HYPOTHALAMIC AND PITUITARY TUMOURS.

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Introduction.

The hypothalamus is a small and sharply circumscribed area of the brain. Its anterior limit is marked by the anterior commissure and lamina terminalis, and its posterior limit by the central branches of the posterior cerebral arteries which enter the brain just behind the corpora mammillaria. Laterally its extent is that of the floor of the third ventricle, and it is bounded here by the anterior inferior margins of the optic thalami and the head of the corpus striatum. Looking at the inferior surface of the brain in the hypothalamic area from before backwards there is seen the optic chiasma, the infundibulum from which arises the pituitary stalk, and on either side of this the prominences of the tuberal nuclei, and most posteriorly the corpora mammillaria. In relation to and forming these structures

Diagram illustrating the Hypothalamic and Pituitary Region.

1. Thalamus.	7. Mammillary Body.
2. Fornix.	8. Nucleus of Luys.
3. Anterior Commissure.	9. Posterior Hypothalamic Nucleus.
4. Optic Nerve and Chiasma.	10. Para-ventricular Nucleus.
5. Pituitary Stalk.	11. Tuberal Nucleus.
6. Third Nerve.	12. Supra-optic Nucleus.

are the various hypothalamic nuclei. The pituitary stalk is connected with the posterior lobe of the pituitary gland, and along it runs the supra optico-hypophyseal tract from the hypothalamus to the posterior lobe. While this lobe of the pituitary

gland is composed of a specialised form of glial tissue, the anterior lobe consists of epithelial cells. In it three parts may be recognised; the pars intermedia separated from the anterior lobe proper by the interglandular cleft, and the pars tuberalis which is a narrow epithelial investment of the stalk of the gland. The anterior lobe is developed as an epithelial outgrowth from the primitive stomadæum, but the posterior lobe arises from the neuroectoderm. The hypothalamus and pituitary gland are thus closely related anatomically and physiologically.

The various hypothalamic nuclei are clearly important centres controlling autonomic activity and in this way the hormonal activity of the pituitary and other glands. It has been suggested that the direction of flow of some pituitary hormones is along the infundibulum and that before their absorption they come in contact with hypothalamic cells affecting the activity of these cells or conversely are themselves chemically and functionally altered. There is also the possibility that some hypothalamic nuclei may possess a secretory function. The physiology of the hypothalamus and pituitary gland is therefore one of great complexity. It is as yet only very partially understood, but rapid advances are being made in our knowledge of the subject, and to this progress the clinical study of the signs and symptoms produced by tumours and other lesions has made valuable contributions.

The Pathological Nature of Hypothalamic and Pituitary Tumours.

As a special article in the present issue of this journal is devoted to the pathology of cerebral tumours, it is only necessary to mention here the types of tumour which may occur.

A wide variety of tumours may be found involving the hypothalamic *and* pituitary region, and this is clearly due to the close association of neural epithelial and meningeal structures. These are

(1) *Pituitary Adenomas.*

Three types—(a) Chromophobe adenoma.
(b) Eosinophil ,,
(c) Basophil ,,

These tumours rarely involve the hypothalamus.

(2) *Hypophyseal cysts*, epithelial tumours frequently cystic and which arise possibly from cell rests or by metaplasia. They are variously described as cranio-pharyngiomas, suprasellar cysts, epidermoid tumours, adamantinomas and hypophyseal duct tumours. They grow between the hypothalamus and the pituitary and therefore generally involve both these structures.

(3) *Essentially hypothalamic tumours.* These are much less frequent than pituitary tumours or hypophyseal cysts, and they may arise in the hypothalamus or in adjacent structures. Any of the types of tumour which grow in the brain proper either from the neurones or neuroglia may be found in this area. (These are listed in the pathological article.)

Of all these perhaps the polar spongioblastoma and astrocytoma are the types most likely to arise in and primarily involve the hypothalamus. Symptoms referable to this region may also be caused by such tumours as colloid cysts of the third ventricle, pineal tumours and cholesteatomata and angiomas arising from the meninges of the base.

(4) Both the *pituitary and hypothalamus* are frequently the seat of secondary carcinomas, and they may also be invaded by sarcomas of the base of the skull.

The Clinical Features of Hypothalamic Tumours.

Apart from hypophyseal cysts, which will be considered separately, tumours involving the hypothalamus are not common. This with the possible occurrence of many different types of tumour makes it impossible to present a concise clinical picture which would cover a group of clinical cases. The patient may be of any age, the symptoms may develop slowly over several years, or very rapidly, and signs of increased intracranial pressure may be the prominent feature in one case, and local hypothalamic symptoms in another. The clinical features of hypothalamic tumours will therefore be considered under the following headings:

- (i) The signs and symptoms produced by the local lesion of the hypothalamus.
- (ii) The signs and symptoms produced by local lesions of adjacent structures.
- (iii) General signs of increased intracranial pressure.
- (iv) The signs revealed by special methods of examination.

I. Signs and symptoms produced by the local lesion of the hypothalamus.

Tumours either during their growth or following the additional injuries necessarily associated with their attempted removal have given rise to signs and symptoms which can be correlated with all the known physiological functions of the hypothalamus. These signs and symptoms are

(I) *Polyuria and polydipsia.* Normally the intake of fluid and the quantity of urine passed in twenty-four hours averages about 1500 c.c.'s, but in some cases of hypothalamic tumours as well as other lesions this may increase to 5 or more litres. The injection of antidiuretic hormone from the posterior lobe of the pituitary gland generally controls the thirst and polyuria, but this is not always the case. Lowering of the basal metabolism from hypothyroidism or hypopituitarism lessens the severity of the condition. The symptom is generally associated with anteriorly placed hypothalamic tumours involving the supraoptic-hypophyseal tract or the tuberal nuclei. A secondary carcinoma involving the pituitary stalk or posterior lobe is a not infrequent cause of the condition, but it may occur with any type of tumour in this region. The physiological explanation of the symptom has not been definitely established, and the most likely theory is that suggested by Biggart (1935). He considers that the antidiuretic secretion is most probably formed in the pars tuberalis and pars intermedia, but possibly also in the pars nervosa of the pituitary under the control of nervous influences reaching the secreting cells along the supraoptic hypophyseal tract. The direction of flow of this secretion is posteriorly through the posterior lobe, and either along the interstitial glial network or along the hypophyseal portal vascular system. This latter is a term applied to venous channels which connect with the sinusoids of the glandular portion of the pituitary, run along the pituitary stalk, and break up into capillaries around the nerve cells of the tuber cinereum. It is probable therefore that the antidiuretic factor comes in contact with these cells, and thus in some way controls water metabolism either primarily through nervous influences from the tuber cinereum or by the elaboration of new hormones acting chemically on the body metabolism.

Tumours therefore which lead to destruction of the supraoptic nuclei or the supraoptic hypophyseal tract will give rise to a diabetes insipidus which can be controlled by pituitary injections, but if the growth of the tumour is such as to destroy widely the tuberal nuclei and infundibulum, a diabetes insipidus refractory to pituitary injections may develop. The condition sometimes lessens or disappears during the clinical course of a progressive tumour. This is difficult to understand,

but it may be due to general depression of body metabolism or to the possibility that a further secretion of antidiuretic hormone takes place despite the interruption of the supraoptico-hypophyseal tract.

(2) *Obesity and genital dystrophy.* These symptoms are generally associated in lesions of the hypothalamic pituitary region. Previously there was discussion as to the relative part played by the pituitary gland and the hypothalamus in their production, but there is now no doubt that tumours confined entirely to the hypothalamus can produce these symptoms. The adiposity may precede the depression of sexual function. It is similar in distribution to the obesity associated with pituitary tumours, affecting predominantly the lower abdomen and proximal parts of the limbs, but it is generally much greater and is not accompanied by any failure of body growth. Age appears to have an important influence, as it is generally found most marked in young subjects. Tumours responsible involve the anterior hypothalamus forwards from the tuberal region, so that it is not infrequently associated with polyuria. Fröhlich's or the adiposogenital syndrome which is simply hypothalamic obesity and sexual dystrophy has been described as commonly due to hypophyseal cysts involving the hypothalamus, and it has also been described in purely hypothalamic tumours. The physiological explanation of the condition is not clear, but it seems likely that the anterior hypothalamus has some neural control over the hormones connected with fat storage and genital function.

Fulton and Bailey (1929) have recorded an interesting case illustrating very well a slowly growing hypothalamic tumour. This was a young married woman of twenty-eight, who, six years before her death began to complain of amenorrhoea, polyuria, increase in weight and drowsiness. She was able to continue her work up to eight months before her death when the polyuria diminished greatly, but the drowsiness became more continuous, and headaches, vomiting, failure of vision and impaired memory developed. She was found on examination to have optic atrophy and bitemporal hemianopia. After a right temporal decompression she became comatose, with a temperature of 104 deg., and died eight days later. A small tumour, classified as a perithelial sarcoma was found in the floor of the third ventricle just above the stalk of the pituitary gland.

(3) The relation of the hypothalamus to sexual function is further evidenced by the occurrence of *precocious sexual development* in other cases of hypothalamic tumour in young children.

In these cases the tumours are generally slow growing astrocytomas involving the posterior part of the hypothalamus, especially the corpora mammillaria. In one case described by Dott (1938) the child developed fits shortly after birth, began to menstruate at six months, and grew rapidly up to four and a half years of age and thereafter slowly. She had no complaints apart from the epileptic attacks, and symptoms of increased intracranial pressure did not develop before death took place following scarlet fever, at eight and a half years. An astrocytoma was found replacing the hypothalamus behind the posterior wall of the tuber cinereum. Other similar cases have been described, mostly in boys, and it is now considered probable that the sexual precocity previously associated with pineal tumours is most probably due to involvement of the posterior part of the hypothalamus in the tumour.

(4) *Hypersomnia.* This has long been recognised as a symptom of tumour of the infundibular region of the hypothalamus. The state may be continuous over long periods, or occur in well defined attacks, and it may also be associated with cataplectic attacks. It is important to distinguish between the somnolence, stupor and sluggishness which may develop in the course of tumours in other regions from increased intracranial pressure, and true hypersomnia associated with hypothalamic

tumours. The early onset of the condition during the course of the illness, its resemblance to normal sleep, and the absence of gross signs of increased intracranial pressure will justify hypothalamic localisation of the symptom. Again the physiological explanation is not understood. It seems most probable that hypothalamic activity is necessary for the waking state, so that destruction of this region to a greater or less extent, or of its efferent pathways posteriorly may result in a state of somnolence.

(5) *Disorders of body temperature.* Hyperthermia and hypothermia have both been observed as symptoms of hypothalamic tumours. The former is especially liable to follow operative interference with hypophyseal cysts involving the anterior hypothalamus, but it may also be a preoperative symptom of this or other hypothalamic tumours. The presence of a temperature in such cases has been known to lead to the erroneous diagnosis of encephalitis lethargica. The hyperthermia may be slight and only present for one to two days, or it may mount rapidly to a fatal height; or it may persist for several days, leading eventually to death from emaciation and exhaustion.

Hypothermia is possibly a less common symptom. It also may occur in attacks; or it may be persistent. Davison and Selby (1935) have described in a young man of twenty-one, hypothermia (93° F.) for long periods, absence of perspiration, adiposity, somnolence, attacks of dyspnoea, and a low blood pressure, due to an angioma involving the floor of the third ventricle.

The bodily functions which have to do with the conservation of body heat, or conversely its loss, and also those concerned with increased or diminished production of heat are clearly under the control of the autonomic system, and as the hypothalamus is the region for integration of the functions of this system, it is not surprising that disturbance of body temperature may result from hypothalamic tumours. There is some evidence to suggest that anteriorly placed lesions may be associated with hyperthermia, and posteriorly situated or very gross lesions with hypothermia.

(6) *Emotional and mental symptoms.* Symptoms of this order have been frequently observed at one or other stage in the clinical course of hypothalamic tumours. They are more frequent, however, as temporary symptoms due to acute disturbances of hypothalamic functions following operations. Maniacal excitement, sleeplessness, talkativeness, indecent conduct, pathological laughing and crying, exaggerated erotic mood, abnormal anger and aggressiveness, have all been observed. Emotional symptoms may, however, be the initial symptoms, and Roussy and Lhermitte (1924) have described a young girl of twenty-four who gradually became quiet and morose with suicidal ideas, indifferent to her parents, and neglectful of her religious devotions. In the midst of her depression she would have periods of abnormal gaiety, motor agitation and laceration. These symptoms were later followed by obesity, polyuria, narcolepsy, hyperthermia and failing vision, and radiotherapy of the hypothalamic region led to disappearance of both the somatic and psychic symptoms.

(7) *Glycosuria.* Periodic glycosuria is not an uncommon symptom of tumours in the hypothalamic area, especially following operative interference. It may occur with or without hyperglycaemia. The hypothalamus through a neurohormonal mechanism has clearly important influence over carbohydrate metabolism, and with this mechanism the symptom of glycosuria can be correlated, although its explanation is not yet clear. Hypoglycaemia has also been observed, but more rarely.

(8) *Polycythæmia* and *neutrophil leucocytosis* have both been described as symptoms of hypothalamic tumours. So far no explanation of their occurrence is forthcoming.

(9) *Other symptoms.* Alteration of blood pressure in either direction, disturbances of visceral mobility and tone such as meteorism and flaccid distension of the bladder, hyperpnoea or apnoea and hypersecretion of the gastric juice sometimes associated with fatal gastric or duodenal ulceration, have all been observed in acute hypothalamic disturbances associated with tumours. These symptoms most probably result from disturbances of the autonomic innervation of the region involved, and clearly such can arise in the hypothalamus.

(10) *Hypothalamic autonomic attacks.* Focal epileptic attacks indicating the region of cortex involved are common in tumours of the cerebral hemispheres. Similar local attacks have been described in tumours involving the hypothalamic region. In Penfield's case of cystic tumour of the third ventricle the attack would last five to twelve minutes. The patient first asked for cracked ice, then her face and arms flushed a deep red, her respiration became slow, tears rolled from her eyes, and saliva ran from the corner of her mouth. Her eyes were open, the eye-balls protruded and the pupils large and the pulse strong and rapid. Hiccoughing sometimes occurred, and the temperature would fall to 97°F. During the attack she remained quiet, but could be roused. Occasionally she lost consciousness with slowing or even cessation of respiration, but this was probably associated with increase of intracranial pressure which may have been the excitant of the attack. Cases in which such major hypothalamic attacks are the presenting feature are rare, but it is probable that minor attacks of the same order are more frequent.

II. Symptoms and signs due to involvement of adjacent structures.

(1) *Visual symptoms.* The optic chiasma is frequently pressed on by anteriorly situated hypothalamic tumours, resulting in three important clinical signs, namely, diminution of visual acuity, alteration of the fields of vision, and optic atrophy. These will vary with the position and rate of growth of the tumour. The field defect may be a bitemporal hemianopia partial or complete, an homonymous hemianopia, or blindness in one eye with a temporal defect in the other which may also involve the nasal field near the fixation point. In large tumours filling the third ventricle some degree of papilloedema may later develop, so that the optic discs may show a combination of the primary optic atrophy and papilloedema.

(2) *Sensory disturbances.* These are due to involvement of the thalamus. Different degrees of thalamic sensory loss characterised by central pain, hyperalgesia with diminution of superficial and deep sensation may result. Vasomotor and trophic disturbances have also been described in such cases.

(3) *Extrapyramidal disturbances* may occur from damage to the anterior part of the globus pallidus, and more posteriorly situated hypothalamic tumours may extend backwards and involve the nuclei of Luys, giving rise to *involuntary choreiform movements*.

(4) *Oculomotor and other cranial nerve palsies* may result from involvement of the posterior part of the midbrain or of the cranial nerves at the base of the skull.

(5) *Pyramidal disturbances* in greater or less degree may also occur.

III. The general symptoms of increased intracranial pressure.

Headache, vomiting, papilloedema, giddiness, lethargy and drowsiness, vary greatly, depending on the actual site and nature of the tumour. Slowly growing tumours may be present for years and give rise to local hypothalamic symptoms

without increased intracranial pressure. In another case early extension of the growth into the third ventricle may lead to blocking of the foramina of Monro or the aqueduct of Sylvius and give rise to early papilloedema, severe periodic headaches and vomiting. Again headache and vomiting may be severe and the cerebrospinal fluid pressure be greatly raised without papilloedema, as the actual position of the growth pressing down on the optic nerves may prevent the appearance of this sign. In such cases optic atrophy is likely to develop quickly.

IV. Special methods of examination, namely X-ray, and ventriculography, may furnish valuable aids to clinical diagnosis. Ordinary X-rays may reveal erosion of the clinoid processes, calcification in hypophyseal cysts, in basal cholesteatomas or in gliomas involving the hypothalamus. By careful ventriculographic studies it is possible to detect deformities of the third ventricle, and it is probable that by this method tumours of the ventricular floor, especially hypophyseal cysts, may be diagnosed in their early stages. It is only by the correlation of all the information obtained from an accurate clinical history, accurate clinical examination, and such special examinations as may be advisable, that an accurate diagnosis can be evolved, the prognosis judged, and the best possible treatment planned.

The Clinical Features of Hypophyseal Cysts.

These tumours, the frequency of which has been estimated at 4.5 per cent. of all intracranial neoplasms, give rise to characteristic clinical signs and symptoms which nevertheless vary somewhat with the age of the patient. They most frequently arise above the sella diaphragm, but they may actually arise within the sella itself. They are tumours of youth or early middle age, and approximately 40 per cent. give rise to symptoms before the age of fifteen and 75 per cent. before the age of forty. In children headache and vomiting are usually early symptoms. The headache may be generalised or predominantly frontal, and has the general features characteristic of headaches due to increased intracranial pressure. Some degree of papilloedema is also common in children, but the effects of direct pressure of the tumour on the chiasma is likely to lead to atrophy of the discs much sooner than would be the case with tumours in other situations. This will lead to rapid failure of vision and changes in the visual field, and in elderly patients these symptoms with primary optic atrophy are likely to be the prominent symptoms. The field defects indicating chiasmal pressure are one of the most important signs of these tumours. The chiasma is most likely to be pressed on from above and behind, so that a bitemporal hemianopia which commences first in the lower portion of the field on one or other side is the commonest finding. Irregular field defects such as lateral homonymous hemianopia, central scotomas and irregular changes are also common, due to variability in the site of origin and growth of the tumour. They may progress to complete blindness in one or both eyes. Symptoms from hypothalamic and pituitary derangement are always present in greater or less degree. These children are generally underdeveloped, their growth is retarded, their skin thin and hairless. They may be thin and emaciated, or slightly obese, or more rarely the typical Fröhlich syndrome may be found. In young adults sexual underdevelopment, loss of libido, impotence and amenorrhoea are prominent symptoms, and they are generally slightly obese with pale, delicate and hairless skin. The picture of emaciation, wrinkling of the skin and premature senility associated with gross pituitary changes is more rarely seen.

It is probable that in the production of these symptoms both pituitary and hypothalamic disturbances are responsible in varying degree. The hypothalamic symptoms have already been described, so that it is sufficient to say that the

pituitary disturbance is entirely responsible for the retardation of growth, and in greater part for the sexual dystrophy. Some of the tumours grow entirely upwards into the third ventricle and produce predominantly hypothalamic symptoms and signs of increased intracranial pressure. These are, however, rare, but it is to be noted that in association with cases of this type, either before or after operative interference, many of the acute disturbances of hypothalamic function already described have occurred.

Local symptoms may develop in advanced cases due to spread of the tumour and involvement of the oculomotor nerves, the fifth cranial nerves and the pyramidal tracts.

X-ray examination of the skull generally reveals an erosion of the clinoid processes, flattening of the sella turcica, and narrowing of the sphenoid sinus. Calcification is frequently present in the tumour, so that patchy shadows above or even inside the sella are often found.

Ventriculography may be helpful in the early diagnosis, as it may be possible to demonstrate filling defects of the third ventricle, and in those cases where the cyst fills the third ventricle it may even be necessary for the correct clinical diagnosis owing to the absence of local signs.

The Clinical Features of Pituitary Adenomas.

It is usual to divide the signs and symptoms of pituitary adenomas into those due to local pressure and those due to endocrine disturbances. The endocrine disturbances are, however, in part also due to local pressure, and in part due to the hyperpituitarism produced by the eosinophil adenomas. They vary therefore with the type of growth, but the pressure symptoms present a fairly constant picture for all types of growth.

Pressure Symptoms.

Headache is an early symptom. It is due to expansion within the sella, and is frequently bitemporal in distribution and bursting in character. It may cease for a time, later to recur in a more generalised manner when the growth breaks through the diaphragm of the sella. Visual symptoms are also an early and important feature. They are diminution of visual activity, alteration in the visual field, and pallor of the optic discs. The visual field defects generally present characteristic features. As the chiasma is pressed on from below the upper portions of the fields are first affected. This generally commences as a peripheral defect or a paracentral scotoma in the upper quadrant of one field, and gradually enlarges to involve the whole temporal field. A similar defect gradually develops in the opposite field so that a bitemporal hemianopia is produced. Some diminution of central vision is likely to be present, but even with a bitemporal hemianopia the visual activity may be 6/6 in both eyes. The visual loss extends to the normal field of the eye first affected, and may progress to blindness in this eye. Complete blindness in both eyes is only likely to be found in very late stages of the growth. Irregular field defects may however occur, such as lateral homonymous hemianopia and central scotomas which may give rise to early diminution of visual activity. The pallor of the optic discs may be very slight in the presence of considerable field defects, but later well defined optic atrophy is likely to be found in both eyes. Pituitary adenomas do not give rise to papilloedema, and also signs and symptoms referable to pressure on the hypothalamus, the adjacent cranial nerves and cerebral peduncles are rare, and when they do occur are very late symptoms. X-ray examination is an important aid to clinical diagnosis, as a general enlargement of the sella with thinning of its walls is always found.

Endocrine Symptoms.

Eosinophil adenomas give rise to gigantism if they develop before growth has ceased and acromegaly in adults. Acromegaly occurs in a few cases in which there is no tumour but only a general increase of eosinophil cells in the gland, otherwise it is always due to a tumour. In one third of the cases, however, this may not have grown large enough to give rise to visual symptoms. Space forbids the description of the clinical and pathological changes of acromegaly. These are due to the hypersecretion of the eosinophil cells. It is to be noted, however, that hyperglycæmia and glycosuria and also enlargement of the breasts and lactation sometimes occur in association with eosinophil adenomas and acromegaly. These symptoms may be due to overaction of other pituitary hormones. General impairment of sexual function, however, is common in acromegaly and is most likely due to hypopituitarism produced by the pressure effects of the growing adenoma.

Chromophobe adenomas. These tumours occur generally in adult life, and the endocrine symptoms are probably due to the destructive effect of the tumour on pituitary function. They very frequently resemble those produced by hypophyseal cysts. There is depression of sexual function, the skin becomes soft and pliable, there is loss of hair over the face, trunk and limbs, and moderate obesity frequently develops. Mixed adenomas are described in which the endocrine features are a mixture of hypopituitary and acromegalic features, but such tumours are excessively rare.

General Differential Diagnosis of the Hypothalamic and Pituitary Tumours.

Pituitary adenomas and hypophyseal cysts are much more common than the various tumours of the glioma group which may involve the hypothalamus, and difficulty in diagnosis between a chromophobe adenoma and a hypophyseal cyst may readily arise in middle aged subjects. The presence of any papilloedema, even superimposed upon a primary optic atrophy, is in favour of a hypophyseal cyst, but if the general clinical features are very similar, the X-ray appearances may alone be distinctive. Calcification is very rare in pituitary adenoma; and there is a great difference between the shallow widened and eroded sella turcica found in a hypophyseal cyst, and the greatly enlarged sella turcica found in pituitary adenomas. It is important to note that this enlargement is rarely regular, and can be readily distinguished from the smoothly enlarged or ballooned sella with tapering clinoid processes which is found in hydrocephalus of long standing. This is a point of great importance, because hypothalamic and even visual symptoms may occur in chronic hydrocephalus from posterior fossa tumours. These may first produce papilloedema which gradually subsides into atrophy and the local pressure of the dilated third ventricle as well as leading to ballooning of the sella, may produce field defects from chiasmal pressure. Clinically the differentiation may be very difficult, and attention must be paid to the early symptoms of the case. Ventriculography, however, will reveal the hydrocephalus with dilated third ventricle; or it may, on the other hand, show deformity or filling defect of the anterior part of the third ventricle if the tumour is in this location. The main diagnostic features of tumours of the hypothalamic region are the signs and symptoms which have been described. Ventriculography and the absence of marked X-ray changes in the region of the sella are additional aids. Special clinical features to be remembered are the periodic intense headaches sometimes associated with loss of consciousness which are found in third ventricle tumours, especially the colloid cysts. Gliomas of the optic nerve generally occur in children. They lead to primary optic atrophy and irregular visual field defects. A characteristic feature is dilatation of the optic

foramen on X-ray. These tumours are not a common cause of hypothalamic symptoms.

Pituitary and hypothalamic tumours must also be distinguished from (1) meningiomas arising from the dorsum sellæ. These tumours generally occur in middle aged adults, cause primary optic atrophy, with little headache or signs of increased intracranial pressure. Endocrine and hypothalamic symptoms are absent, and X-ray may show slight hyperostosis of the tuberculum sellæ or actual calcification in the tumour. Some of these tumours more anteriorly placed may lead to anosmia as an early symptom.

(2) Chronic circumscribed arachnoiditis may give rise to headaches and irregular visual field defects from chiasmal pressure. Cystic formation may even press on the hypothalamus and cause symptoms referable to this region. Clinical diagnosis is extremely difficult and in most cases failing vision requires exploration to exclude a removal cause, and it is in this way that the diagnosis is arrived at.

(3) Chronic meningovascular syphilis is a not infrequent cause of headache, primary optic atrophy, visual field defects, and also hypothalamic symptoms, especially diabetes insipidus. The clinical diagnosis may be difficult. Variability of symptoms and the early appearance of oculomotor nerve palsies may be helpful points. Definite serological changes in blood and cerebrospinal fluid will, however, be present.

(4) Congenital aneurism. These are most commonly found attached anteriorly or posteriorly to the circle of Willis. Anteriorly they may give rise to such symptoms as headache, visual failure, optic atrophy and oculomotor palsy. Their diagnosis may be extremely difficult if at no time of their history have they given rise to blood in the cerebrospinal fluid.

The association of pyrexia with some cases of hypophyseal cysts has led in the past to the possible diagnosis of encephalitis lethargica in cases of such tumours, but the differentiation of acute inflammatory diseases of the hypothalamus and tumours is not likely to be a matter of great difficulty.

Treatment and Prognosis.

Two lines of treatment are available for the large group of tumours which has been considered, and these are

(1) Surgical removal or (2) Radiation.

No tumour in the pituitary or hypothalamic region readily lends itself to surgical intervention. The pituitary adenomas are the most hopeful, and in these cases the prognosis is good. In cases of acromegaly or even in chromophobe adenomas radiation may be used without surgery, but only if there is no danger of visual loss. The acute hypothalamic symptoms which sometimes follow the opening and removal of hypothalamic cysts are a surgical difficulty. In these cases the prognosis is, on the whole, poor. The nature of the tumour makes its complete removal practically impossible, and they are not susceptible to radiation. Some cases have been dealt with by a two stage operation; one through the third ventricle, and a second approach via the chiasmal region. With regard to pure hypothalamic tumours, these are generally infiltrating gliomas, and radiation with or without a right temporal decompression may be the only possible treatment. Third ventricle cysts can, however, be dealt with surgically, and in suitable cases they furnish one of the major triumphs of cerebral surgery.

REFERENCES.

- BIGGART, J. H. (1935), *Brain*, **58**, 86.
DAVISON, C. and SELBY, N. E. (1935), *Arch. Neur. Psychiat.* **33**, 592.
DOTT, N. M. (1938), Henderson Trust Lecture **16**, Oliver and Boyd, Edinburgh.
FULTON, J. F. and BAILEY, P. (1929), *J. Nerv. Neurol. Dis.* **69**, 159.
ROUSSY, G. and LHERMITTE, J. (1924), *Rev. Neurol.* **31**, 65.