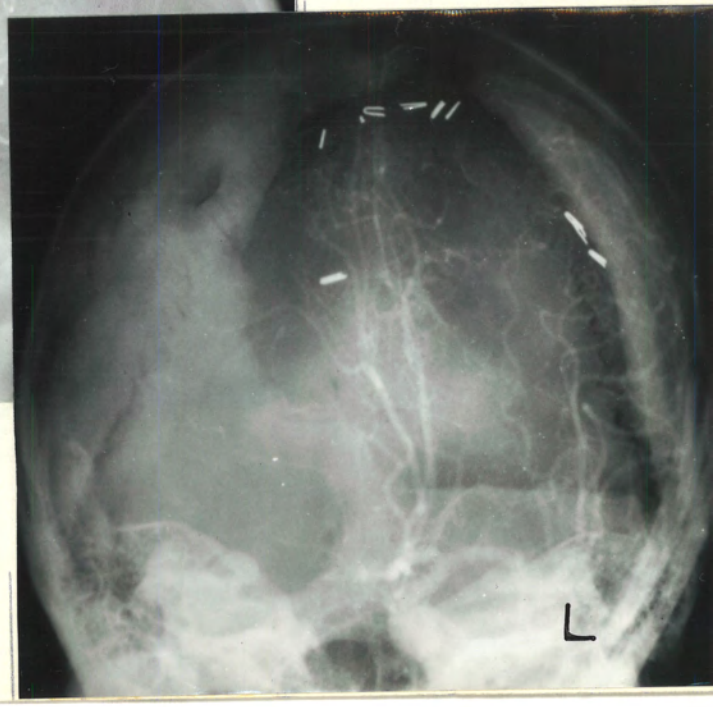


a.





b.



RECURRENCE : RADIOGRAPHIC

DIAGNOSIS

Figure xlviii Recurrent meningioma of undifferentiated histology (case 5, appendix C).

(a) left carotid angiogram before primary operation.

(b) left carotid angiogram showing recurrence ten years later. The irregular vascular pattern is probably suggestive of this type of tumour.

a.

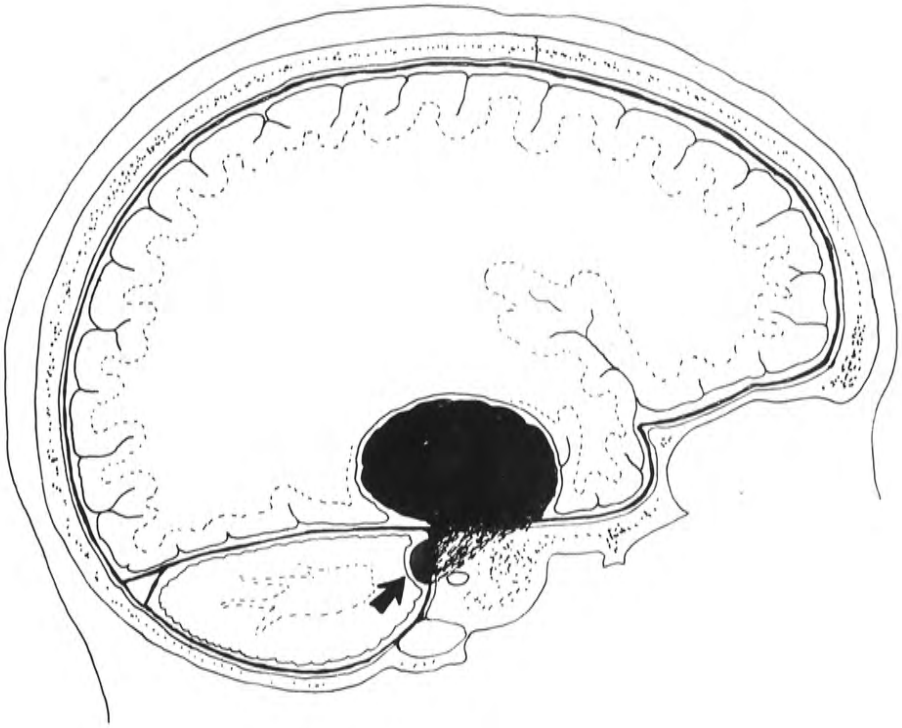
b.

RECURRENCE : CAUSES.

Figure xlix. A recurrent meningioma without apparent attachment : presumably an implant metastasis (Case 24, appendix C).

Figure 1. Diagram showing subtemporal meningioma invading petrous bone; the arrow indicates a nodule in the posterior fossa - a cause of recurrence.

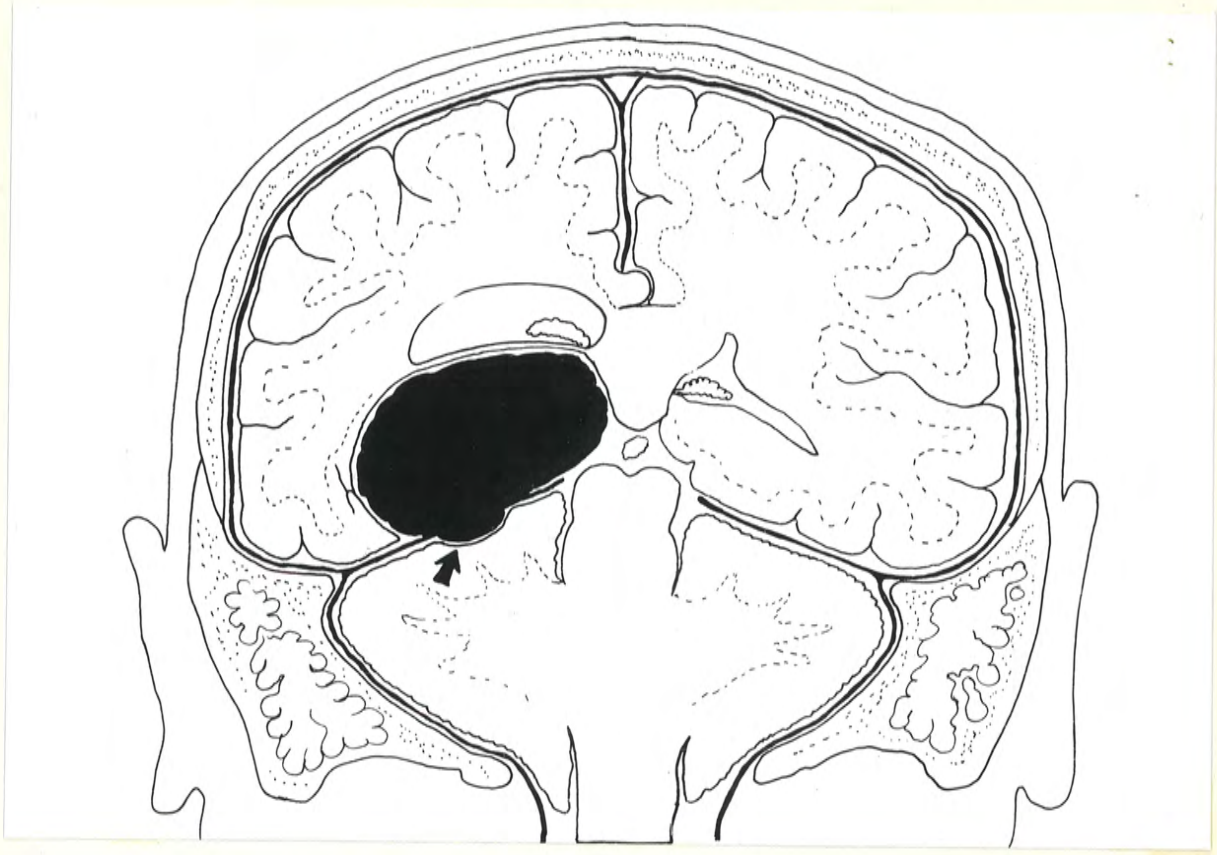
xlix



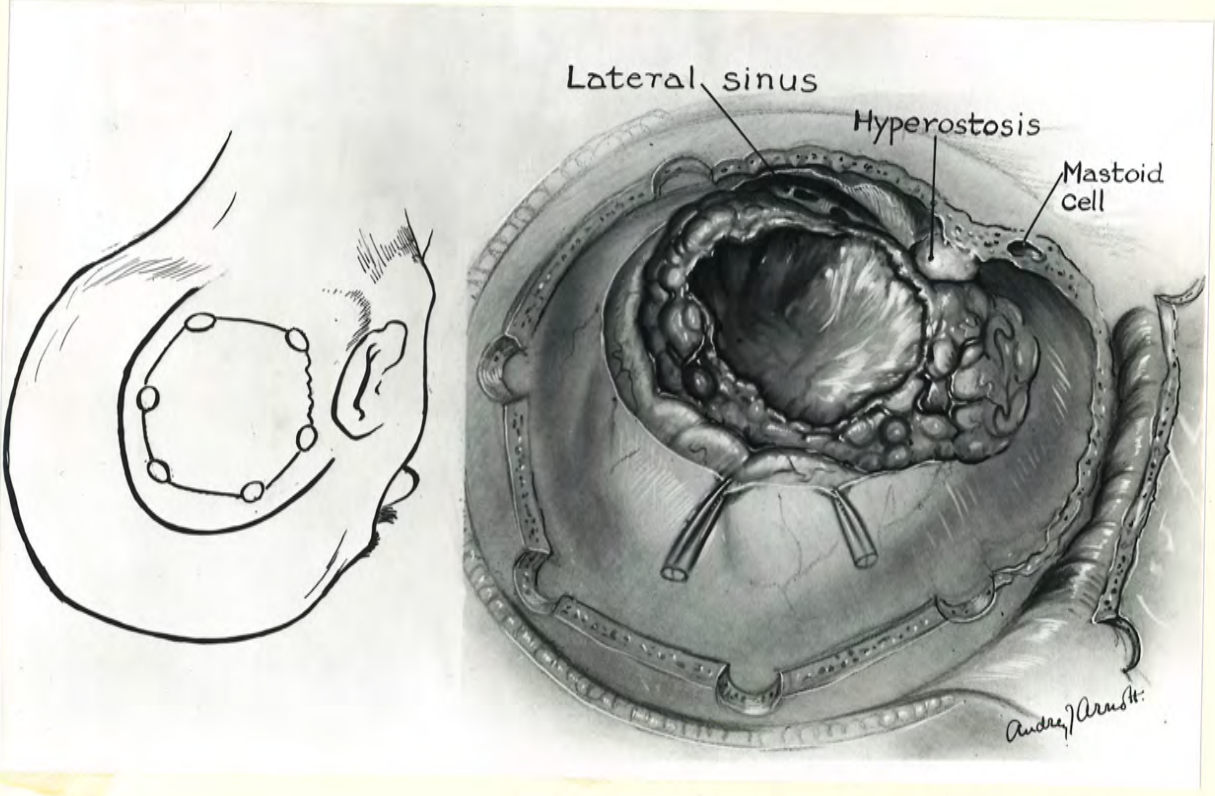
RECURRENCE : CAUSES

Figure 1i. Diagram showing supra-tentorial meningioma; the arrow indicates trans-tentorial extention into the posterior fossa - a cause of recurrence.

Figure 1ii. Operative removal of transverse sinus meningioma (Oxford case). This is a comparatively unusual situation. Radical resection would involve a wide excision of the mastoid bone, and some risk of meningitis.



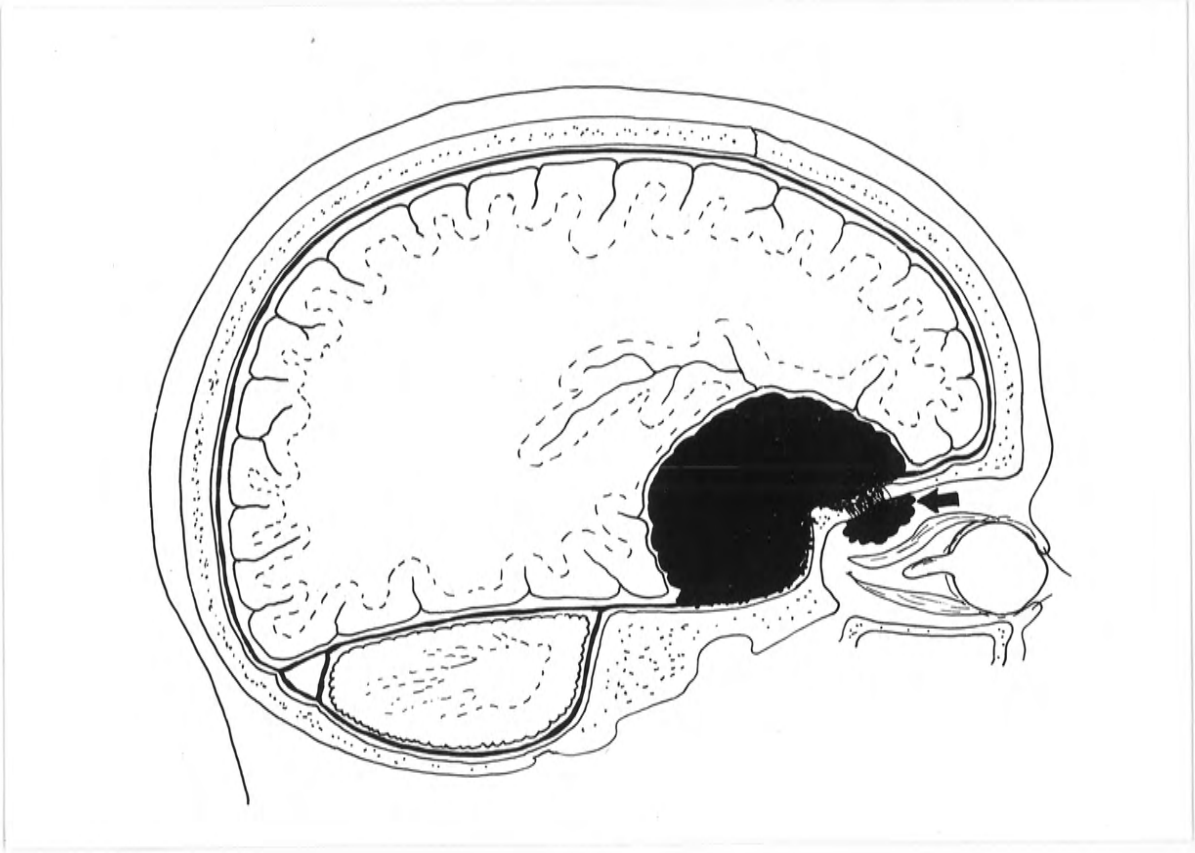
li



liii

RECURRENCE : CAUSES

Figure liii. Diagram showing intraorbital extension of a sphenoidal ridge meningioma - a cause of recurrence.



liii