TUMOURS OF THE FRONTAL LOBE.

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General Considerations.

The difficulties in diagnosing frontal tumours have been well recognised, not only by all writers on the subject, but by all clinicians whether they have contributed to the written word or not. The reasons for this are not hard to find and centre chiefly round the fact that large though the frontal lobes are they contain no structure whose destruction must necessarily cause an obvious alteration in the patient, an alteration that could not have been produced by a lesion elsewhere. Objections to this statement come to mind, for it will be remembered that the motor area and the pre-motor area both lie within the frontal lobe. They demarcate, however, its extreme posterior border and it is clear that unless a tumour is so far back in the frontal lobe that it almost ceases to be a pure frontal tumour no disturbance of motion will result. On the left side is also the so-called motor speech centre, or Broca's area, so that difficulties in the exteriorisation of speech might well be found with a frontal tumour far enough back to involve these mechanisms. We must not be unduly impressed with the importance of the gray matter of the cortex at the posterior end of the left third frontal convolution. Tumours, and for that matter other lesions as well, more commonly produce their effects by interference with the white matter, by cutting deep association and projection fibres, than by destruction of the layers of cells in the cortex. It is more probable that defects of speech are due to damage to these deep fibres than to loss of cells with a special function in the cortex. This belief has led in more recent years to speech defects being referred to damage of "the region of the insula (island of Reil), a brain area that belongs as much to the temporal lobe as to the frontal. Tumours have a way of transgressing the anatomical boundaries of tradition; a tumour may be temporal as well as frontal, temporal as well as parietal, occipital as well as both temporal and parietal. When therefore one wishes to speak of the signs of a tumour in any area it is best to confine the examples to lesions which are entirely local. Hence frontal tumours of classical description will only slightly, if at all, encroach on the motor area, nor will any of those even on the left side lead to deficiency in speech. Is there then within the frontal lobe no other structure, is it an unbroken mass of white matter with the usual gray matter covering it? There lies within it the caudate nucleus and the front end of the lateral ventricle. It may be that the tremor to which Grainger Stewart first drew attention in 1906 and has since been noticed by many as a peculiarity of frontal tumours, is due to partial involvement of the caudate nucleus and basal ganglia. The anterior horn of the lateral ventricle could have no neurological significance, but it is important that the foramen of Monro lies within the frontal lobe and if a tumour is so situated that it could block it, a great rise in intracranial pressure must follow. Otherwise the pressure within the skull tends to be low with anteriorly placed tumours, as Stopford first pointed out though not for the reason that he adduced (pressure on the vein of Galen).

In this review of the neural structures of the frontal lobe, in the search for areas whose destruction might lead to outspoken signs or symptoms, no mention has been made as yet of intellectual processes. Are not the frontal lobes the "organs of the mind," the organisers of personality, the censors of conduct,

almost one might say the seat of the soul? Although the frontal lobes are concerned in these things, and probably more concerned than any other part of the brain, all the evidence points to these qualities being more diffusely spread throughout the brain than had recently been thought. It is possible for a patient to have a large frontal lesion and yet no alteration in his memory or personality or moral sense. Sometimes of course these things are disturbed, but much less commonly than would be the case if the frontal cortex was an exceedingly highly specialised mosaic where all our intellectual and (for want of a better word) spiritual potentialities or achievement were lodged. This fascinating subject will be dealt with a little more fully below.

Symptoms and Signs of Frontal [Lobe Tumours.

As a result of the analysis of frontal lobe tumours which have been made during the past thirty years a certain uniformity of description has emerged. Writers differ in the emphasis which they place on this or that symptom or sign; such emphasis tends to be individualistic and what has helped one observer may be thought unimportant by another, even though he agrees that the observation is correct. However desirable it may be for teaching purposes to produce a syndrome, a formula, something which shall represent the photographic likeness of a disease entity, we know very well that in practice the resemblance will be a family rather than an exact one. It is exceedingly rare for any case to show every sign which the closest scrutiny of a large number of cases has proved to be a possibility. Only too often but one or two of the theoretically possible diagnostic critical points are all there is to work on.

We will begin with a list of symptoms and signs and first amongst them we must place those of that rise in intracranial pressure which is the general rule in intracranial tumours.

1. **Signs of raised intracranial pressure**—headache, choking of the optic nerve heads, vomiting, paralysis of cranial nerves at a distance, usually the abducens, and (in the later stages) drowsiness.
2. **Signs and symptoms due to interference with the brain mass of the frontal lobes—**
 - (a) Epileptic fits.
 - (b) Memory defects, personality changes, incontinence, inertia, loss of powers of concentration and of introspection, facetiousness, unwarranted good humour (Witzelsucht, euphoria).
 - (c) Weakness of the contra-lateral limbs, perhaps a "grasp reflex."
 - (d) "Motor" aphasia, if the lesion is left-sided in a right-handed person.
 - (e) Tremor of the arms, often ipsilateral.
 - (f) Pseudo-cerebellar signs—dizziness, ataxia, nystagmus.
3. **Neighbourhood signs**, due to compression of nearby structures—
 - (a) Anosmia, uni- or bilateral.
 - (b) Optic atrophy, especially when it is unilateral. Central scotomata. Foster Kennedy—Paton syndrome.
4. **X-ray evidence of**
 - (a) Calcification in the benign frontal gliomas.
 - (b) Hyperostosis of the floor of the anterior fossa or of the vault, associated with some, but not all, meningiomas.

Ventriculographic evidence need not concern us. In some cases studies of this kind may be imperative, especially in those with unexplicable fits and no other signs.

Discussion. If all the signs mentioned above occurred always we should have a very clear picture indeed, unless the cerebellar signs were also outspoken. There might then be a conflict in the observer's mind as to which signs were the more reliable. It is better not to get involved in that problem at this stage, so we will go back to the signs of raised pressure. It might be thought that unless these were outspoken the idea of a tumour being present would be scarcely likely to arise. This is, alas, only too true and many a patient with a frontal tumour has been thought to be a hysteric or to be at fault in some system other than the nervous. It is a good working rule to attribute nervous symptoms to the nervous system. The practitioner is not always so ready to do so as he should be. Headaches are often dismissed as bilious or migrainous, vomiting as due to gastric or other sub-diaphragmatic disorder, and the symptoms otherwise generally attributed, if sex and age make that possible, to menopausal disturbances. Unless the patient has a fit or the doctor an ophthalmoscope things may drag on indefinitely in this way until the tumour is inoperable. A fatality at this late stage may confirm the doctor's impression that brain tumours are very risky things and that most patients die of them. Although there must of course be a substratum of truth in such an opinion, otherwise it could not have arisen, the more conscientious would more properly wonder whether the picture would not be different if tumours were diagnosed when they were small. They never will be recognised at that stage unless the practitioners to whom the patients first go with their complaints are "tumour conscious" and ready to suspect a brain lesion on little evidence. The last ten years has shown a remarkable improvement in this direction in this country, for which praise must be given to him to whom it is due, the family doctor.

ANALYSIS OF THE SYMPTOMS OF 50 FRONTAL LOBE TUMOURS.

						20 cases of Meningioma. %	30 cases of Glioma. %
1.	<i>Pressure signs.</i>						
	Headache, vomiting, visual disturbances, etc. ...					90	77
2.	<i>Symptoms and signs attributable to the frontal lobe.</i>						
	(a) epileptic attacks						
	generalized					20	50
	localized					10	27
	minor					15	13
	(b) contralateral pareses					20	27
	(c) other pyramidal signs					25	23
	(d) early apathy, loss of concentration, memory defects, euphoria, personality changes ...					30	20
	(e) grasp reflex					5	3
	(f) aphasia					25	10
	(g) hypersomnia					15	3
3.	<i>Pseudo-cerebellar signs.</i>						
	(a) ataxia					25	0
	(b) tremor					10	7
	(c) vertigo					25	20
	(d) nystagmus					5	3
4.	<i>Neighbourhood signs.</i>						
	(a) anosmia					25	7
	(b) optic atrophy, and Foster Kennedy-Paton syndrome					25	7
5.	<i>X-ray evidences.</i>						
	Calcification, hyperostosis					40	33

I. General pressure signs : There is nothing very noteworthy about the headaches from which these patients suffer. They are often not very severe, but they are continuous and progressive. They do not have the paroxysmal qualities of the pain produced by some tumours in the posterior fossa. The pain may be unilateral, and then it is generally on the same side as the tumour. It has to be differentiated from migraine: then the pain is commonly unilateral, may be accompanied by fleeting visual disturbances (teichopsia) and by vomiting, but it dates back commonly over years, is well spaced in time, and periodical. It does not have the continuously worrying character of tumour headache. Some patients with tumour, and even with very high pressure, have no headache at all. We do not know why that is.

Changes in the optic discs, papilloedema and congestion of the nerve-heads, are present in most cases. It is undoubtedly possible for a tumour in the anterior fossa to attain some size before any pressure signs arise. The brain does not so tightly fill its membranes and bony capsule that the slightest encroachment on the intracranial space leads to clearly recognisable cerebral embarrassment. A small tumour in the posterior fossa will cause trouble much earlier than one in the pre-frontal region because it will interfere with the circulation of the cerebro-spinal fluid. In that case the mass of fluid in the dilated ventricles must be added to that of the tumour itself if we wish to compare tumour sizes with tumour effects. Equally a small meningioma springing from the sphenoidal wing, burying itself in the brain, and hindering the outflow of cerebro-spinal fluid from the lateral ventricle will, in the end, cause more disturbance than a much larger tumour at the frontal pole. The outflow of cerebro-spinal fluid may be interfered with by the cerebral oedema which is so common an accompaniment of the gliomas, and which itself adds to the bulk of the tumour proper. It is less common in meningiomas (though it can occur with these as well) and thus it comes about that a frontal tumour springing from the meninges of the convexity may attain a considerable size over a number of years before its bulk is comparable with a glioma. Some of the gliomas, to be sure, are very slow growing and it is not so rare as might be imagined to have a five year, a ten year or even longer history with tumours of this sort. Nearly all of these are astrocytomas. And since this tumour tends to weave itself amongst the normal neural structures, and even to push them on one side, disturbances of function are not nearly so obvious or so early as they are with the malignant types of glioma (especially the dreaded spongioblastoma multiforme, at present an incurable lesion). Vomiting is a rare and always a late symptom, as will be deduced from the foregoing considerations, for it requires for its production involvement of centres either in the region of the third ventricle, the hypothalamus (a diencephalic structure) or the posterior fossa.

II. Signs and symptoms due to interference with local brain mechanism :

(a) *Tremor* has already been mentioned and is rarely an outstanding sign or complaint. Much more important are *epileptic fits*. These occur in about 50 per cent. of frontal tumours, and they are often almost, or even quite, indistinguishable from the idiopathic variety. They are commoner in glioma than in meningioma cases. If the tumour spreads far back towards the motor area the myoclonic movements may preponderate in the contralateral limbs and may rarely be Jacksonian. Most often the convulsions come without warning or with an uninformative aura. The importance of this lack of characteristic is that the fits may be the only sign of a tumour for months or years. How are we to distinguish fits of this kind from the idiopathic? Only by general inference and by auxiliary tests. The vast majority of idiopathic epilepsies begin before

the patient is twenty years old. As age advances true idiopathic epilepsy becomes rarer, and it is our duty to search most carefully for a cause in all patients in whom it starts during the third, fourth, fifth, and later decades of life. The fact that the fit begins with turning of the head to the opposite side is not diagnostic, because a great many youthful epileptics do that. James Collier (1929) thought that point important, but something else that he observed seems to the writer much more so—the tendency of these fits to be multiple, to approach or to attain “status epilepticus,” if there is a tumour in the frontal lobe. This has certainly been so in some of my own cases. If therefore a man or woman in the forties, let us say, begins to have generalised fits and at the same time headache and some unaccountable falling off in working powers we ought certainly to suspect that a frontal tumour is present. If there is as yet no papilloedema the best plan will be to examine the cerebro-spinal fluid for pressure and for raised albumen content, and to make pneumograms or electro-encephalograms.

(b) *Loss of memory* for recent events, some subtle alteration in personality, loss of application at work and failure to recognise that duties must be completed, loss of reticence and decency, are frequently encountered in patients with frontal tumours. Complete moral breakdown so that the patient becomes delinquent or liable to imprisonment for his acts is in the writer's experience very uncommon (one case only). Much more common is it to find the patient good humoured and docile, though given at times to periods of unreasonableness impenetrable to persuasion or argument. Few of my frontal tumour series have realised the seriousness of their condition, few have been worried at the prospects of an operation, which to the lay mind is particularly fraught with danger, few have been bothered about money matters, the expense or duration of their illness has brought no anxieties or questionings. They have a certain amount of insight, for they may be brought to understand perfectly what is the matter with them, but even then they seem to be spared anxieties of a really worrying kind.

FIG. 1.

(a) Situation of frontal tumour causing fits only

(b) Situation of frontal tumour infiltrating the corpus callosum and causing profound mental alteration.

There is no doubt whatever that all of the mental troubles so firmly linked in our minds until recently with tumours of the frontal lobes also occur with tumours elsewhere. As the result of experiences in the unilateral removal of the frontal lobes in man the writer has been driven to the conclusion that although the frontal lobes have much to do with the workings of the intellect, and of all the faculties subsidiary to it, that they are not its one and only seat. Nor can any differences be detected whether it be the right lobe or the left that is excised. If a frontal lobe is removed the patient is left quantitatively with less neural tissue than he had before to carry on his life and thought, to direct his conduct. So much is obvious. But what could not have been foretold is that the deprivation makes remarkably little difference to him. It is clear that thought processes are not so intensively cultivated in the frontal cortex that removal of a part leads to permanent loss of such and such a faculty of the mind. It would have been very interesting if it were so, for a careful correlation study of pathological material and of the observed clinical facts would have led to the establishment of individual human faculties in different areas of the cortex. Some might have been in the right lobe, some in the left. Such an arrangement would have completely justified the phrenologists, Gall and Spurzheim, the first localisers of function.

The facts are, of course, quite otherwise. Function is diffusely sown in the brain, though no one would deny that it is heavily concentrated in certain parts. The greatest mental defects are caused by bilateral frontal lesions or by tumours of the corpus callosum, which by cutting commissural fibres impair the activities of both lobes. Mesially placed frontal tumours are very apt to invade the corpus callosum. Severe symptoms will always, therefore, suggest callosal involvement. Mental power, in Foster Kennedy's (1911) words, depends on the exquisite integration of the entire brain. Disturbances of commissural fibres and tracts leads to an upset in this integration far more than does cortical damage, unless more widespread than is ever seen in human pathology.

Remarkable disturbances of personality sometimes follow left temporal lesions, neoplastic or otherwise. High intracranial pressure, wherever the lesion, interfering as it does with the actions of the brain as a whole, is capable of causing great changes in alertness and in thought, and examples could be brought forward of a clear frontal lobe syndrome when the tumour was later proved to be elsewhere. We must therefore be wary of accepting mental peculiarities as incontrovertible evidence of a frontal lesion. If these changes are present in a person with no signs of high pressure that would be better evidence. A word must be added about incontinence. In the highly compressed drowsy or stuporous patient this calls for no special comment. But it is another matter if it occurs when the patient is conscious. It is then strongly suggestive of a frontal lesion. In the analytical table of 50 frontal tumours it will be observed that mental and memory defects occur as an early sign in less than one-third of the patients. As a late sign there are few patients who do not show some alteration for they must all eventually become drowsy and incontinent. These alterations are due to high pressure and are very similar whatever part of the brain the tumour affects.

(c, d) Better still would be the additional presence of an aphasia, a difficulty in saying what the patient wishes though he declares that he is perfectly clear headed. This can only occur when the tumour is on the left side (with the usual reservation of right handedness) and far back. Similarly slight pyramidal signs, absent abdominal reflexes, may suggest the side of the tumour if not its site. Sachs has stressed particularly weakness of the face on the opposite side; this

certainly occurs but it is as frequent with temporal tumours. None the less Sachs' studies of frontal tumours are important; he regards fits, mental changes, and nystagmus as most important signs. A grasp reflex may be present, that reflex action by which the patient will always clench hold of anything which so touches his palm. It has been admirably described by Adie and Macdonald Critchley (1927). Weakness of the leg is rare in frontal tumour patients, because the motor area slants forward offering the face area most readily to the tumour.

(e) The cerebellar signs shown by some frontal tumours will best be dealt with in the differential diagnosis.

III. Neighbourhood signs: The olfactory tracts are so closely applied to the under surface of the frontal lobes that their compression by sub-frontal tumours is well imaginable. Complete anosmia, on one or both sides, is rare unless the olfactory bulbs are disorganised, as happens chiefly when there is an olfactory groove meningioma. Elsberg has introduced more delicate tests for estimating depression of the sense of smell short of complete loss. Special, even though simple apparatus, is necessary and outside hospital it will suffice if the clinician tests the sense of smell with whatever easily identifiable odours he can find to hand. These tests must be remembered, for especially if the loss is unilateral, the patient may be unaware and does not mention it. When it is bilateral (in the absence of nasal disease) it is always important, always organic, though it can be a false localising sign. (Cushing, 1916).

Unilateral optic atrophy caused by the pressure of a frontal tumour bearing heavily on the nerve of the same side is an extremely important sign. It was first given diagnostic significance by Leslie Paton, and worked up with illustrative cases in an important paper by Foster Kennedy, whose name is usually attached to the syndrome of atrophy of the optic nerve on the side of the tumour, papilloedema in the uncompressed nerve of the opposite side. Of recent years the significance of unilateral optic atrophy has more and more impressed itself on ophthalmologists and neurologists. It is an organic sign of the first order, and never more so than when the opposite disc is oedematous. Its presence means exactly what the facts indicate. The optic atrophy can be as well produced by a temporal tumour as by a frontal (see Fig. 124 in W. R. Henderson's essay on the anterior basal meningiomas, 1938). Also one must beware of being deceived by an atrophy consecutive to severe choking of the discs which has become more complete on one side than the other.

IV. No special comment is required by the **X-ray evidences** except to say that a number of the benign gliomas calcify and that the patterns of these calcifications need an expert eye to recognise. They may be very faint and easily overlooked.

Differential Diagnosis.

We will assume that the fits and mental changes from which our hypothetical patient could suffer have been proved non-syphilitic by a negative Wassermann reaction. The chief differentiation necessary will be between either temporal or cerebellar tumours. Temporal tumours equally produce raised pressure (only more early because they tend to compress the third ventricle), facial weakness and fits. There are two points peculiar to temporal lobe tumours—uncinate fits and homonymous visual field defects. If neither of these is present, differential diagnosis can only be arrived at by mechanical means.

The possibility of cerebellar signs in frontal tumours has already been mentioned once or twice. This possibility of confusion is brought about by the important pathways which leave the frontal lobes and run to the pontine nuclei, there to be relayed to the cerebellum and labyrinthine apparatus. But it can be said at once that a full-fledged cerebellar picture is never given by frontal tumours. The symptoms and signs are suggestive and no more. Why then should difficulties ever arise? The reason is that cerebellar tumours themselves frequently give rise to symptoms and signs which are scarcely more obtrusive or classical. The clinical picture which Gordon Holmes (1922) has made so well known is best seen in injuries or vascular insults of the cerebellum. It can, of course, occur in patients with tumours, too, but not so often as might be thought. Even nystagmus itself may, if rarely, be minimal or absent in cerebellar lesions. It is quite certain that the coarse, unmistakable nystagmus of some cerebellar tumours never occurs with frontal. In cases in which there is a real doubt ventriculography is the only means of ensuring a correct operative approach, of solving the old problem of frontal or cerebellar location.

Operations on Frontal Tumours.

In general the attack on a frontal tumour follows the lines generally adopted in neuro-surgery. It is assumed that the aim is the removal of the tumour. This can sometimes be effected by enucleation or without sacrifice of the frontal lobe, in other cases the extent and position of the tumour make the sacrifice of the lobe unavoidable. Further, the lobe may have to be excised to give access to a tumour beneath it. The steps of the operation are as follows. An incision is made in the mid-line backwards from a point just above the glabella to one inside the hair line. The cosmetic result is superior if the incision is very accurately placed in the mid-line. Having reached the higher point the incision curves over the scalp to fall vertically towards the ear which it should reach. The scalp flap should be first marked out with iodine and then with a scratch. Novocaine-adrenalin solution (one per cent.) is then injected along the proposed line of section. The whole scalp flap is dissected downwards and forwards, free from the bone. Great care must be taken by finger compression to keep the blood-loss during the cutting of the scalp flap down to a few c.cs. Suitable points are now chosen for making drill holes, avoiding the frontal air sinus. The bone dust obtained in making the holes is saved for replacement at the close of the operation. The holes are most safely made by brace and perforator and burr worked by hand. After separation of the dura mater from the bone the holes are connected with the Gigli saw. The base of the bone flap in the temporal fossa may be narrowed with de Vilbiss forceps; it is then broken down, hinged on the temporal muscle. The bleeding from the exposed dura is usually negligible, and is well controllable with wet cotton or lintine. If bleeding is severe either there is a meningioma beneath the dura with a wide attachment to it, or the anæsthetic is wrong, or the air-way imperfect. It is a great handicap to good surgery to have a high intracranial pressure, hence the need for early diagnosis. The patient's chances of recovery are greatly endangered if the brain tends to bulge irresistibly through a dural incision. If the pressure cannot be lowered by puncture of an intracerebral cyst or of the ventricle it will be wiser to break off the operation before more harm is done and try again under local anæsthesia alone later. Supposing that the dura can be safely opened this is next done, cutting it below, in front, and behind. The cortex is now inspected for evidence of tumour, which may be very clear.

If not it will be found by puncture. The recognition of the presence of a tumour, of its extent, and especially of its nature needs considerable culture. It is on this vital point that the general surgeon is so constantly defeated. If excision of the frontal lobe is decided upon the cortical veins entering the superior longitudinal sinus are first coagulated so that the falx is clear. This necessitates a bone incision exactly on the mid-line. A half or one-inch overhang will greatly hamper the securing of these veins. When clearly seen they are easily diathermised and divided. The line of cortical incision is next planned on the surface of the brain, the veins to be cut coagulated, and the arteries occluded with silver clips. The line of this section will commence below, as a rule, at the junction of the anterior and middle fossæ. The incision into the brain is best made with a narrow blunt dissector, which allows the recognition of deep vessels. The anterior horn of the lateral ventricle may be cut across if the tumour has not pushed it too far back. This does not matter. The only difficulty may be the clipping of the anterior cerebral artery on the mesial surface deep in. After the orbital surface of the brain has been cut through, the whole lobe is lifted out. All bleeding points are secured, the large cavity filled with Ringer's solution and the dura closed. A small drain can be left in between bone and dura for 24 hours, but it is certain that daily aspirations of fluid will have to be made during the next week or ten days. The dead space eventually settles down, it may permanently communicate with the ventricle.

Lobectomy gives the patient the best chance of long survival and obeys the surgical maxim of block removal of non-enucleable tumours. In none of the writer's cases has there been any important mental, moral, or other disability as the result of it.

REFERENCES.

1. ADIE, W. J., and CRITCHLEY, M. (1927), "Forced Grasping and Groping" *Brain*, **50**, 142.
2. COLLIER, J. (1929), "Diagnosis of Frontal Tumours," *Lancet*, **2**, 661.
3. CUSHING, H. (1916), "Anosmia and Sellar Distension as Misleading Signs in the Localisation of a Cerebral Tumour," *Jour. New. Ment. Dis.*, **44**, 415.
4. ELSBERG, C. A. (1935), "The Sense of Smell," *Bull. New York Neurol. Inst.*, **4**, 1.
5. HENDERSON, W. R. (1938), "The Anterior Basal Meningiomas," *Brit. Jour. Surg.*, **26**, 124.
6. HOLMES, GORDON (1922), "Croonian Lectures on the Clinical Symptoms of Cerebellar Disease and their Interpretation," *Lancet*, **1**, 1177.
7. JEFFERSON, GEOFFREY (1937), "Removal of the Right or Left Frontal Lobes in Man," *Brit. Med. Jour.*, **2**, 189.
8. KENNEDY, FOSTER (1911), "Retrolubar Neuritis as an Exact Diagnostic Sign of certain Tumours and Abscesses in the Frontal Lobes," *Amer. Jour. Med. Sci.*, **142**, 355.
9. SACHS, E. (1930), "Lesions of the Frontal Lobe; Review of 45 Cases," *Arch. Neurol. Psych.*, **24**, 735.