MENINGEAL TUMOURS: A REVIEW

BY

DOROTHY S. RUSSELL

From the Bernhard Baron Institute of Pathology, the London Hospital

The tumours to be considered here are those arising primarily in the meninges, or gaining access to them as secondary growths. It will be necessary to consider not only the dura and leptomeninges that invest the brain and spinal cord, but also their extensions into the brain as the tela choroidea and stroma of the choroid plexuses, and the sheaths of the perforating blood-vessels that form the outer boundary of the Virchow–Robin spaces. In the vertebral canal the separation of the dura from the bone by the epidural adipose and areolar tissue, and the resolution of the arachnoid and pia into two distinct membranes, introduce additional factors that are of importance, especially in the direct spread of tumours and the dissemination of their cells by the cerebrospinal fluid.

Although little has been heard of it lately, the old controversy as to whether the meninges are of mesodermal or of ectodermal origin cannot be regarded as satisfactorily resolved. In practice, however, it is undisputed that the primary meningeal tumours (meningiomas) display many features in common with meso-dermal tumours in other parts of the body ; the question of embryological origin is thus purely academic.

PRIMARY TUMOURS

The most important group to be considered includes the different varieties of meningioma. Before dealing with these it will be convenient to review a number of rarer tumours, composed of tissues or cells ordinarily foreign to the meninges, which are to be regarded as derivatives of embryonal remnants. These in general mostly occupy the leptomeninges in the mid-sagittal plane over the surface of the brain, though they may be laterally situated. In the vertebral canal they are often associated with congenital malformations, especially spina bifida.

Epidermoid and Dermoid Cysts

These are not sharply separable as distinct groups. The epidermoid, in which the squamous epithelial lining of the cyst is devoid of skin appendages, is far commoner than the classical dermoid. The best known form is the pearly tumour of Cruveihier, which arises in the leptomeninges as a smooth, often lobulated mass with a charac-teristic sheen derived from the concentrically laminated exfoliated keratin, mixed with cholesterin, which fills the interior and imparts so brittle a character to the mass. These tumours, which may develop to a considerable size, are usually found at the base of the brain either in the mid-line or in the cerebello-pontine angle ;

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occasionally in a lateral ventricle or over the corpus callosum. The lining of the cyst is a simple squamous epithelium. Smaller cysts lined with a similar epithelium have been identified in the pineal body and spinal cord. In the latter situation they are usually situated in the pia, but they may be embedded in the substance of the cord (Falconer and Hooper, 1941 ; Black and German, 1950). Epidermoid cysts and cystic tumours situated in the region of the sella turcica are usually not pearly and are often partly solid growths derived from remnants of Rathke's pouch. This conception of their origin is strongly supported by the frequency with which small nests of squamous cells can be identified under the microscope in and about the pituitary gland, its stalk and the adjacent leptomeninges. The content of these cysts is usually more or less fluid, turbid and brownish, with a suspension of abundant cholesterin crystals. The lining of the cyst may, as in the pearly tumours, be of a simple squamous character. More often, however, it is elaborated into papillary and trabecular formations which include cells of basal type as well as Malpighian cells, supported by connective tissue which is apt to undergo mucinous degeneration. Calcification and even bone-formation are frequent secondary changes in the solid parts of the tumour. Those forms in which the basal cells are conspicuous often receive the name of " adamantinoma." The propriety of using this term is, however, questionable since there is no sure evidence that these cells have any relationship to the ameloblasts of the enamel organ ; the resemblance is but superficial. The *dermoid cysts* are not clearly separable from the epidermoid. In fact Montgomery and Finlayson (1934) described a tumour, incorporated in the dura of the middle and posterior fossae, which was in part epidermoid only but in part dermoid. Occasionally cysts arise in the vermis which earn the title of dermoid from the presence within them of hairs, but are otherwise epidermoid. The fully developed dermoid cyst (Fig. 1) is rare ; that illustrated, which showed all the usual skin appendages, occupied the basal part of the frontal lobes.

FIG. 1.—Dermoid cyst from base of brain showing sebaceous glands and hair-follicles. H. and E. × 65.

Other teratoid tumours and typical teratomata may be encountered within the skull and vertebral canal but more frequently involve the tissues of the central nervous system than its integuments. In the spinal cord, however, they may abut on the meninges. A series of 15 such tumours arising in childhood has recently been described by Ingraham and Bailey (1946) ; eight of these were intracranial and seven intraspinal. Of the latter, five were associated with spina bifida.

Lipoma

Islands of adipose tissue, representing another variety of these embryonic remnants, occasionally manifest themselves as lipomata of the leptomeninges. As a rule they remain small, and are merely pathological curiosities disclosed during the routine examination of the brain. Bailey and Bucy (1931) found records of 60 reported cases. They usually lie over the corpus callosum or the tuber cinereum ; occasionally they are embedded superficially in the corpora quadrigemina, but have not been known to excite symptoms with the possible exception of Taubner's case (quoted by Bailey and Bucy, *loc. cit.*).

In the spinal cord larger lipomata may arise at the site of a spina bifida, and are sometimes intimately blended with the cord in addition to the meninges. A more diffuse involvement of the cord by lipomatous tissue, apart from spina bifida, may be accompanied by neurological symptoms, as in the well-documented case of Baker and Adams (1938), in which lipomata were found in the choroid plexus of the left lateral ventricle, the left cerebello-pontine angle, and throughout almost the whole length of the spinal cord.

Melanoma

A well-defined though rare condition, recognized first by Virchow (1859) and named " melanosis " of the meninges, is clearly a naevoid form of neoplasia in which the leptomeninges over the base of the brain are especially apt to be affected. There is diffuse pigmentation from the infiltrating cells, which may penetrate deeply into the nervous tissue along the sheaths of perforating vessels. Hydrocephalus is a recognized sequel (Russell, 1949). Extensive cutaneous pigmented naevi may be associated with the cerebral abnormality. These cases have been reviewed by Schnitker and Ayer (1938).

Circumscribed melanotic tumours of the meninges and adjacent brain substance have also been reported by several observers, and doubtless certain of these are acceptable as arising primarily in this situation. But doubt must be entertained concerning this point in examples where a complete necropsy has not been performed, and there are many reports in which fuller particulars are desirable. The histological appearances may be those of a malignant tumour ; even when histologically benign the liability to recurrence after operation seems to be considerable (Christensen, 1941). It is desirable to distinguish between this group and the occasional examples of meningioma, to be described later, in which melanin pigment may be produced by the tumour cells.

Chordoma

Remnants of notochordal tissue may linger in the region of the basisphenoid and basiocciput, and give rise either to ecchordoses or chordomas, which are usually disclosed in the adjacent meninges. The ecchordosis, a chance finding at necropsy, is a small jelly-like mass of greyish-white tissue which generally lies over the basilar artery, and is attached by a delicate stalk to the dura over the clivus. The notochordal cells of which it is composed are usually in advanced stages of degeneration ; the mass is essentially inert and incapable of further development.

The chordoma, on the other hand, is an invasive tumour capable of penetrating the meninges and exerting pressure within the cranium, or upon the nerve-roots

in the sacro-coccygeal region. Since these tumours are related primarily to the bone rather than the meninges they will not be discussed further.

Meningioma

This group is one of the most important of the intracranial tumours, forming from 12 to 16% of the total in large published series from various neurosurgical centres. The name now so generally adopted was originally introduced by Cushing in 1922. Its significance is clearly generic, and it comfortably evades the controversy that inevitably ensues when attempts are made to devise a suitable name with cytological implications for a group of tumours with the most diverse microscopical appearances. The old name " dural endothelioma " held pride of place until it came to be recognized, following the work of M. B. Schmidt (1902), that the source of origin of such tumours lay in the nests of ara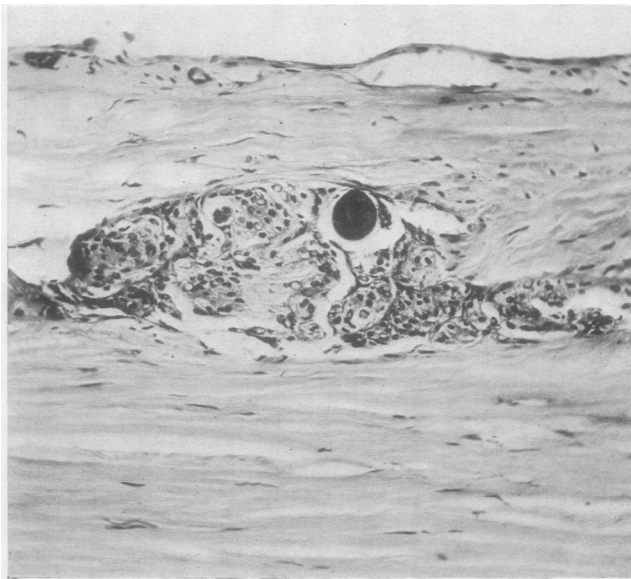chnoid cells included in the dura as arachnoid villi (Fig. 2). But neither " arachnoid fibroblastoma " (Mallory, 1920) nor " meningeal fibroblastoma " (Penfield, 1927) can be regarded as satisfactory equivalents for a tumour which often appears quite devoid of fibroblasts.

FIG. 2.—Arachnoid villus projecting into dural vein remote from a main sinus. The dark circular mass is a calco-spherite. H. and E. × 160.

The diversity of cell type that goes to form the meningiomas is best understood in recollecting that the arachnoid cells form the macrophages of the cerebrospinal pathway in the meninges, are vitally stainable with trypan blue and are thus a component of the reticulo-endothelial system. Their polyblastic character is reflected then in the cytological and architectural variations in the neoplasms to which they give rise, and this has found expression in a considerable number of suggested classifications. The best known of these are by Bailey and Bucy (1931), Globus (1937), Cushing and Eisenhardt (1938), and del Rio Hortega (1941). I attempted to tabulate these in terms of their synonymous types, but the existence of transitional forms that are recognized and named by some workers but not by all, and the consequent lack of a precise equivalence in the definition of the accepted types by these authors, made the task impracticable. Again variations in experience have led to the inclusion of sundry rare types in one classification or another, but not in all: for example, chondroblastic meningiomas (Cushing

and Eisenhardt), and melanotic (Bailey and Bucy). It is perhaps better to pass by these discrepancies and difficulties, with the recognition that they exist, than to elaborate their details. For Cushing and Eisenhardt (p. 54) frankly state: "We regard most of the subdivisions, i.e., variants, under a given type as fundamentally unimportant. Indeed, we find, somewhat to our surprise, that there is essentially little difference even between certain of the main types, either from the standpoint of histo-functional differentiation or life history of the tumour." Further, as will be shown, any rigid attempt to relate histological varieties to one or other of the three meninges as the tissue of origin is to invite contradictory experience.

Cushing's opinion is certainly endorsed by the results of tissue-culture in various histological types of meningioma (Bland and Russell, 1938). We found a considerable range of variation in the patterns of growth and in the morphology of the cells, ranging from sheets of flat, polygonal cells of "epithelioid" appearance to spiky growths of narrow spindle cells. But these variations appeared in different cultures of the same tumour, and could not be correlated closely with the morphology of the cells of the parent tumour.

It is proposed, therefore, to adopt the simpler scheme of Courville (1945), who suggested five main types: (i) syncytial, (ii) transitional or mixed, (iii) fibrous, (iv) angioblastic, and (v) sarcomatous. These are tolerably well recognizable as equivalents in the other main classifications. After summarizing these some attention will be devoted to the rarer varieties that perhaps hardly merit recognition as "types."

(i) **Syncytial Type** (Meningotheliomatous meningioma of Bailey and Bucy; leptomeningioma of Globus; meningothelial meningioma, Type I, of Cushing and Eisenhardt; exotelioma difusa of Rio Hortega).—This form, as the name suggests, is composed of sheets of polygonal cells subdivided irregularly by vessels and collagen fibres; fibroglial fibrils and reticulin are absent (Fig. 3). The cell-boundaries are often poorly defined. This type was designated "endotheliomatous" by Bland and Russell (1938) and we found that it accounted for 56.6% of our series.

(ii) **Transitional Type** (Psammomatous type of Bailey and Bucy would be included here; also the "primitive meningioma" of Globus; meningothelial Type II of Cushing and
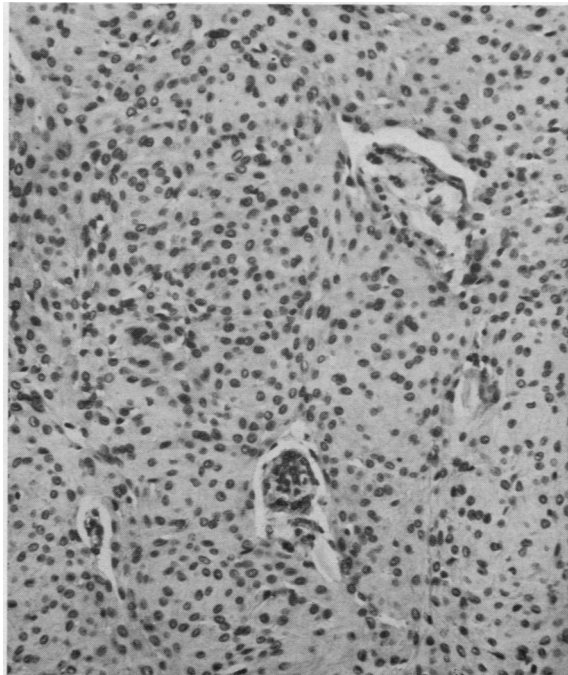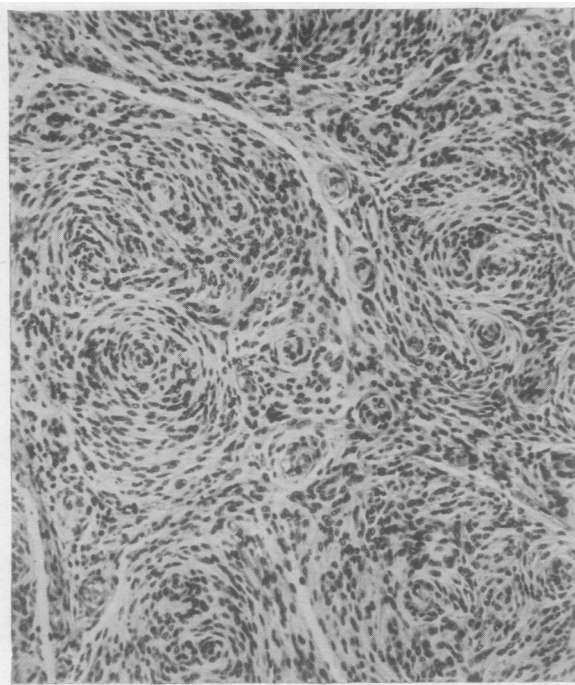

FIG. 3.—Meningioma: syncytial type. H. and E. × 165.

FIG. 4.—Meningioma: transitional type.   H. and E. × 133.

Eisenhardt ; exotelioma nodular and lobulado of Rio Hortega). —It is generally agreed that many examples of the syncytial type show a greater or less tendency to the formation of whorls, in which groups of the cells are wrapped round one another recalling the appearance of an onion in transverse section (Fig. 4). The intervening cells between the whorls tend to be spindle-shaped and to contain fibroglial fibrils. This tendency is recognized by Cushing and Eisenhardt in their description of four variants of Meningothelial Type I, and in their separation of a Meningothelial Type II in which the outstanding feature is the predominance of whorls a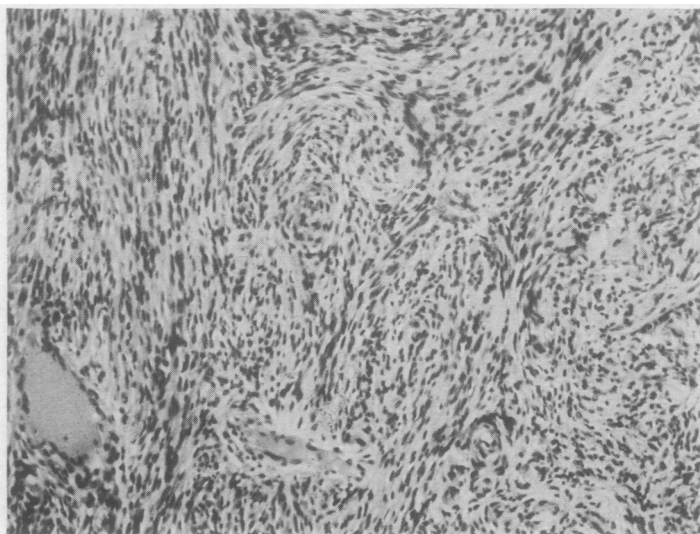nd their further conversion into psammoma-bodies. There is obviously no sharp distinction here, but a smoothly graded series in which the progressive development of whorls and psammoma-bodies, separated by collagen and spindle cells, comes to dominate the histological picture. A convincing interpretation of this ultimate s t r u c t u r a l arrangement has been advanced by Orville Bailey (1940), who likens the polygonal cells to the functional arachnoid cells of the villi and Pacchionian bodies, where they form the cap cells ; whilst the spindle cells, containing fibroglial fibrils, are interpreted as stroma cells such as the covering arach-

FIG. 5.—Meningioma: fibroblastic type.   H. and E. × 123.

noid cells require for their support, and might be expected to evoke. Bailey found no evidence that the fibroblastic cells were derived by differentiation from the arachnoid type of cell. Moreover the rate of growth and prognosis do not appear to differ substantially with the development of fibroblastic cells within these tumours. The clinical features of these two types, syncytial and transitional, which together accounted for 65% of Cushing and Eisenhardt's series, thus reflect in no way their histological diversity.

(iii) **Fibroblastic** (Bailey and Bucy; Cushing and Eisenhardt; dural fibroblastoma of Globus; exotelioma laminar of Rio Hortega).—The fibrous meningioma of Courville may also be included, but his description of the additional features of whorls and psammoma bodies does not allow of a clean separation from (ii). The tumour described by Bailey and Bucy is regarded by Cushing and Eisenhardt as being rather of a fibrosarcomatous nature; the reason for this is not clear since it seems to have behaved like a benign tumour. In general, however, this type is rich in stout collagen fibres, between which the spindle cells lie. These cells form interweaving bundles, and occasionally loose whorls such as are seen in the acoustic nerve tumours (Fig. 5). Fibroglial fibrils are conspicuous (Fig. 6). Though some are attached to the dura, excellent examples may arise from the pia of the spinal cord, and the intraventricular meningiomas are generally of this group. The term "dural" fibroblastoma (Globus) is therefore inappropriate.

(iv) **Angioblastic** (Bailey and Bucy; Cushing and Eisenhardt; Globus classifies this as a sub-type both of pial meningioma and of leptomeningioma; Rio Hortega separates it from the meningioma group altogether).—This is a distinctive

FIG. 6.—Meningioma: fibroblastic type showing fibroglial fibrils in cells. P.T.A.H. × 440.

type of cellular tumour in which numerous small and larger blood-spaces of capillary structure are separated by plump polygonal cells which are often foamy and may show mitosis (Fig. 7). Fine reticulin fibrils form a dense network throughout the tumour (Fig. 8). Some of these tumours are identical in appearance with the haemangioblastoma of the cerebellum (Lindau's tumour), and in this connexion it is of interest that Cushing noted their predilection for the tentorium and the peritorcular region. But undoubtedly a good many are of pial origin and we have encountered a classical
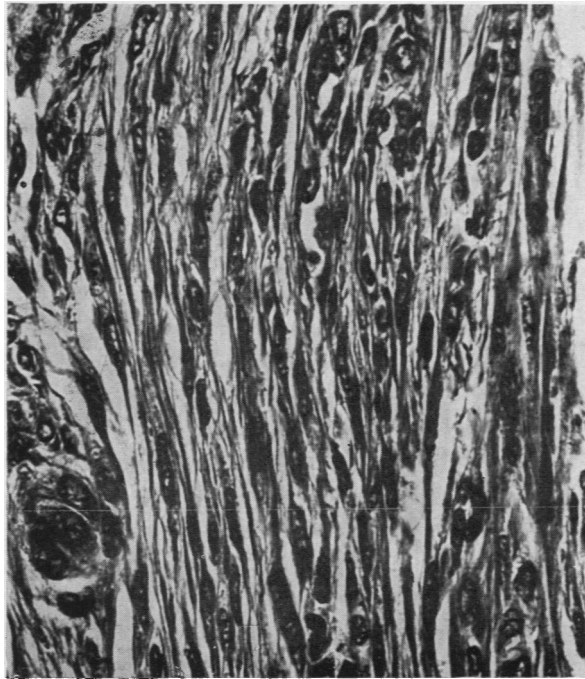
FIG. 7.—Meningioma: angioblastic type. P.T.A.H. × 380.

example arising in the pia of the spinal cord and in the lepto-meninges of the cerebrum. It is therefore pertinent to inquire into the propriety of including the cerebellar tumours in this group; a question upon which there is no agreement. These cerebellar tumours are cystic or solid growths arising in the mid-line or laterally; occasionally the tonsil is the site of origin. Others, however, may spring from the dorsal aspect of the medulla oblongata, in the region of the area postrema. In the cystic examples the wall of the cyst is composed of smooth neuroglial tissue which is occupied at some point by a reddish-brown nodule of the tumour proper, the "mural nodule," which may be very small in proportion to the whole. The cyst contains clear straw-coloured fluid, rich in protein, which is regarded as a transudate from the capillaries of the tumour nodule. Microscopically the tumour is composed of a mesh of blood-spaces, of capillary structure but of varying calibre, supported by a stroma of plump polygonal cells. The cytoplasm of these cells appears vacuolated in paraffin sections, and is characteristically laden with doubly refractive Sudano-phil material in frozen section. Reticulin stains show a wealth of fine fibrils
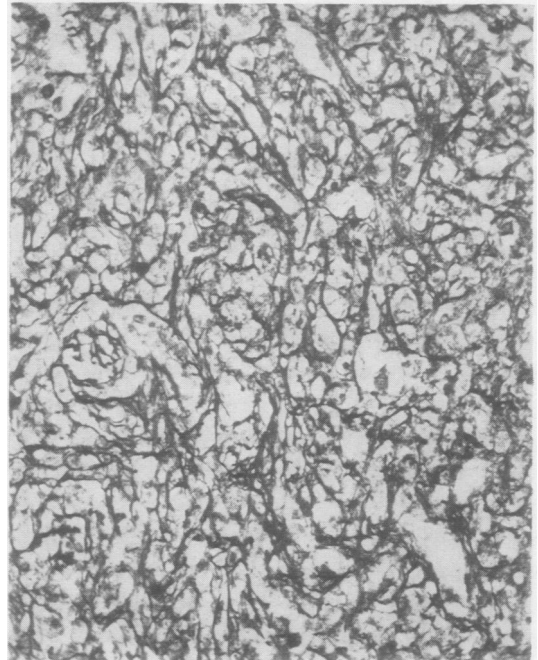

FIG. 8.—As in Fig. 7 to show reticulin. Laidlaw × 380.

supporting these cells and forming the basement-membranes of the blood-spaces.

The obvious similarity between these tumours and the angioblastic meningiomas has provided the theme of several studies (Wolf and Cowen, 1936 ; Bailey and Ford, 1942 ; Corradini and Browder, 1948) in which the attempt has been made to decide whether or not they were clearly separable. In general the influence of Bailey, Cushing, and Eisenhardt (1928), who originally favoured their separation, seems to have prevailed. The chief grounds for this view lie in the apparent dural origin of most of the supratentorial tumours and their non-cystic character, whereas the cerebellar examples appear to be embedded in the neural tissues. No single criterion, however, appears absolute in actual experience. The supratentorial examples may arise independently of the dura, as already noted. Further they may be cystic, as in the case reported by Barnard and Walshe (1931), though this is clearly exceptional judging by the lack of similar cases in the literature. The cerebellar haemangioblastoma may be solid and, although it is regarded as being intracerebellar and usually devoid of any attachment to the leptomeninges (Corradini and Browder), there are reasons for doubting this. We have already noted (Bland and Russell, 1938) that " many of these cerebellar tumours are contiguous with, and in some cases involve, the pia." I have recently reviewed a series of 33 cases of this group obtained both from biopsy and necropsy in this Institute. There is evidence of direct continuity between the tumour and the pia in 21 of these ; in the remainder (biopsies) the material is insufficient for the analysis. It is proposed to substantiate these observations in a separate communication. Here it must suffice to state that the relationship between these cerebellar haemangioblastomas and the pia appears to be of so intimate a character in such a large proportion of examples that their pial origin cannot reasonably be denied. The reader's attention is directed to Fig. 106 on p. 148 of Cushing and Bailey's m o n o g r a p h (1928) illustrating the presence of tumour tissue over the surface of the cerebellar cortex in an example of cerebellar haemangioblastoma, and to the article by Bailey and Ford (1942) in which (case 2) a cerebellar tumour of this type is described as arising from the leptomeninges, and is interpreted by the authors as transitional between the two groups of tumour under discussion.

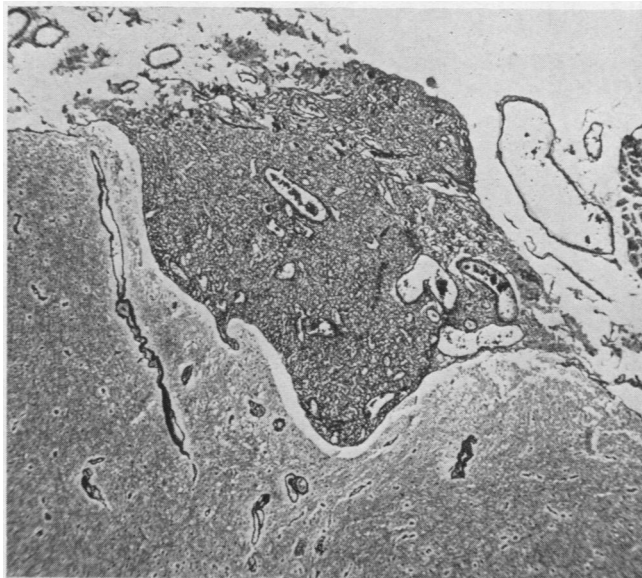It must also be noted that the capillary haemangioblastoma can occur in the spinal

FIG. 9.—Capillary haemangioblastoma in pia over spinal cord in a case showing Lindau's syndrome. Laidlaw × 27.5.

cord and, when deeply embedded in the cord tissue, is liable to be complicated by syringomyelia. But again there is continuity between the tumour and the pia and examples are occasionally encountered in which the pial origin of the tumour is obvious (Fig. 9). This illustration is taken from a case that displayed the features of Lindau's syndrome (infratentorial capillary haemangioblastoma with multiple pial tumours in the spinal cord, von Hippel's disease, multiple cysts of the pancreas and solid and cystic tumours of benign Grawitz type in the kidneys).

Lindau (1931) listed angioma of the retina (von Hippel's disease), cystic pancreas, cysts of the kidneys and " hypernephromata of the kidneys or the suprarenal glands " as the ingredients of the syndrome that goes by his name. He particularly mentioned the cystic pancreas as characteristic. This curious assortment of pathological conditions constitutes an inherited disease, but accompanies a small proportion only of these infratentorial haemangioblastomas, and has not so far been recorded in association with the supratentorial angioblastic meningiomas. This alone suggests that the infratentorial tumours possess an individuality that demands their consideration as a separate group.

FIG. 10.—Meningioma of spinal theca containing much lamellar bone. H. and E. × 11.

Histological Variations.— Before proceeding to the malignant, or sarcomatous, forms of meningiomas it is proposed to deal briefly with certain histological variations which, if rare, are nevertheless important in gaining a general view of these neoplasms and their potentialities. These are concerned with the presence of bone, cartilage, melanin, and doubly refractive Sudanophil fatty substances.

(a) *Bone.*—Meningiomas of the first three types described above occasionally contain bone, which may be coarse-fibred or lamellar or bot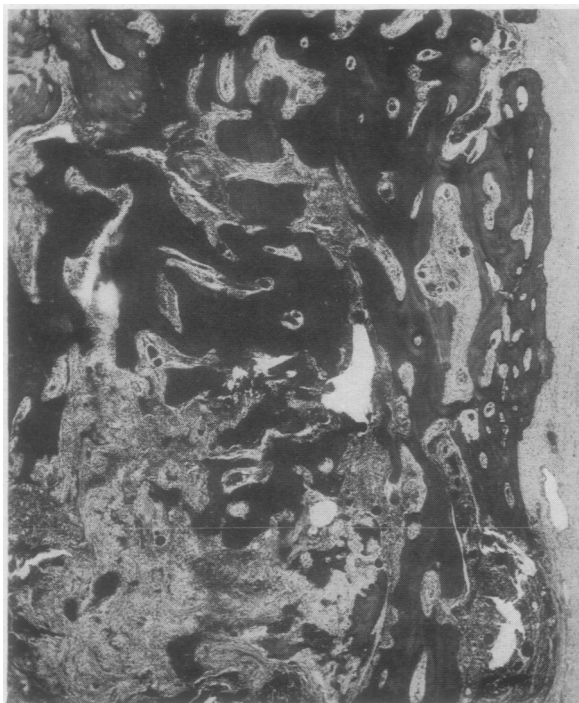h. Sometimes the bone is laid down in relation to calcified psammoma bodies, but usually it is independent of these. This should not be confused with the well-known hyperostosis of the adjacent cranium which will be considered separately. Indeed, in our experience, it is the spinal examples that are most liable to be osteoblastic (Fig. 10). The anatomical separation here of the dura from the bone exemplifies well the distinction between these two features.

(b) *Cartilage.*—The presence of cartilage in meningiomas must be exceedingly rare. Bailey and Bucy do not mention it, and in Cushing's series there is only one

such case, which proved to be a chondrosarcoma. Cushing and Eisenhardt mention seven others from the literature, one of which (Wolf and Echlin, 1936) also was malignant. Recently Forsythe, Baker, Dockerty, and Camp (1947) in reporting a large osteochondroma, apparently arising in the dura over the cerebral convexity and falx in the same style as a meningioma, state also that approximately 38 cases of primary solitary intracranial cartilaginous tumours had been reported to date. It is doubtful how many of these should be interpreted as chondroblastic meningiomas in the sense described by Cushing and Eisenhardt. Some may indeed arise from cartilaginous rests, as suggested by Wolf and Echlin, but they also pointed out that such rests had not been identified in the dura or pia-arachnoid. I have, however, once encountered a cartilaginous rest in the falx of a kitten ; the possibility is thereby strengthened.

(c) *Melanin.*—This pigment is normally present in the pial cells over the ventral surface of the medulla oblongata and upper cervical cord ; it is less frequent elsewhere. Melanin therefore appears in occasional examples of meningioma, particularly of the posterior fossa and spinal cord. Surprisingly this phenomenon is not mentioned by Cushing and Eisenhardt. Bailey and Bucy describe one example, in a girl of 9, who had multiple small pigmented tumours in the cerebral leptomeninges and in the floor of the fourth ventricle, without evidence of a primary source elsewhere in the body. Microscopically the tumours were composed of polyhedral cells containing melanin and scantier spindle cells in bundles. Abundant reticulin fibres divided the tumour cells into alveoli. Mitoses were noted as " common throughout." The account of this case raises considerable doubt concerning its real nature. The peculiarities of malignant melanomas in general certainly invite caution in their interpretation. Occasionally, however, a meningioma is encountered with the characteristic appearances of the t r a n s i t i o n a l or fibroblastic type but differing in the conspicuous, though often patchy, development of melanin granules in the cytoplasm of the tumour cells.

(d) *Fatty Substances.*—Meningiomas of types (i) and (iv) quite often contain so much intracellular Sudanophil lipoid that they are opaque and yellowish macroscopically, and foamy in stained paraffin sections (Fig. 11). The appearances suggest a storage process rather
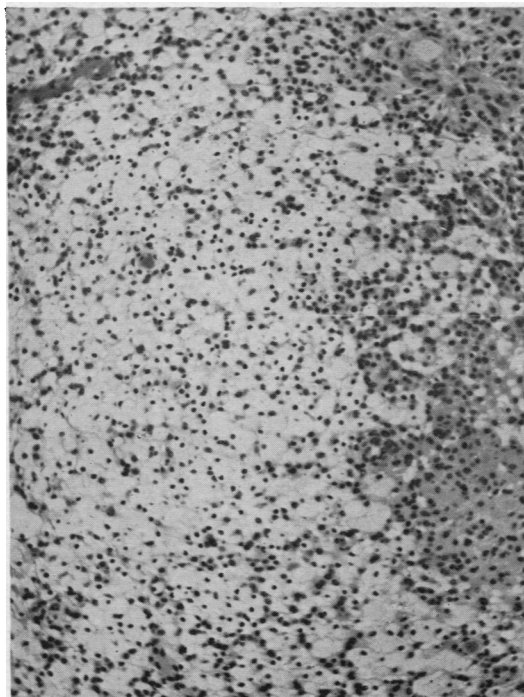

FIG. 11.—Meningioma of syncytial type with conspicuous xanthomatous areas. H. and E. × 109.

than degeneration since the nuclei are well preserved and the lipoid is doubly refractive.

(v) **Sarcomatous Meningiomas.**—The forms so far considered have been benign. When incompletely removed they usually recur, but it is seldom that they display a greatly increased rate of growth, histological evidence of malignancy, or diffuse invasion of the adjacent brain. But when these occur there may be a striking alteration in the cytological appearances and architecture of the tumour, as in Cushing and Eisenhardt's case, Doroth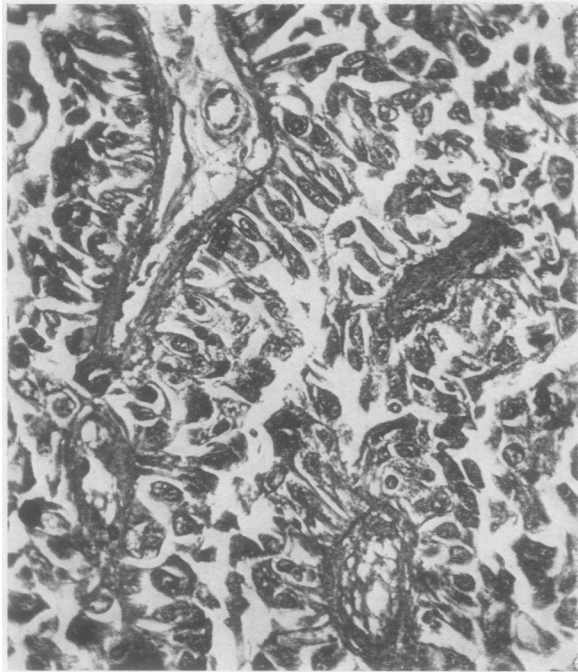y May Russell, who underwent 17 operations for removal of recurrent growth and finally, at necropsy, was found to have pulmonary metastases. Starting as a spindle - celled tumour this example ended with a papillary epithelial structure which was reflected in the metastases. I have twice observed a similar papillary appearance in undoubted meningiomas (Fig. 12). Malignancy was suggested in one of these by invasion of the brain ; in the other, in a girl of 16, a fatal recurrence of the growth followed operative removal. Though Cushing and Eisenhardt attributed sarcomas to the fibroblastic type of meningioma, and thus wrote of fibrosarcomas, it seems that potential malignancy is not the exclusive attribute of any one type. The angiomatous meningioma in particular carries a relatively poor prognosis, being of rapid growth and apt to recur after radical treatment, and prone to invade the brain at late stages. Histologically this tumour often contains a considerable number of mitotic figures.

FIG. 12.—Meningioma with papillary structure. Silver carbonate × 350.

Swingle (1949), however, has reported a case in which, like Cushing's, the tumour was of fibroblastic character. Eight years after radical treatment a recurrence was partly removed and the patient, a male aged 39, died five years later with pulmonary metastases. An example, recently examined in this Institute, is of interest in showing a profound alteration in the cytology and general character of a frontal para-sagittal meningioma at successive operations. The patient, a man aged 24, was admitted first to the London Hospital in 1948 under the care of Mr. D. W. C. Northfield. The tumour removed then.was a well-defined growth of typical and benign appearance, with numerous whorls separated by short spindle cells (Fig. 13). As shown in the photomicrograph a narrow fringe of cerebral tissue, adherent in places

to the surface, is indented by bosses of tumour tissue, but not obviously invaded. The recurrence, removed a year later, is a spindle-celled fibrosarcoma with great variation in the size of the cells and the chromatin content of their nuclei. Mitoses are numerous (Fig. 14). It invades the brain diffusely, with the segregration of islands of neural tissue within its advancing borders (Fig. 15). This case is of importance not only in showing this change of cell type in the acquisition of malignancy, but also in supporting Orville Bailey's view that the fibroblastic type of meningeal cell is not a product of differentiation.

Occasionally no such transition from a benign to a malignant form of meningioma is observed : the tumour is a sarcoma when first seen. A group of this kind has been described by Globus and others (1944). Particularly when such tumours are disclosed in chil-

FIG. 13.—Meningioma removed at first operation showing benign, whorled type of growth, and its relationship to adjacent cerebral tissue. H. and E.× 175.

dren and young subjects it seems likely that they have been sarcomatous from the start. Histologically they may be highly cellular fibrosarcomas, or of a primitive mesenchymal character as exemplified in a recent report of a fibro-myxosarcoma of the skull and meninges in a child of 3 (Baker, Dockerty, and Kennedy, 1950).

Metastasis.—In Cushing and Eisenhardt's malignant example, mentioned above, a sarcomatous change in the primary tumour was followed by pulmonary metastasis, disclosed at necropsy. There are few other records of blood-borne metastasis, and the meningiomas appear to share with other intracranial tumours a notable reluctance to spread in this way. Abbott and Love (1943) reported a malignant haemangioblastic meningioma of the frontal region in a man of 32 ; this, after two operations for resection of the growth combined with radium therapy, metastasized as nodules of firm grey tissue to all lobes of both lungs. The total length of the history was three years and nine months. Other metastasizing meningiomas have been reported by Jurow (1941, one case), Russell and Sachs (1942, three cases), Hamblet (1944, one case), and Swingle (loc. cit.).* The cases of Jurow and Hamblet are remarkable for the typical appearances of the secondary deposits, which displayed well-developed whorls of arachnoid-cell type. The authenticity of Russell and Sachs' three cases has been questioned by some writers, in particular their case 2 in which 13 years intervened between an operation for the removal of the meningioma (which did not recur locally) and the appearance of metastases
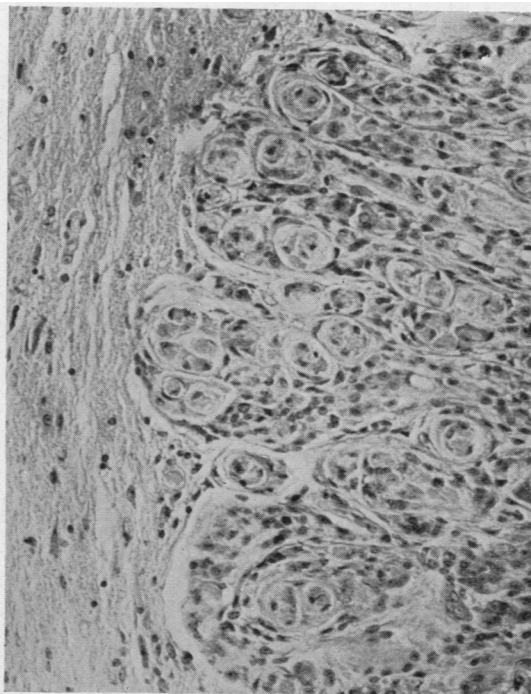
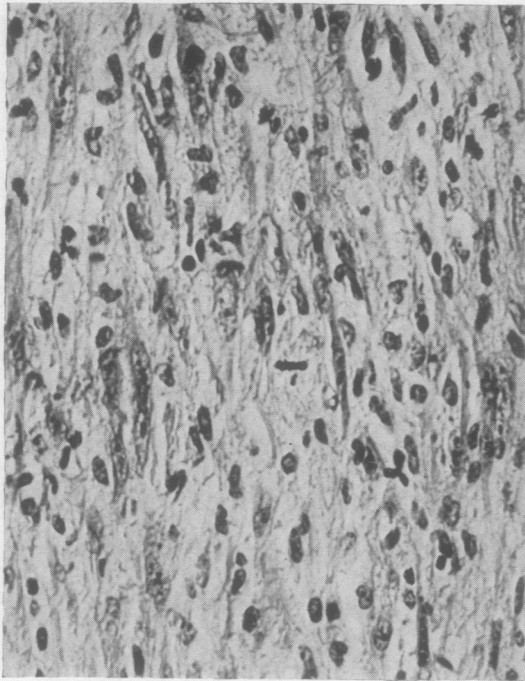* Recently Christensen, Kiaer, and Winblad (1949) have reported two further examples.

FIG. 14.—Meningeal fibrosarcoma from second opera-
tion (see Fig. 13).   Mitosis at centre of field.   H.
and E. × 370.

elsewhere. Their case 3 is certainly difficult to interpret, but their case 1 appears to be indisputable. Six of the reported cases are therefore acceptable.

Sites of Origin and Methods of Local Spread.—With few exceptions there is no close association between the histological varieties of the meningiomas and their topography. While most of them are firmly attached to the dura over the brain or spinal cord, a few are found to embed themselves in the nervous tissues, and to be attached to the pia or leptomeninges only ; an important group is related to the ventricles of the brain. The origin of many of the dural tumours is traced to the presence within that membrane of nests of arachnoid cells, forming the villi and Pacchionian bodies. Hence the meningiomas frequently arise in relation to the main dural venous sinuses, especially the anterior half of the superior longitudinal sinus. Their origin at more remote sites over the cerebral convexities may be traced to the development, increasing with age, of similar arachnoid nests as pointed out by Schmidt (1902). Alternatively, as Orville Bailey has argued (1940) a meningioma arising primarily in the leptomeninges may gain a secondary dural attachment upon breaching the arachnoid membrane.
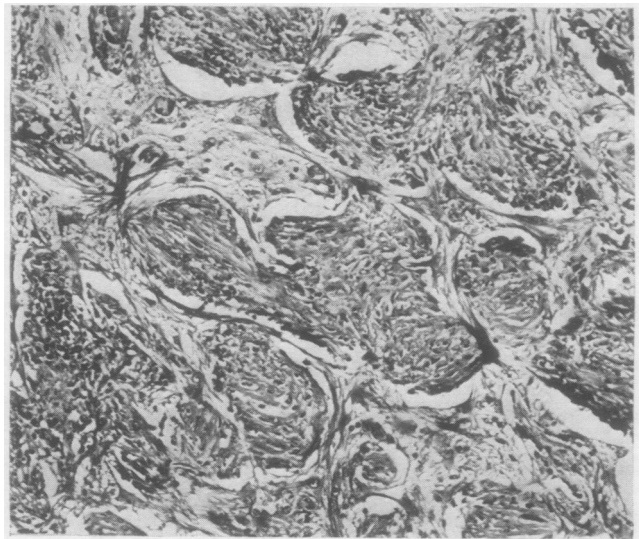

FIG. 15.—Same specimen as in Fig. 14 ; margin of growth showing
inclusion of islands of nervous tissue (lighter areas) within
spindle-celled growth.   Masson's trichrome × 130.

Clinically the anatomical situation of these tumours is the predominant considera-tion, and they are usually classified accordingly in practice rather than upon the more academic aspects of their cytology. Such an arrangement is found in Cushing and Eisenhardt's important monograph, to which the reader is referred for fuller details. Here it must suffice to point out that the meningiomas frequent the anterior part of the cranium more than the posterior. The parasagittal examples may penetrate the falx to become embedded in both frontal lobes; they have been carefully studied by Olivecrona (1934). The lumen of the sinus is often invaded, and even occluded, by the growth but without metastasis taking place. The region of the Sylvian fissure as it traverses the ventro-lateral border of the cerebrum, the olfactory groove (Fig. 16),

the tuberculum sellae, the lesser wing of the sphenoid, the cavern-ous sinus, and the sheath of the optic nerve are additional sites. The last men-tioned is relatively rare, but a menin-gioma may arise here, especially in child-hood, as a dumb-bell mass constricted by the optic foramen. Craig and Gogela (1950) have re-ported two cases of bilateral and one of unila-teral foraminal tumours with slowly progressive blindness as the sole symptom.
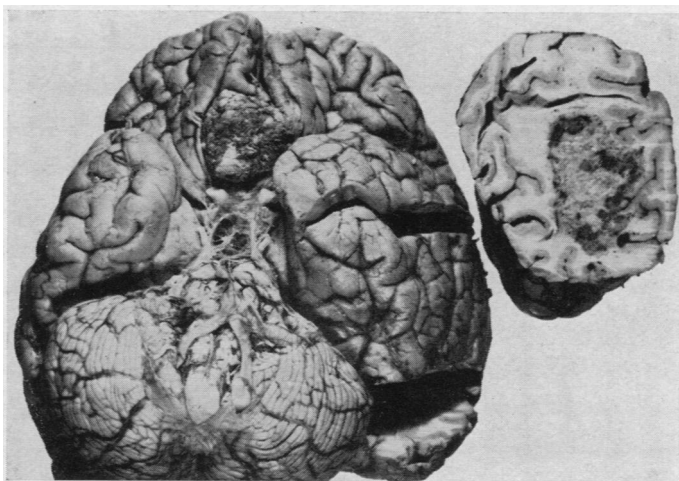

FIG. 16.—Combination of meningioma of olfactory groove and spongioblastoma multiforme of left occipital pole.

In relation to the posterior part of the brain, meningiomas may arise over the convexities, the main dural sinuses including the torcular, from the posterior aspect of the petrous bone or in relation to the foramen magnum.

As already mentioned meningiomas of fibroblastic type may occur in the ventricles. Here they arise in the stroma of the choroid plexus, or in the velum interpositum. It is remarkable that, like the choroid plexus papilloma, they seem to have a preference for the left lateral ventricle which is gradually distended by a firm globular mass of growth, to the surface of which the remnant of the plexus is attached. It has been argued as to whether the tumour arises in the stroma of the plexus at the confluence of the occipital and temporal horns, or whether it extends laterally into the ventricle from the tela choroidea, pushing the plexus before it. Support is gained for the former view by the observation in this Institute (P.M. 92.1945) of a small example measuring 2.5 × 2 × 1.5 cm. at this point of the plexus (Fig. 17). The tumour was symptomless. The intraventricular meningiomas have been reviewed by Abbott and Courville (1942), who found reports of 50 cases in the literature. As they point out, the tumour may occasionally take the form of a sausage-like thickening of the whole length of the plexus. A remarkable
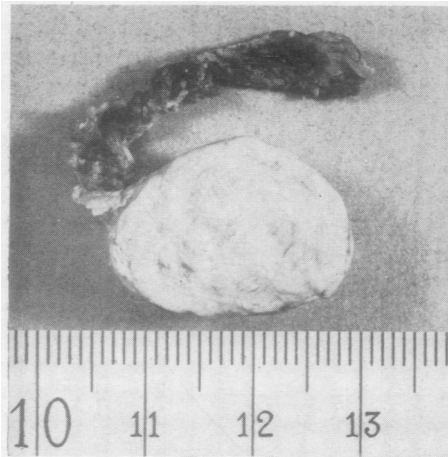
FIG. 17.—Small meningioma arising in choroid plexus.

example of this, affecting both plexuses of the lateral ventricles in a symmetrical fashion, occurred in this Institute many years ago (P.M. 36.1924) in association with von Recklinghausen's neurofibromatosis. The case is briefly mentioned by Cushing and Eisenhardt (p. 114). In distinction to the usual fibroblastic type, the tumours in this case were highly psammomatous.

Corresponding tumours of the fourth ventricle seem to be far rarer and more debatable ; they are fully discussed by Cushing and Eisenhardt.

The meningiomas of the vertebral canal are the commonest tumour of this region according to some, but in other neurosurgical centres the nerve-root tumours slightly preponderate. As in the cranium, they are usually attached to the inner aspect of the dura. The arachnoid villi, from which they arise, are formed where the arachnoid membrane is brought into apposition with the dura at the emergence of the nerve roots. Occasionally, however, the tumour arises in the pia and becomes deeply embedded in the substance of the cord. The commonest levels at which the meningiomas occur are the thoracic segments, according to Elsberg (1941), who had a unique experience with these and other spinal-cord tumours. He records that 80% of his 73 cases were in women.

Hyperostosis.—In addition to penetration through the dura and occupation of adjacent venous sinuses, the convexity meningiomas show a notable tendency to invade the overlying bone, and may even penetrate the pericranium, muscles, and cavities of air-sinuses. But such invasion is no indication of malignancy, in terms of cytological change or remote metastasis. Involvement of the bone usually leads to a conspicuous thickening, or hyperostosis, of the part affected. The mechanism of this bony change is still warmly debated. Bailey (1940), Courville (1947), and Freedman and Forster (1948) have discussed the rival theories. From these and other papers it is clear that there is no agreement as to whether or not the tumour cells are directly responsible for the deposition of new bone. Obviously, as already noted, the meningiomas are capable of producing bone within their substance. But tumours displaying this propensity seem seldom to be associated with a hyperostosis of their cranial attachment. On the other hand there is a good deal to suggest that the meningioma, like certain carcinomatous metastases, exerts an osteoplastic effect in which the tumour cells themselves cannot be directly responsible for bone-production. Thus in some examples of convexity meningioma the inner table of the adjacent skull shows a nipple-like protrusion towards the centre of the attached growth, without histological evidence of invasion of the bone by growth. The medullary spaces of the region are occupied by fibrous tissue containing scanty spindle cells. Another possible factor, responsible perhaps for the "sun-ray" pattern of some hyperostoses in x-ray photographs, is the stimulation of periosteal

bone-formation which, following Ribbert (quoted by Courville and Crockett, 1948), is due to the stretching of vessels entering Volkmann's canals when a mechanical strain is exerted upon the periosteum or dura. Such a pattern is characteristic both of certain primary bone-tumours and of some secondary deposits, such as those derived from a neuroblastoma of the suprarenal medulla, that cause an elevation of the periosteum.

The incidence of hyperostosis in meningiomas varies widely in different reported series. Figures ranging from 25% to 4.5% are quoted by Courville, who considers that the smaller figure is the more acceptable. Undoubtedly the tumours related to the vault of the skull are those most productive of hyperostoses, especially when related to the intersections of the mid-sagittal and coronal suture-lines (Cushing and Eisenhardt). From this it has been considered that diastasis of the sutures from trauma may be an important aetiological factor. Nevertheless hyperostosis may also accompany tumours at the base of the skull, particularly those overlying the lesser wing of the sphenoid, and occasionally those over the tuberculum sellae.

Multiplicity and Associations with Other Types of Primary Growth.—Multiple tumours of the meninges and of other regional tissues are usually the manifestation of the central type of von Recklinghausen's neurofibromatosis. But occasionally two or more meningiomas may be found in a case that displays no evidence of this disease. We have observed seven examples of this kind at necropsy. Usually a large tumour, producing clinical symptoms, is associated with an unsuspected, small, and remotely situated tumour. Mufson and Davidoff (1944) have reviewed the literature and report two additional cases, in one of which 10 meningiomas were removed from the right cerebral convexity at four operations. At necropsy several more were found, including a flattened mass in the right side of the tentorium. When multiplicity is an accompaniment of von Recklinghausen's neurofibromatosis the meningiomas are associated with bilateral acoustic-nerve tumours, and often with other primary growths of the cranial and spinal nerve-roots ; gliomas may also be found.

Apart from neurofibromatosis there are also instances in which an intracranial meningioma has been associated with a glioma in some other area of the cerebrum. Such an example has been reported by Alexander (1948), who finds only four similar cases in the previous literature and concludes, from the rarity of the association, that it is probably coincidental. A fifth has been reported by Kirschbaum (1945): the combination of an intrasellar meningioma with multiple cerebral glioblastomas. The latter, from his description, probably represented intraventricular metastases and not independent growths as he postulated. Examination of the spinal cord, which might have settled this point, was not carried out. We have observed three examples in which a meningioma was associated with a glioma ; the latter was invariably a spongioblastoma multiforme (Fig. 16).

Reticuloses

Allowing that the cells of the leptomeninges form part of the reticulo-endothelial system, it is in no way surprising that these should on occasion participate in the cellular proliferations that affect this system in other parts of the body. But such proliferations involve principally the lymphadenoid tissues, and hence it is mainly in the manifestations known as lymphosarcoma and reticulo-

sarcoma that the meninges, and their extensions along the perforating vessels of the central nervous system, may be involved.

Hodgkin's disease is, in its histological aspects, a granulomatous form of cellular proliferation. But there are many who prefer to regard it as a neoplasm and there is certainly a form, often referred to as Hodgkin's sarcoma, which macroscopically and microscopically lends some support to this interpretation. Involvement of the nervous system in this form of Hodgkin's disease is discussed by Sparling, Adams, and Parker (1947) and briefly by Jackson and Parker (1947). In the first of these two contributions the authors describe three cases in which tumour masses were identified within the brain substance ; in one there seems little doubt that this was the primary site to be involved. The relationship between such tumours and the reticulosarcomas, and also the proliferations within the central nervous system that have been described by Russell, Marshall, and Smith (1948) as " microgliomatosis," is at present impossible to decide. Since the microglial cells are of mesodermal origin and can therefore undoubtedly be derived, amongst other sources, from the perivascular sheaths, their proliferation within the brain is primarily related to the blood-vessels with the production of perivascular cellular foci, and tumours arise by the confluence of these foci. Jackson and Parker regard the reticulum cell as identical with the histiocyte, and therefore the microglial cell. Since the careful application of silver techniques reveals important differences in the affinities for silver on the part of these cells (Robb-Smith, 1938) there are grounds for disagreeing with this assumption. The reticulum cell should preferably be regarded as a more primitive type, but capable of differentiating into a variety of forms including the histiocyte. Further observations will doubtless clarify the relationships between microgliomatosis and the reticulosarcomas of the brain (also discussed by Sparling and others, 1947, and by Kinney and Adams, 1943).

The reticuloses are perhaps more important in their relation to the spinal cord. Hodgkin's lymphogranuloma, and the form termed by Robb-Smith (1938) " lympho-reticular medullary reticulosis," sometimes give rise to masses in the epidural fat, causing compression of the cord. Hodgkin's lymphogranuloma affecting the vertebrae, or paravertebral soft tissues, may also invade the spinal roots and dura but seldom penetrates the arachnoid membrane. Nevertheless instances are occasionally encountered in which even the substance of the spinal cord is invaded by direct extension.

In *generalized lymphosarcomatosis* and in *myeloid leukaemia* extensive infiltration of the epidural tissues by tumour-like masses may lead to paraplegia, either from compression of the spinal cord or ischaemia resulting from local circulatory disturbances. Four such examples, complicating leukaemia, were reported by Critchley and Greenfield (1930), who reviewed the literature and discussed the pathology at length.

SECONDARY TUMOURS
Of Dura Mater

Secondary deposits in the dura are usually the outcome of a direct spread from foci of metastatic growth in the adjacent bone. In childhood these are most commonly derived from a primary neuroblastoma of the suprarenal medulla and as a rule the periosteum of the bones tends to be involved. Hence the dura is often elevated by bosses of soft grey tissue in which new bone is usually laid down.

In the adult, carcinomatosis of the bones may include either the vault or the base of the skull, or both. The dura is then often diffusely infiltrated and thickened by plaques of the growth which replace the normal glistening under-surface of the meninx. In some instances extensive permeation of the veins and capillaries of the dura leads to varying degrees of pachymeningitis interna haemorrhagica and even subdural haematoma (Russell and Cairns, 1934). At the base a similar permeation may lead to profound disturbance of pituitary function, and even acute pituitary cachexia from necrosis of the anterior lobe when the nutrient vessels of the gland are extensively permeated.

Of Leptomeninges

Secondary tumours here may be discrete or diffuse, the latter giving the appearances of a chronic meningitis. As a rule they are dependent upon the presence of a neoplasm within the central nervous system which, by the involvement either of the surface of the brain or cord, or of the ventricular ependyma, is enabled to metastasize by way of the cerebrospinal fluid. Such neoplasms may be either primary, or blood-borne metastases from a remote site.

Primary Tumours of the Central Nervous System.—These tumours, especially the gliomas, are now well recognized as capable of metastasizing in this way. The medulloblastoma of the cerebellum, being a highly malignant tumour, is a notable offender, and its situation in relation to the fourth ventricle and basal cisterns is peculiarly favourable to such spread. The metastases are usually discrete though poorly defined ; they may be massive and confluent. In the spinal cord they tend to involve the posterior surface rather than the anterior, and the cauda equina is a favoured site. All types of glioma, even the most differentiated, are, however, capable of behaving in a similar way. Tarlov and Davidoff (1946) have reported three cases in which spinal deposits complicated an ependymoma. The oligodendroglioma, long regarded as a relatively benign type, may spread as vigorously in the leptomeninges as any medulloblastoma and prove as rapidly fatal ; on the other hand the cells may provoke a chronic reactive meningitis and the clinical picture of internal hydrocephalus, which may be prolonged for as much as seven years (Beck and Russell, 1942) or even 14 years (Blumenfeld and Gardner, 1945). The naked-eye appearances, in such protracted cases, may be very difficult to distinguish from chronic fibrous meningitis. The primary tumour, which will probably be discovered in relation to the third or a lateral ventricle, may be so small that it has excited no localizing symptoms, and hence may be missed unless the brain is carefully examined after fixation.

Such possibilities need to be recalled before any example of gliomatosis of the meninges is classified as a primary condition ; indeed it is questionable whether such occurs. In any doubtful case the spinal cord should be examined, because an intramedullary glioma at any level is capable of spreading through the meninges, even to the surface of the cerebrum. The literature relating to this interesting phenomenon has been reviewed by O'Connell (1946), with the addition of three personal observations. An intramedullary oligodendroglioma of the cervical enlargement which spread in this way, causing internal hydrocephalus as the principal clinical disturbance, has been described by Russell (1949).

Secondary Tumours within the Brain.—These tumours may involve the lepto-meninges by direct extension at the surface. But whereas the gliomata, particularly spongioblastoma multiforme, may gain attachment to the opposing dura this is less often seen in carcinomatous metastases.

Of greater interest is the diffuse carcinomatosis, or meningitis carcinomatosa, that may arise when a secondary deposit within the brain breaks through the ependyma of the adjacent ventricular wall. The meningeal spread may then con-stitute the main cause of clinical symptoms. Evidence of chronic meningitis, sup-ported by the presence of excess of protein and mononuclear cells in the cerebro-spinal fluid, may be combined with symptoms of cranial nerve-root involvement resulting from their infiltration with tumour cells. Recently a remarkable example was personally observed in which the cerebral metastasis, situated in the floor of the left lateral ventricle, was quite small (Fig. 18) and symptomless. But metastases in each foramen of Luschka gave rise to a clinical picture suggest-ing bilateral acoustic nerve tumours. The primary growth was in a bronchus.

A similar diffuse spread of growth through the lepto-meninges, especially at the base of the brain, may complicate primary carcinomas of the upper part of the nasopharynx or of the middle ear. Special mention should also be made of the malig-nant gliomas of the retina which are apt to
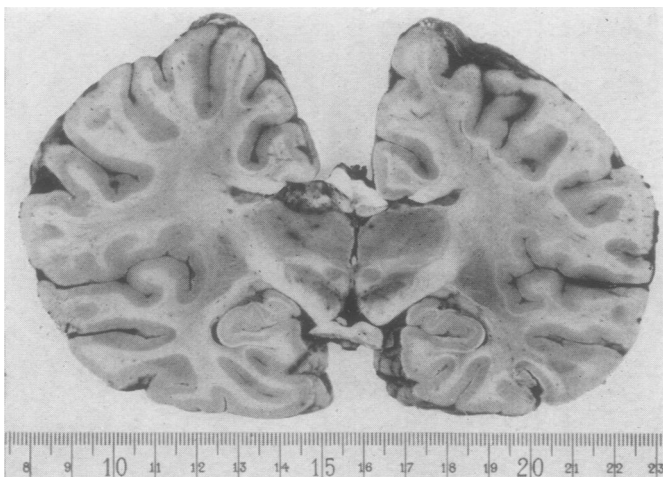

Fig. 18.—Coronal section of brain showing small metastasis from primary growth of bronchus in floor of left lateral ventricle. Metastasis by C.S.F. gave rise to bilateral tumours of cerebello-pontine angle.

extend along the optic nerve to the chiasma and thence throughout the leptomeninges of the brain and spinal cord. The growth in such cases may be luxuriant, forming thick sheets of soft tissue that obscure the blood-vessels and nerve-roots at the base of the brain.

But in most instances of leptomeningeal metastasis, whether this be related to a primary tumour of the brain or to secondary carcinoma, the meningeal deposits are not conspicuous to the naked eye. On close scrutiny they are detected as thin, greyish-white plaques that obscure the surfaces of the subjacent structures. They are most readily detected where they overlie sulci. Microscopically there is a vari-able degree of low-grade inflammatory response in relation to these deposits, and in places it will be found that the tumour cells penetrate the brain along the peri-vascular sheaths of the perforating vessels.

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