Onderstepoort Journal of Veterinary Research,
Volume 26, *Number* 4, *September,* 1954.

The Government Printer, Pretoria.

STUDIES IN COMPARATIVE NEUROPATHOLOGY.

I.—GLIOMAS OF THE DOMESTIC FOWL: THEIR PATHOLOGY WITH SPECIAL REFERENCE TO HISTOGENESIS AND PATHOGENESIS; AND THEIR RELATIONSHIP TO OTHER DISEASES.

CECIL JACKSON, Onderstepoort Laboratory.

CONTENTS.

Received for publication on 6th January, 1953.—Editor.

I. Introduction.

Gliomas of the domestic fowl have been reported by Belmonte (1935)—one case, by Jackson (1936)—two cases, and by Jungherr and Wolf (1939)—two cases. In more recent years the opportunity has occurred to study a very large series of cases, in many of which proper neurohistological technique could be applied. The material has been supplied chiefly by Prof. D. Coles, of this Institute, and its study has extended over a period of some ten years. The results have led me to disagree with some of the most important conclusions of previous authors —not only as regards the nature of the tumour cells (and therefore the nomenclature to be applied to these gliomas), but especially with such conceptions as exist of the growth, spread, and pathogenesis of these tumours. A preliminary note mentioning some of these conclusions has already been published (Jackson, 1948). It is not within the scope of this communication to survey the comparative pathology of gliomas of lower *mammalian* species. For this purpose reference may be made to the reviews of Christensen (1), Barboni (2), and Jungherr and Wolf (*loc.* cit.).

During the progress of the study here reported, the present lack of precise knowledge and at the same time the importance of gliomas (and related lesions) of submammalian species became increasingly plainer. If the unique Onderstepoort material was not largely to be wasted, it appeared essential to provide a fairly comprehensive *atlas* of this poorly understood histopathology. Every effort has therefore been made to meet the need for illustrations to serve as a guide through this *terra incognita.*

II. Note on Technique.

(In collaboration with W. H. Gerneke, B.Sc.)

So far as possible, arrangements are made to receive specimens in the fresh state, so that smears may be made, the colour of lesions noted, fixatives decided on and the duration of fixation controlled. Smears are of inestimable value in studying tumours of the nervous system. Apart from providing a means of rapid diagnosis in many cases of urgency, they provide an indispensable supplementary study of cytological details. This is even more especially the case in fowls, where often one has to study simultaneously glia cells and mesenchymal derivatives (haematogenous cells), distinction between some of the latter elements being virtually impossible in sections alone. Contrary to a present vogue in pathological neurohistology, we find dry-fixed smears of much greater value than moist-fixed preparations and also that Romanovsky staining gives much more information and incomparably more brilliant pictures than the customary use of a single basic dye (e.g. toluidin blue).

It is now a usual routine at this Institute to fix avian brains in formol-bromide, so that Cajal and Hortega impregnations are always possible where required. We find that the bromide in no way detracts from the other methods employed and indeed, notably in the case of Romanovsky staining, have suspected that the performance of aniline dyes has thereby been improved.

---

(1) Christensen, N.O. (1946). Om Gliomer. Repr. from *Medlemsbl. f. Den. danske Dyrlaegef.* Vol. 29, pp. 28.

(2) Barboni, E. (1940). Contributo allo studio dei gliomi dell' encephalo nei bovini. Repr. from *Tumouri,* Vol. 26, pp. 361–393.

In Cajal gold sublimate (and Hortega's silver carbonate) impregnations the time allowed for the action of the bromide fixative is crucial. Yet precise periods cannot be prescribed owing to variation in size, texture, etc. of the material, and of room temperature (3). In our experience, whereas 22 days was the maximum time for successful Cajal impregnation of human material, brilliant results have been obtained on fowl material after as long as 35 days. It has been our usual practice to carry out the Cajal impregnation at a temperature of 20°–22° C. (viz. in an air-conditioned room, which happens to be our only available constant temperature within the limits of temperature for success). In cases where the material has been beyond the optimum time in formol-bromide, prolonging the impregnation time for the usual 4–6 hours to overnight may result in attaining the desired intensity without serious non-specific deposition. In cases where fowl brains had been fixed in formalin, we had to resort to Globus' modification of the Cajal method, which gave fair or in some cases brilliant results. In the case of Hortega's IVth variant, a period of 8–10 days in formalin is the minimum fixation time, but our results are equally good using formol-bromide. In this method the material may alternatively be left for a virtually indefinite period before impregnation.

On embedded sections, the most useful single method is Giemsa. This gives good pictures of the cytology of many gliomas and at the same time facilitates the study of the mesenchymal elements mentioned. It satisfactorily replaces the Nissl stain and is capable of staining axis cylinders simultaneously in addition to Nissl substance. It replaces thionin (or toluidin blue) for metachromatic substances. It can replace histochemical tests (Berlinerblau) for certain iron-containing pigment which has been of great interest in these studies. For early encephalitic lesions to be described, it gives better "Übersichtsbilder" than does haematoxylin-eosin. Lastly, it has proved indispensable in the study of additional aspects of neurohistology to be dealt with in later communications. It is thus a most economical method to use, having perhaps as its only serious drawback the fact that it does not reveal glia fibrils. But Giemsa must be properly used (colophonium-acetone, not acid-alcohol differentiation!) otherwise its brilliance becomes miserably impaired. And unless the mounting medium be carefully chosen, excellently differentiated sections may be ruined by further differentiation beyond the desired degree, accompanied by precipitation of the basic component of the stain. We use thick cedarwood oil as mountant, although it dries slowly. In general it is well to examine Giemsa-stained tissues in water immediately after removal from the stain, so as to observe to what extent the subsequent differentiation and dehydration, mounting, etc. have detracted from the brilliance of the staining more especially of metachromatic substances.

Thus, apart from haematoxylin and eosin, the most useful methods in these studies have been Giemsa (for the many reasons mentioned), Cajal's gold sublimate and Hortega's silver carbonate (for the astrocytic series of elements); Hortega's IVth variant (for general delineations of neuroglia); Mallory's phosphotungstic acid haematoxylin (4) for delineation of the cytoplasm of tumour cells and for the demonstration of glia fibrils (especially for the former, Held's haematoxylin and iron haematoxylin are also very useful); and van Gieson, reticulum and elastic stains for changes in the connective tissues of vascular walls.

---

(3) We most often use room temperature, although higher temperatures shorten the time.

(4) Lieb's (1948) modification of the phosphotungstic acid-haematoxylin method has proved superior to Mallory's original method, at least on material not fixed in Zenker's. But although we use her mordanting in ferric alum, we prefer the spontaneously ripened staining solution to her artificially ripened solution and find it gives superior results in cellular detail.

KEY TO FIG. 2.

Tumour cells: 1, 2, 7, 8, 9, 10, 13, 17, 19..

1. Bipolar endoplasmic cell.
2. Multinucleate (giant) cell.
7. Minotic cell.
8. Large unipolar cell, exoplasm confined to process.
9. Cell showing exoplasm and endoplasm of the cell body. Mucin secretion in early stage and confined to endoplasm.
10. Multipolar cell with cell body composed of endoplasm and processes composed of ectoplasm.
13. Cell in advanced state of mucin-secretion.
17. Bipolar cell with development of ectoplasm in the processes.
19. Unipolar (endoplasmic) cell.

Infiltrating (haematogenous) cells: 3, 4, 5, 6, 11, 12, 14, 16, 20, 21, 22.

3. Macrophage of monocyte derivation.
4. Monocyte.
5. Monoblastic plasma cell.
6. Monocytic plasma cell. Note angular outline and nuclear texture.
11. Medium lymphocyte.
12. Medium (lymphocytic) plasma cell showing nuclear budding.
14. (Monocytic) histiocyte ("macrophage") with "haemofuscin" pigment.
16. Monoblast.
20. Binucleate plasma cell (quite probably also of monoblastic origin).
21. Small lymphocytic plasma cell.
22. Small lymphocyte.

---

15. Free "haemofuscin" pigment.
18. Erythrocyte.

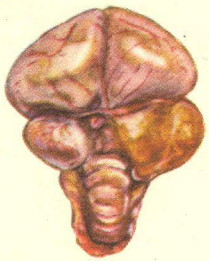

Figure 1.—Gliomatosis of right optic lobe. Note the characteristic orange-yellow coloration. (27562). (Natural size).

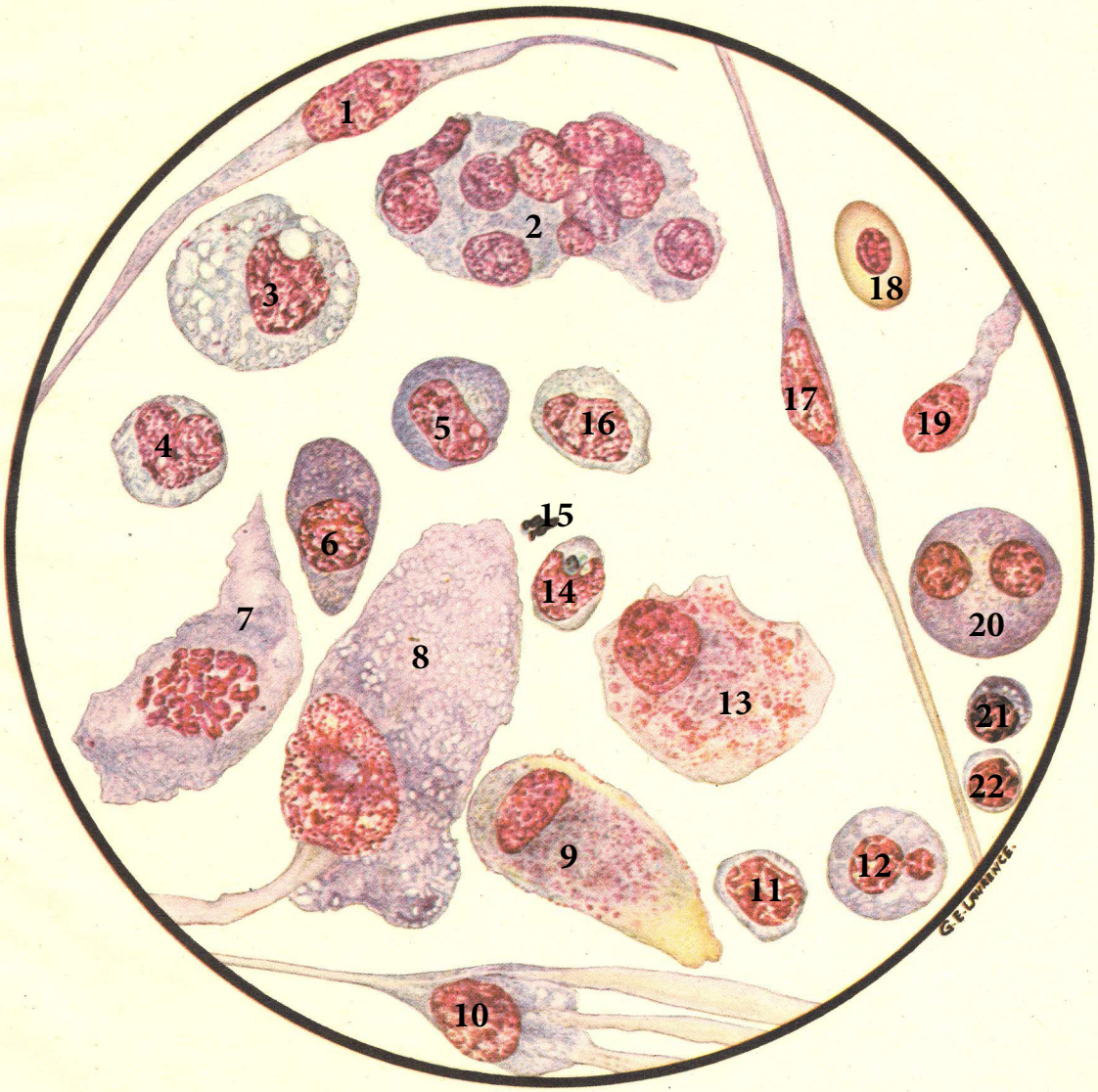

Figure 2.—The chief types of cells encountered in avian glioma. Composite picture constructed from dry-fixed May-Grunwald-Giemsa stained smears from type II gliomas. (X 1300).

III. Pathological Anatomy.

(1) *Gross Pathology.*

Glioma of the fowl (see fig. 1) is seldom solitary (fig. 3). Much more often the lesions are multiple (fig. 4). Even in tumours described as solitary but lobulated, this lobulation will be shown to be due to coalescence of originally separate foci. In size gliomas vary from lesions invisible to the naked eye (and thus disclosed only on microscopic examination) to tumours which for this species are very large in size (i.e. exceeding 1 cm. in diameter).

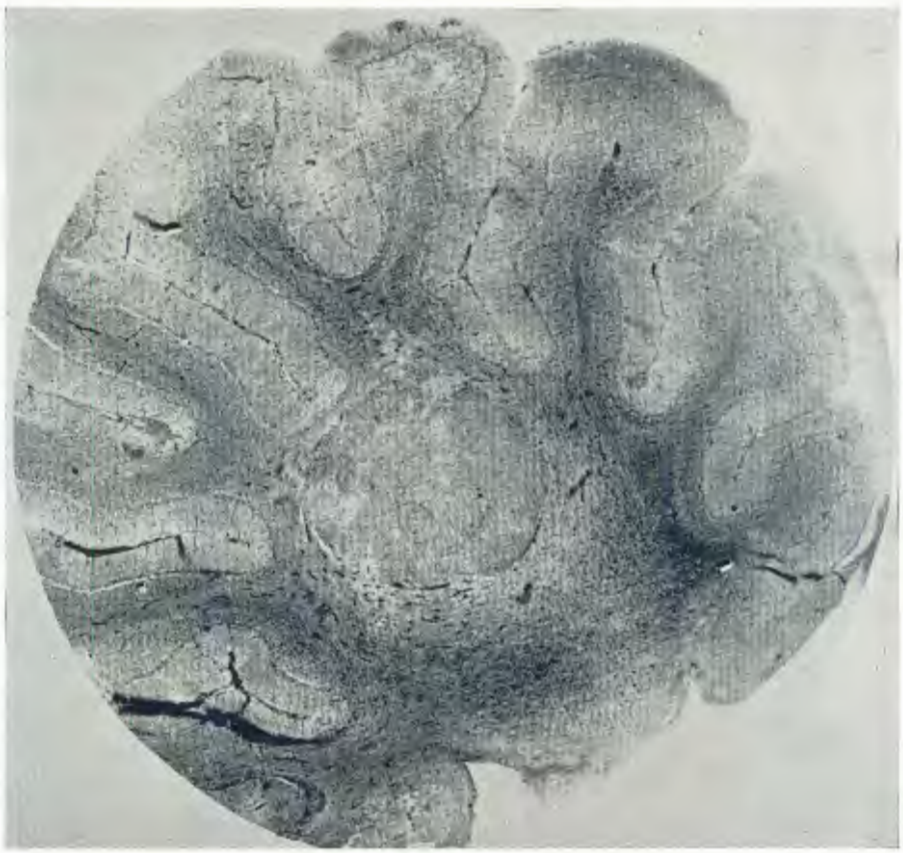

Fig. 3.—Solitary glioma in central grey matter of cerebellum. X 7. (35536.)

Since almost infinite variation occurs in the precise location of the tumours and since further it has been concluded that the detailed location in any one division of the brain is largely fortuitous, it is not intended to continue the practice of detailed descriptions of the topography with reference to tracts and cell-masses. It will be sufficient to indicate that the chief sites of election are the cerebrum and optic lobes, and that the cerebellum is less often affected. Affection of the brain stem is rare and when it occurs is usually due to encroachment of

a tumour originating in a more dorsal situation. However, in one case a solitary glioma was present in the ventro-lateral aspect of the medulla without lesions elsewhere in the brain. Deeply situated tumours are likely to be overlooked at post-mortem until the brain is incised. Many cerebral tumours are deeply placed and in the cerebellum the central grey matter appears to be a favourite site (fig. 3), although tumours have also been observed to originate in the foliae.

The colour of fowl gliomas is very typical (fig. 1). They have a distinct orange to yellow coloration, contrasting with the surrounding brain tissue. This coloration, to which Prof. Coles first drew attention, has for years been a matter of great interest to me and its cause will be dealt with later in this communication. It is unusual to observe none of this coloration, i.e. for tumours to be greyish as described by Jungherr and Wolf (*loc. cit.*). The colour disappears rapidly on fixation (e.g. in formalin) so that one suspects that failure to observe it may have been due to postponing the macroscopic description until after fixation. However it is true that in individual cases it is much fainter than in an average case.

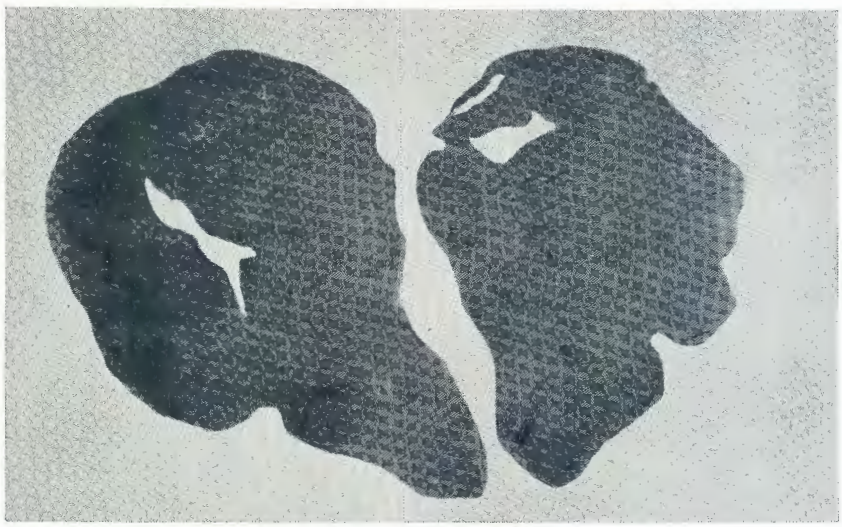

FIG. 4.—Extent of multiple gliomatosis affecting both optic lobes. Note how little brain tissue remains. (H.E.) X 10. (34608.)

2. *Histopathology and Cytology: Classification of the Tumours.*

It will be clearer to state at the outset that I continue to disagree with the conclusion of Jungherr and Wolf (*loc. cit.*) as to the nature of the tumours reported by them, by Belmonte (*loc. cit.*) and by Jackson (1936). I am unrepentant of my original opinion that the tumours hitherto reported were quite fittingly to be compared with *glioblastoma* (*spongioblastoma*) *multiforme* of man, an opinion which in principle was shared by Belmonte. However that may be, an erroneous impression has now come to exist that there is but one histological variety of glioma in the fowl, viz. an astrocytoma. Whereas the facts are that (*a*) two chief types exist, (*b*) neither of which has a structure consistent with the diagnosis of astrocytoma.

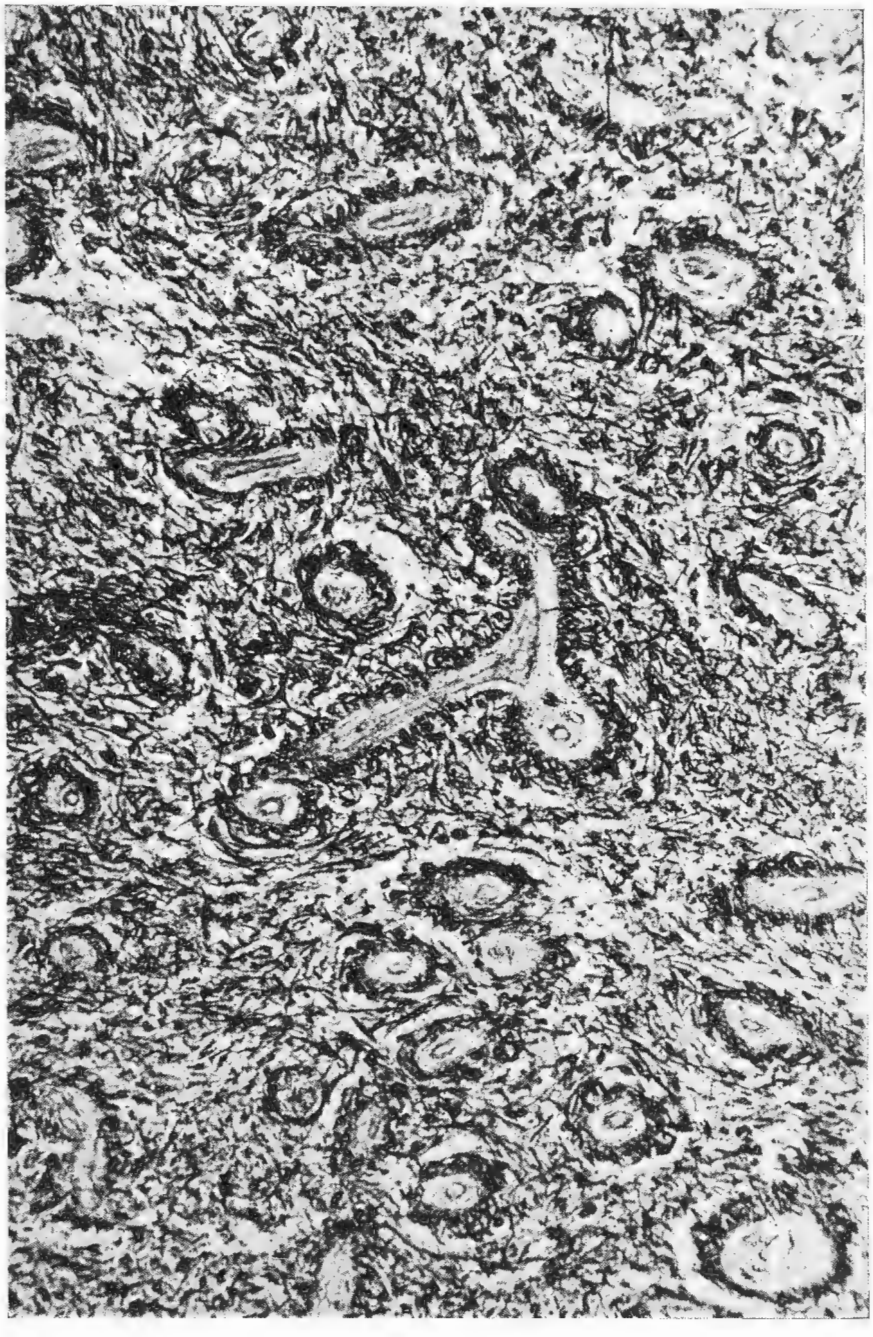

FIG. 5.—Astroblastoma—low power appearance. Regular distribution of bloodvessels around which the tumour cells radiate. Their cytoplasm (including the processes) is deeply impregnated by Cajal's gold sublimate. X 125. (27562.)

The histopathology of these types will bear description in some detail, but particulars already to be found in the literature will be omitted for the sake of brevity. The great bulk of the present work is based on and refers especially to tumours to be described hereunder as Type II, the other types being more rarely encountered.

FIG. 6.—Structure of astroblastoma under high power. Robust process ending in sucker feet are attached to the vessel walls. (Cajal's gold sublimate.) X 300. (27562.)

Type I (*Astroblastoma*) (figs. 5, 6, 7).

This tumour is rare, and I do not believe it is represented by any specimen described in the existing literature. I have encountered it once only. This glioma is characterised by evenly dispersed hypertrophied bloodvessels around which the

FIG. 7.—Astroblastoma. The cytoplasm and processes of the astroblasts are equally well impregnated here by Hortega's silver carbonate. X 300. (27562.)

great majority of tumour cells are radially disposed. These cells exhibit a clearly defined vascular process with terminal expansion (sucker foot) attached to the vessel wall, less robust processes being given off from the other parts of the cell. The cells have large cytoplasmic bodies, often roughly triangular in outline, and eccentric nuclei. Rare mitoses were seen. The cells impregnate readily and deeply with Cajal's gold sublimate (Fig. 5 and 6) and Hortega's silver carbonate (fig. 7) after sensitisation for appropriate time in formol-bromide. Their entire cytoplasm and system of processes become impregnated. Intervening inconspicuously between the perivascularly aligned cells is a looser and less regular arrangement of cells. Glia fibrils were developed in parts of this tumour, absent in others. (For the full report on the histopathology, see Appendix II.)

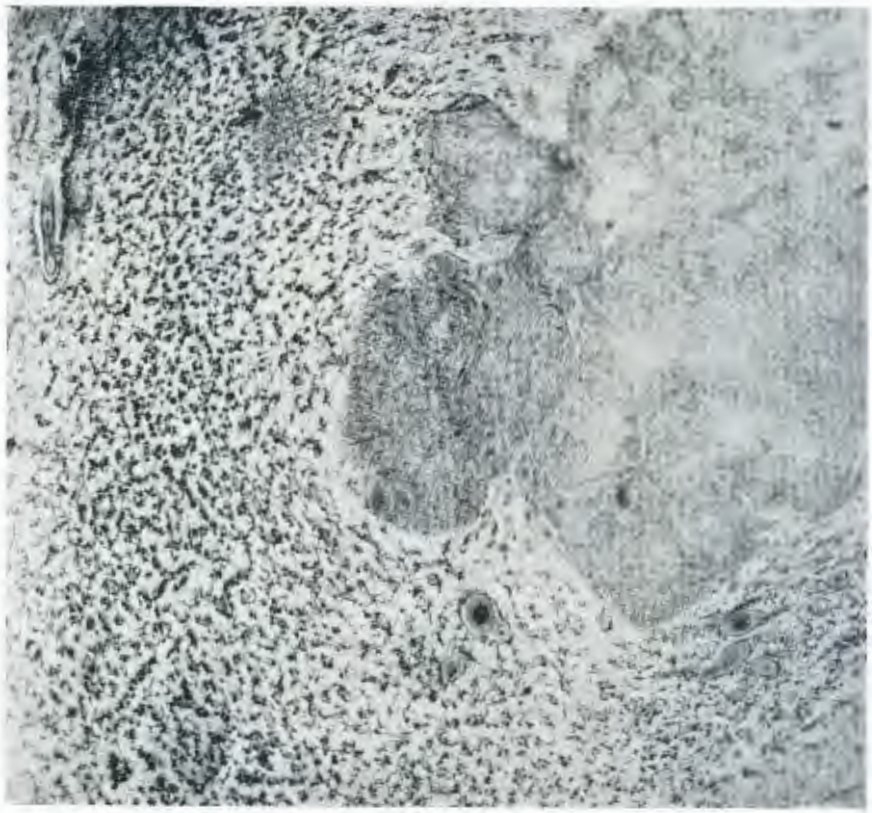

FIG. 8.—"Type II" Glioma. No regular arrangement of bloodvessels or grouping of cells. Failure of the tumour cells to impregnate with gold sublimate, in striking contrast to the deeply impregnated astrocytes of the surrounding brain tissue (left and below) and in contrast to the tumour cells in astroblastoma (Figs. 5 and 6). X 45. (35538.)

The above characteristics need not be laboured in connection with the identification of the tumour cells as astroblasts, and the proper classification of this variant of fowl glioma. A glance at the photomicrographs will be sufficient to convince anyone that we have here to deal with as classical an example of astroblastoma as could be wished, comparable in all essentials with astroblastoma of man, the only exception being that glia fibrils are demonstrable, which is at variance with the usual descriptions of human astroblastoma.

Type II. (figs. 8 to 14).

This is by far commoner and is represented by all the five tumours described in the existing literature. The essential differences are that there is here no even and regular arrangement of blood vessels, the tumour cells are arranged in more patternless and even texture, and any tendency to radiate around vessels is much more rudimentary (fig. 8). They everywhere show a multiplicity of types in respect of size and shape (fig. 2). Many have voluminous cytoplasm and eccentric nuclei similar to the cells of Type I, but in addition there will be found large numbers of smaller bipolar and even unipolar and apolar cells. Giant cells with one or multiple nuclei (usually two or three, occasionally half-a-dozen or more),

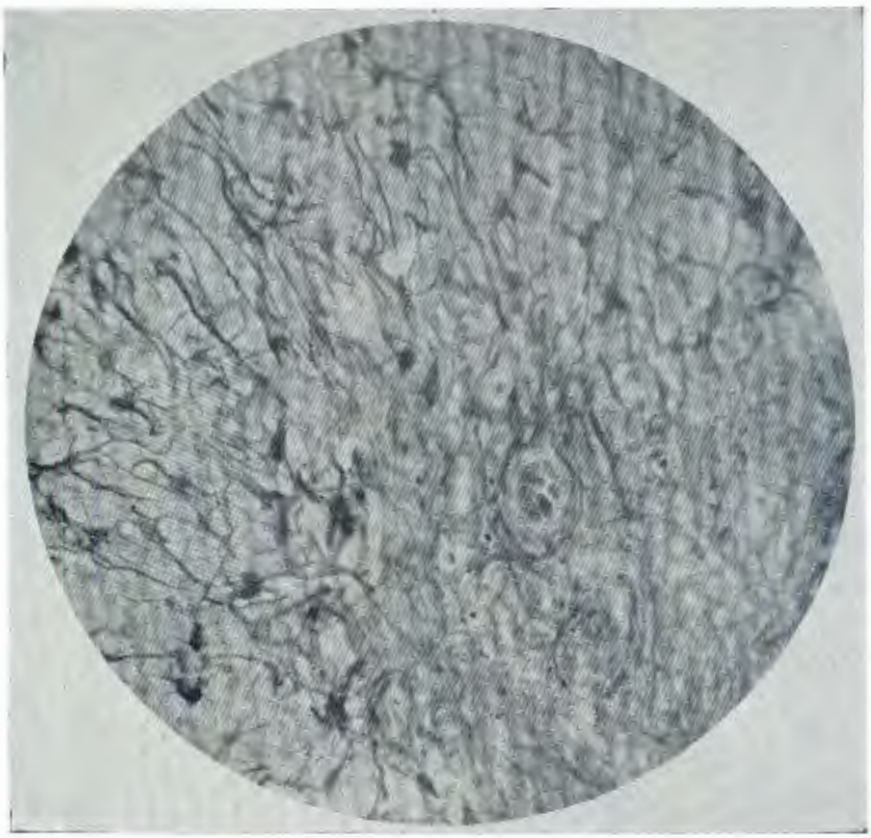

FIG. .9—" Type II " Glioma. Higher magnification. Striking contrast between impregnated astrocytes of surrounding brain tissue (left and above) and unimpregnated tumour cells (below, right). (Cajal's gold sublimate.) X 400. (35538.)

commonly occur. Many of these large cells are flask-shaped or quite rounded off without processes. The cells having processes are seen in smears to be composed of a granular basophilic endoplasm, staining blue to purple with Giemsa, and a clear refractile rather chromophobic exoplasm, which constitutes the processes but often also surrounds the endoplasm of the cell body (fig. 2). This exoplasm stains a faint yellow to very faint clear blue. In sections it can be differentially stained with iron haematoxylin (fig. 14). It must not be confused with glia fibrils,

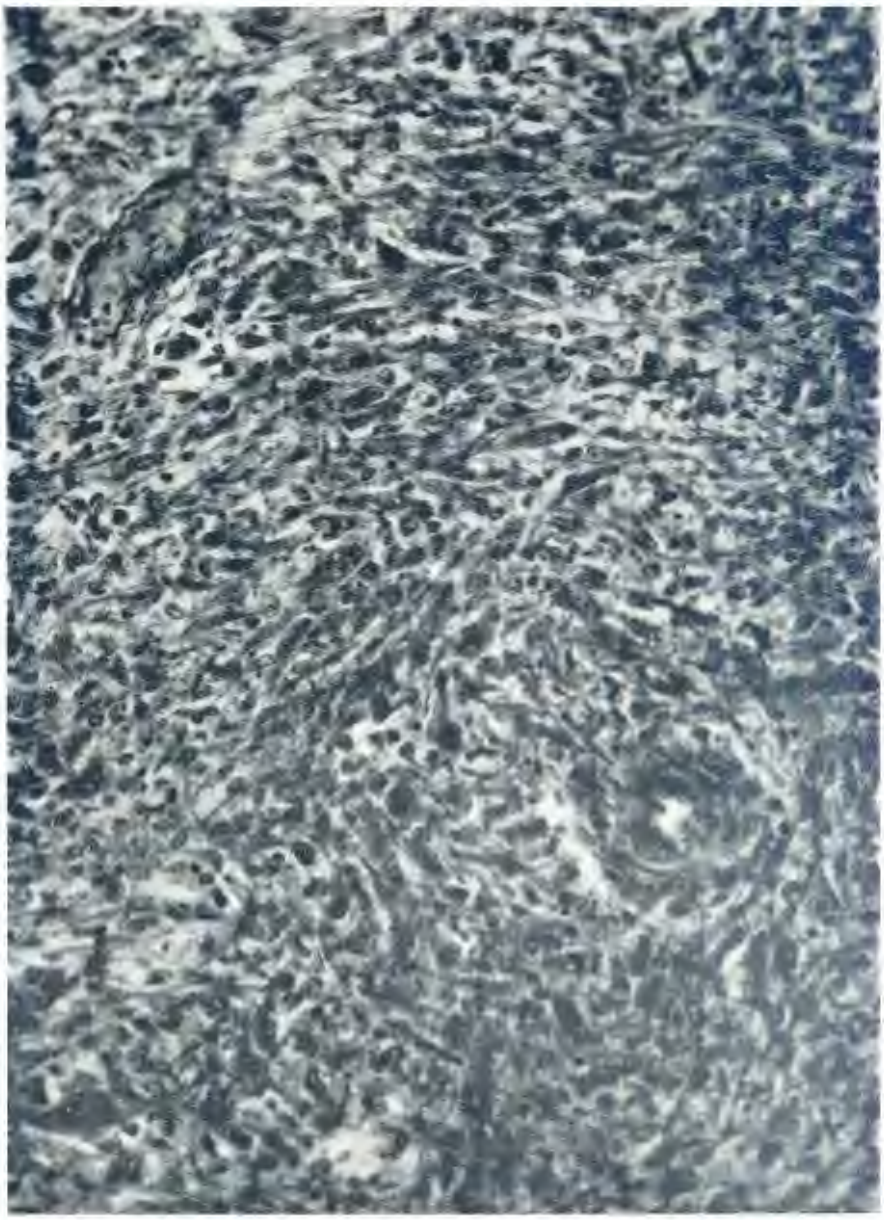

FIG. 10.—Structure of Type II Glioma as seen with Hortega IV impregnation. On account of the failure of the cells to impregnate with the methods for astrocytes and astroblasts (see Figs. 8 and 9) it is necessary to use this technique if metallic impregnation is desired. X 440. (35539.)

which are often closely associated with it. It stains with phosphotungstic acid haematoxylin the same colour as the endoplasm of the cell body (tan) but a slightly deeper shade. The extreme eccentricity of the nuclei of the cells often results in their being wholly contained in the exoplasm, which is widened to enclose them on all sides, including the central edge of the nucleus, which is then demarcated from the endoplasm by an intervening exoplasmic seam. Glia fibrils are sometimes demonstrable (figs. 11, 12, 13). When seen they are often confined to certain areas of the tumour and are absent from other parts. The variations in their degree of development are well portrayed by the illustrations referred to. Mitoses may occur, or may not be demonstrable. They were seen in 10% of cases and when present are usually rather sparse and have to be searched for.

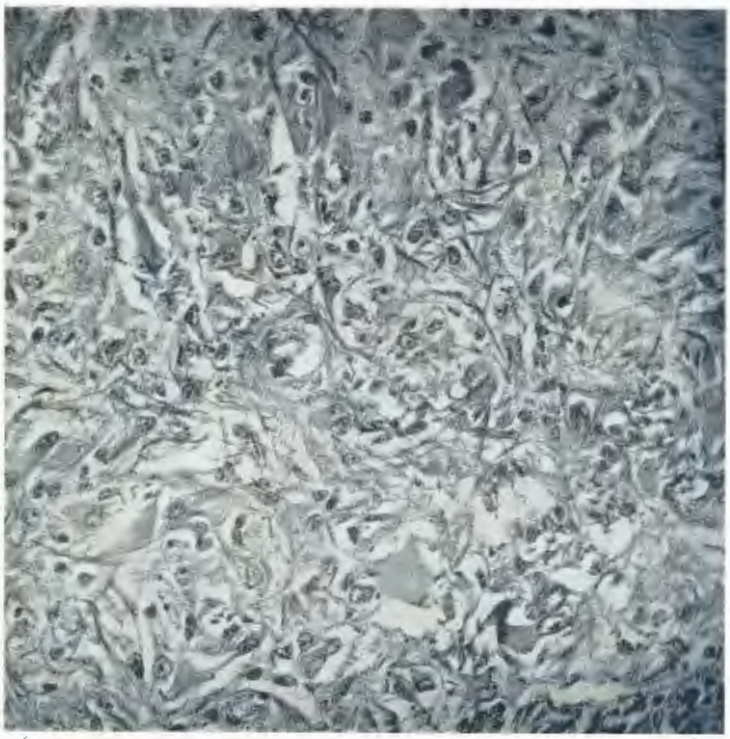

FIG. 11.—An area of Type II glioma rich in glia fibrils. (Mallory's phosphotungstic acid haematoxylin.) The fibrils which appear black in the photomicrograph stain blue, in contrast to the tan-coloured cytoplasm and processes of the tumour cells. X 480. (36409.)

These cells fail to impregnate heavily and readily with the Cajal and Hortega Silver Carbonate methods, in striking contrast to the astrocytes of the surrounding brain in the same block of tissue (figs. 8 and 9) and in contrast to the ready impregnation of the cells of Type I tumours. If metallic impregnation of these tumours is desired, Hortega's IVth variant must be used (fig. 10).

Jungherr and Wolff (*loc. cit.*) seem to have felt confident that if only the correct fixative had been used, they would have been able to demonstrate by

specific gold and silver impregnations that the cells of their tumours were astrocytes. I do not believe that this would have been the case, and the same probably applies to the other tumours reported in the literature.

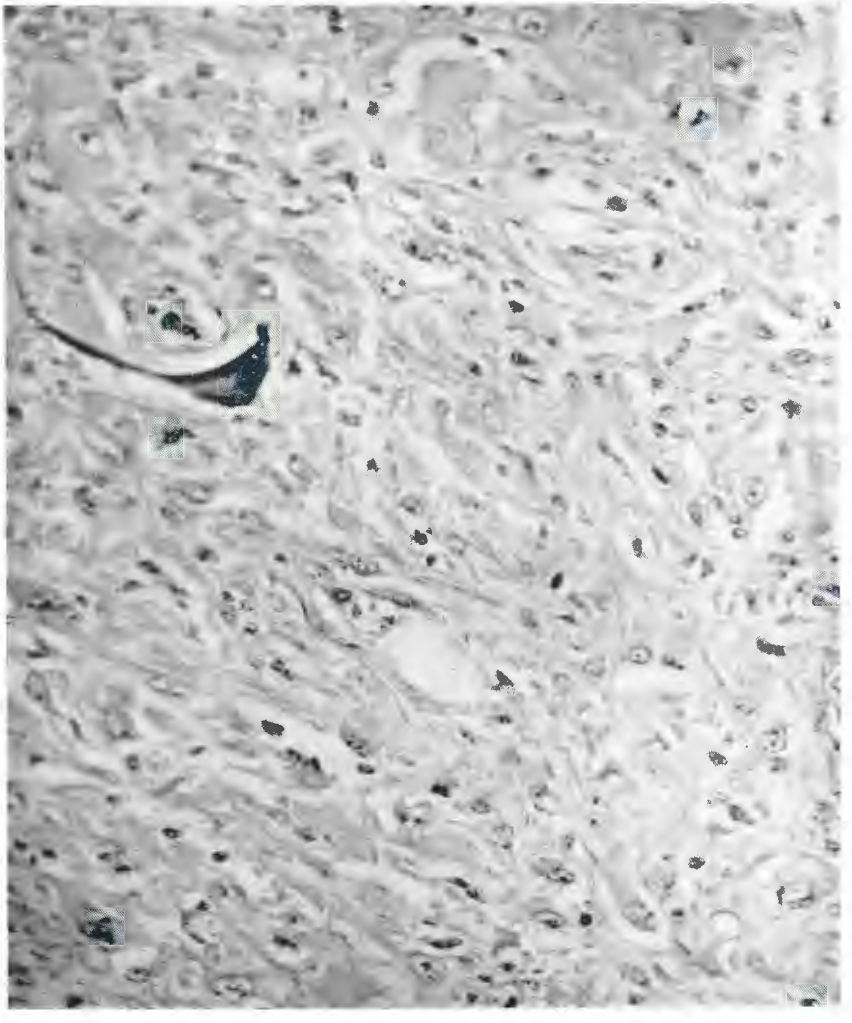

FIG. 12.—An area of Type II glioma (same tumour as Fig. 11) poor in fibrils. The general absence of fibrils in this part of the tumour is emphasised by selecting a field which contains but a single cell showing fibril development. (Mallory's phosphotungstic acid haematoxylin.) X 480. (34609.)

In the multiplicity of cell types in the tumours here described as Type II—multipolar cells, (5) bipolar spongioblasts, unipolar spongioblasts and giant cells,

(5) These are comparable with those cells of human glioblastoma multiforme referred to by Bailey and Cushing as "imperfectly formed astrocytes". The term is probably unfortunate, since, as will be seen later, one is dealing not with degrees of differentiation toward maturer cell types, but with de-differentiation. In actual fact I believe a more correct term would therefore be "incompletely de-differentiated astrocytes".

in the degree of demarcation from the surrounding brain substance, these tumours could be successfully compared with only one well-defined type of human glioma, *viz.* glioblastoma multiforme. It is true there are also points of dissimilarity—e.g. the relative paucity of mitoses and the lesser degree development of giant cells, in an average case. But these are details when compared with the essential features of the cytology. The degree of cellularity, while perhaps not quite so dense as the average human *Spongioblastoma multiforme* (fig. 15), is entirely foreign to one's conception of astrocytoma (fig. 16), even when viewed under low power with ordinary stains. The occurrence of mitoses is not considered consistent with astrocytoma. Further differences from human astrocytoma have

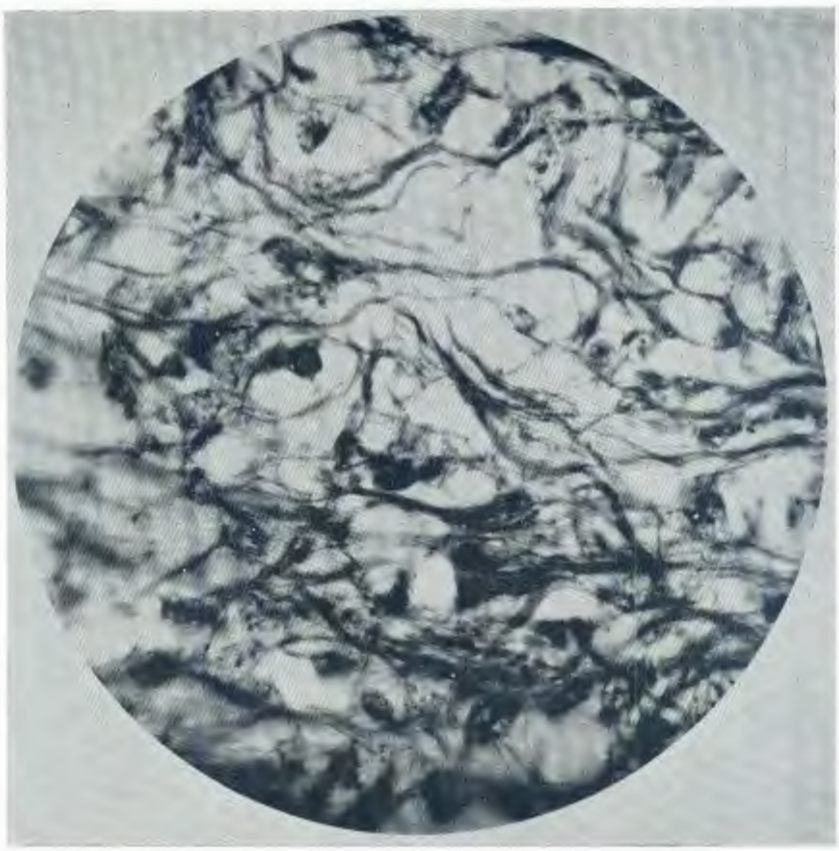

FIG. 13.—An example of an unusually extreme degree of fibril development (Type II glioma). In several places it can be distinctly seen that the fibrils (black in the photograph, but blue in the original) contrast with the ectoplasmic cell processes, running either in them or along them. But in other places it is seen that entire thickness of a cell process has been converted into fibril material, producing the extremely robust fibrils seen. (Phosphotungstic acid haematoxylin—Loeb's modification I.) X 1500. (34537.)

been pointed out by Jungherr and Wolf themselves. Finally the failure to impregnate typically for astrocytes virtually by definition excludes the diagnosis of astrocytoma. More precisely these avian tumours are to be assessed as intermediate between astroblastoma and low grade glioblastoma multiforme of man.

Types II (a) and II (b).

In these types there is admixture of type II glioma with neoplasia of mesenchymal (haematogenous) elements and these impure tumours will be better understood after the mesenchymal reactions occurring in glioma and related lesions have been explained. Their description is postponed to a later part of this article.

3. *Encroachment on the Ventricles.*

This phenomenon has been mentioned by all authors who have described avian gliomas. It is extremely common, and was noted in 68% of the present series of cases. It is well pictured in figs. 17 and 18, and has been studied time and again in my cases. In no case was there any evidence that it was due to implantation of tumour cells circulating in the C.S.F., as a sequel to tumour tissue having broken into the ventricles. This indeed does occur, and fragments

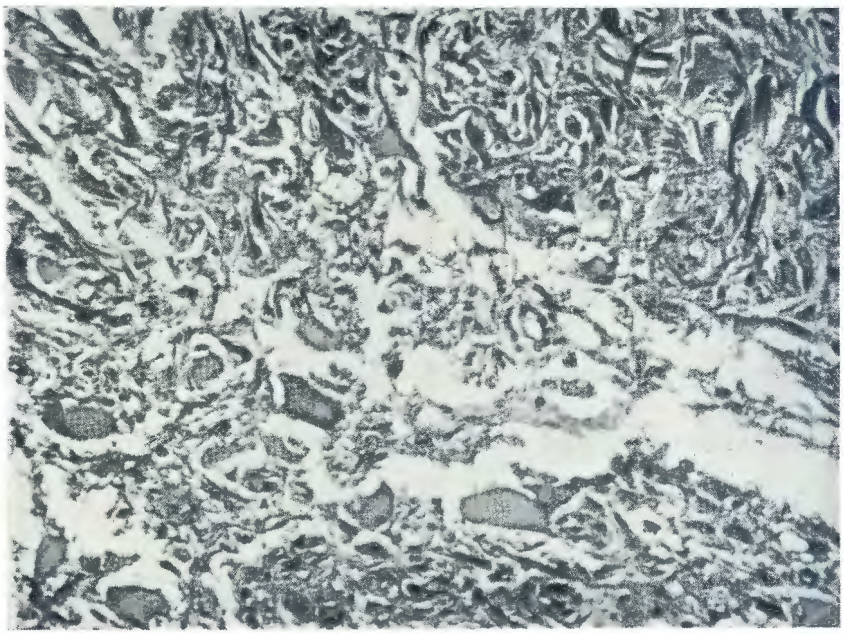

FIG. 14.—Ectoplasm and processes of tumour cells differentially stained with carbol-iron-haematoxylin. The continuity of the ectoplasm of the cell body with the processes is well seen in several cases. The structures revealed thus should not be confused with glia fibrils. Type II glioma (same case as Figs. 11 and 12). X 400. (34609.)

of tumour tissue may be seen loose in the C.S.F., but never did one observe a stage of growth which could be interpreted as implantation. It will be seen later that there is an entirely different explanation for the multiplicity of avian gliomas and their occurrence in the ventricular walls (see page 541 and fig. 46).

Where gliomas involve ventricular walls, one can often make a most favourable study of " collateral hyperplasia " affecting the ependymal cells (figs. 19 and 20). These elements, previously cuboidal, develop long processes from their proximal poles and these processes grow through the underlying tissue to make

contact with a bloodvessel. Subsequently these processes undergo a transformation which results in their staining as for glia fibrils. In other words, adult ependymal cells have been converted into ependymal spongioblasts. However, although the cells readily become mobilised and proliferate in the neighbourhood of gliomas and in ventricles stimulated by encroachment (with resulting debris of tumour cells, inflammatory exudate cells etc.), they do not in the fowl appear to take part in the formation of tumours located in the ventricular wall. Rather does the ultimate fate of ependymal cells overlying such tumours appear to be atrophy, so that the astrocytic tumour cells themselves eventually come to form a new lining to the ventricle at the place where they encroach—in other words the tumour tissue ulcerates through the previous ependymal lining, even if the latter has undergone considerable proliferation previously.

FIG. 15.—Degree of cellularity of Spongioblastoma multiforme of man (an average case for comparison). Two mitoses seen. (Phosphotungstic acid haematoxylin.) X 480. (36727.)

4. *Cavitation of Gliomas—its cause and its Relationship to Secretory Ability of the Neoplastic Cells.*

Jungherr and Wolff (*loc. cit.*) mentioned the occurrence in one of their cases of "several small cysts" in the tumour, "which contained yellowish gelatinous material".

In the present series of cases this phenomenon can be well studied. Relatively huge fluid-containing cavities may ultimately come to exist in these gliomas (fig. 21). The fluid may contain a few infiltrating cells including pigment (see

later), and has even been observed to contain nerve cells previously incorporated in the tumour tissue (see later). In most cases it can be demonstrated that this fluid is rich in mucin. The " mucin " is of a type which stains rather weakly with mucicarmine, but gives a strong metachromatic reaction with basic thiazines (including thionin). As in the case of some other " mucins ", the best way to demonstrate it is by examining sections taken straight out from dilute basic aniline stains (or mixtures) and examined while covered by the stain itself, or soon after mounting in water. Attempts to preserve the metachromatic reaction by dehydrating and clearing are successful in some cases, but disastrous in others. Even mounting in water as suggested may lead to fading within less than an

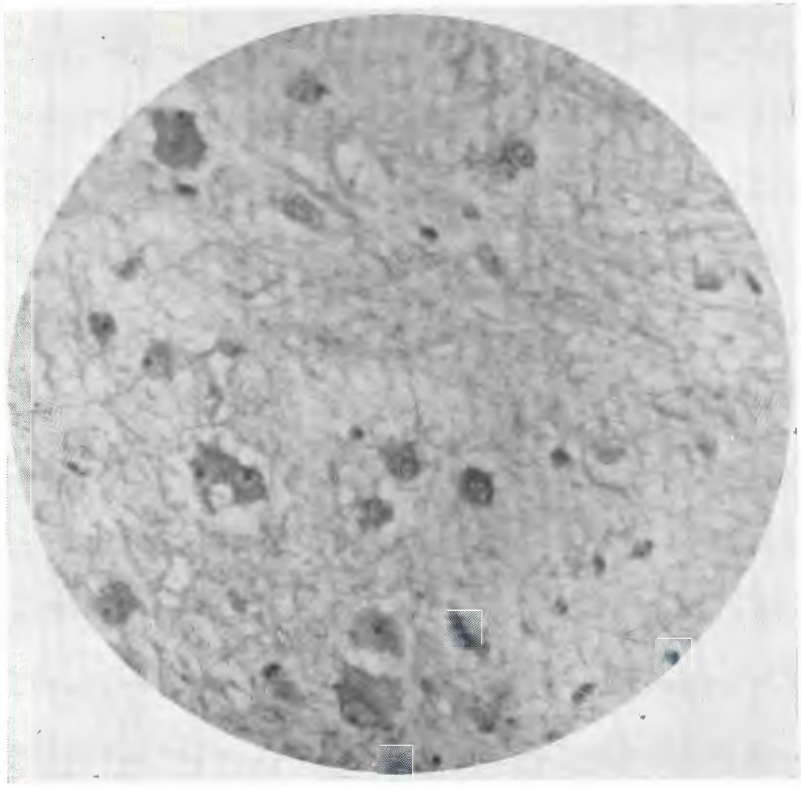

FIG. 16.—Sparse cellularity of human astrocytoma (for comparison with the avian Type II tumours—see e.g. Figs. 11 and 12). (Phosphotungstic acid haematoxylin. X 480. (35399.)

hour. Fig. 23 was photographed within a matter of minutes after mounting in water after removal from the stain (in this case Giemsa). " Mucin " was demonstrated, by one or other of the methods mentioned, in 58% of the cases in which cavitation was present.

Note added in Press.—The mucopolysaccharides (hexosamine-containing polysaccharides) and mucopolysaccharide-containing compounds referred to loosely as " mucins " are nowadays being much more elaborately classified. There are tests to distinguish between the various substances isolated by biochemists *in vitro* and also a whole series of tests have become available which can be applied to

sections of fixed tissues. Unfortunately the significance of the latter results is often uncertain. The material occurring in the cystic cavities of avian glioma behaves as summarised in the accompanying table (tests on formalin-fixed, paraffin-embedded sections).

Reactions of a suspected acid mucopolysaccharide in gliomas.

Mucicarmine	Stains very weakly or not at all.
Metachromasia	"Gamma", but fading during dehydration. It fails to be intensified by preliminary treatment with H_2SO_4.
P.A.S.	Negative.
Steedman's Alcian Blue ("for acid Mucopolysaccharides")	Positive.
Hale's Dialysed Iron ("for acid Mucopolysaccharides")	Positive. In practice this is doubtless the most satisfactory method for selective staining of this substance.
Hyaluronidase	Fast (Metachromasia not abolished by 3 hours exposure to testis hyaluronidase at 37° C.)

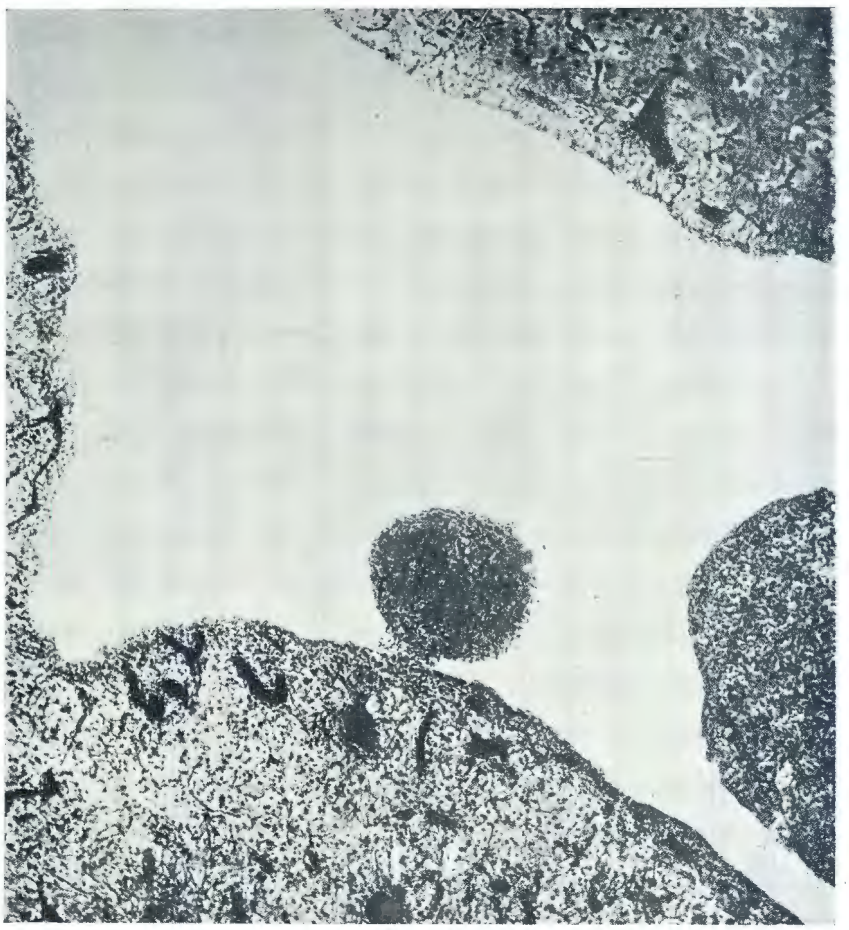

FIG. 17.—Fowl glioma—encroachment on ventricular cavity by a smaller tumour (centre) and a larger tumour (right). (Hortega IV.) X 125. (35306.)

This combination of results provides evidence to suggest that the moiety responsible for the above reactions is an acid mucopolysaccharide; more especially such reactions would theoretically appear consistent with the presence of a chondroitin sulphate. The present state of our knowledge does not allow one to dogmatise. Still further methods could be employed if it were within the scope of this communication to do more than draw attention to this interesting aspect of the chemistry of brain tumours.

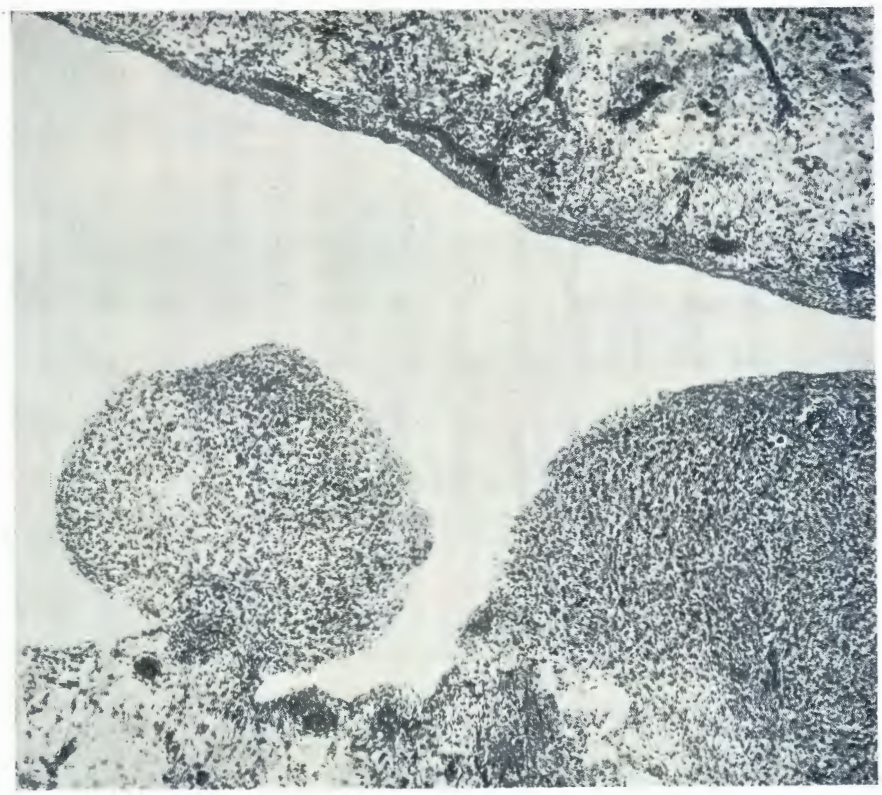

FIG. 18.—More advanced encroachment of fowl gliomas into ventricles. As in Fig. 17, ulceration through the ependymal lining can be appreciated. (Hortega IV.) X 125. (35306.)

All stages in the development of these fluid containing cavities have been followed (fig. 22). As seen in fig. 2 (cells 9 and 13) the metachromatic substance first appears within the cytoplasm of the tumour cells. Later the cell walls break down under the pressure and " microcystic " cavities result. Finally these coalesce into large macroscopic cavities. In smears especially, the accumulation of metachromatically staining substance can be seen to commence in the endoplasm of the cell in a zone adjoining the nucleus, which becomes displaced by the pressure into an eccentric position. Later the secretion spreads to all parts of the cell (see fig. 2).

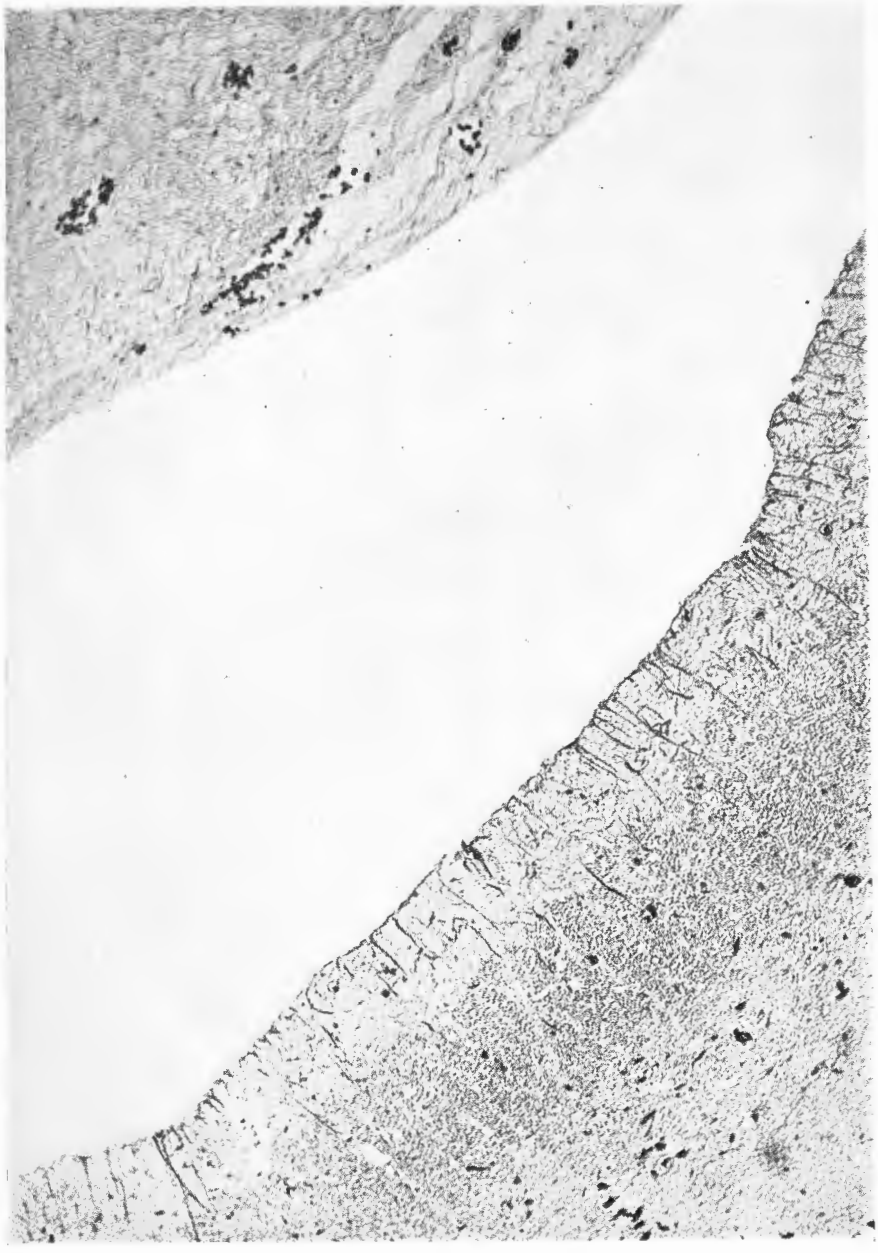

FIG. 19.—Reactivity of ventricular ependyma. Above is seen the edge of a glioma which further to the left protruded into the cavity of the ventricle. Below, the opposite wall of the ventricle shows conversion of the ependymal cells to ependymal spongioblasts, whose long "tails" are deeply stained (blue) by ethyl violet-orange G. X 150. (26503.)

" Microcystic degeneration " is common in human gliomas, including astrocytoma and spongioblastoma multiforme. It is apparently considered to be the result of oedema and degeneration, as the term implies. The fact that in the fowl this phenomenon is due to a secretory process is of considerable interest, more especially when one asks whether this secretion may perhaps be merely an exaggeration of the normal physiology of glia cells. " Microcystic degeneration " in human gliomas would in my opinion bear re-investigation.

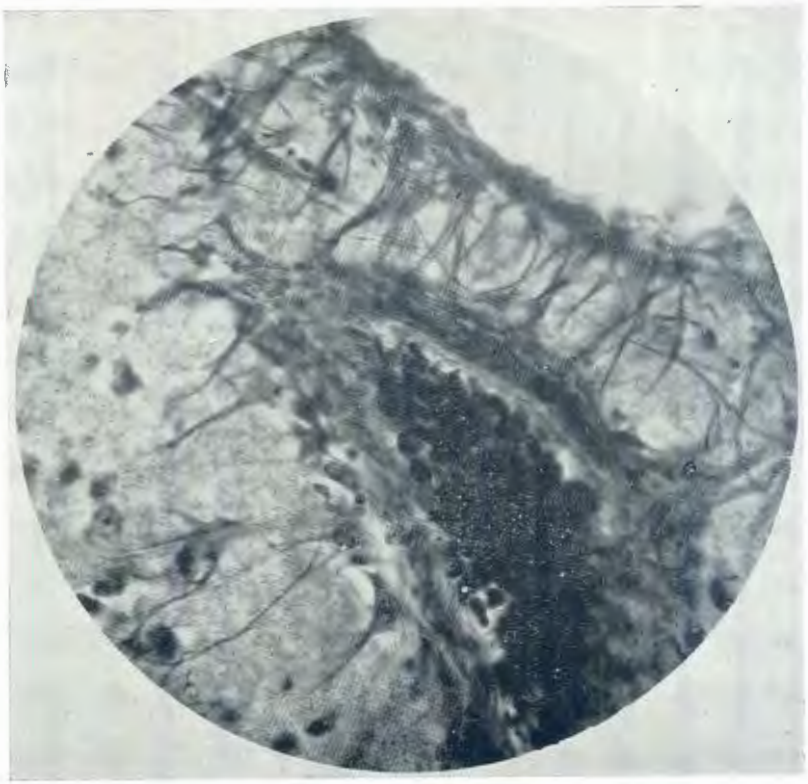

FIG. 20.—Detail of ependymal reaction of a ventricle involved by glioma. The processes of the ependymal spongioblasts, impregnated by Hortega IV, are seen to have grown down to make contact with bloodvessel. (Left, a reaction is seen also among the perivascular astrocytes of the brain tissue.) X 450. (35539.)

IV. HISTOPATHOLOGY OF THE BRAIN TISSUE AT THE MARGIN OF GLIOMAS.

(1) *Changes affecting Mesenchymal Derivatives.*

Perivascular changes have been mentioned by all authors reporting glioma of fowls, but without comment on their significance until the publication of Jackson (1948). Jungherr and Wolff observed lymphocytic infiltration and mild marginal gliosis. Belmonte mentioned a marked reactive gliosis. In the course of years of study my interest in the phenomena occurring in the marginal brain substance has steadily grown until *this tissue interests me even more than the tumour tissue itself.*

It is probably correct to state that the brain tissue in the vicinity of glioma is never normal (fig. 24), although there is variation in the severity of the changes. These changes centre in and around the blood vessels near the tumour, and in most cases are striking.

FIG. 21.—Large central cystic cavity in fowl glioma. A smaller cavity is developing in the tumour lobule to lower right. (H.E.) X 30. (34784.)

Vascular Changes.

The vessels are affected by both hypertrophy and hyperplasia of the endothelium (fig. 25). These cells are swollen to an extent where there is partial (sometimes complete) obliteration of the lumen, and mitoses may be observed. The whole vessel wall also increases in thickness due to deposition of elastic tissue (fig. 26) as well as of collagen. There is an actual multiplication of capillaries, which become altered into thick-walled vessels; and dense congeries of such vessels are often seen transected at the margin of the tumour (fig. 25). These changes affect very largely capillary (or pre-capillary) vessels whose structure becomes altered so that they come more to resemble arterioles. Pigment may be seen in these vessel walls (see later).

FIG. 22.—Development of cavitation by confluence of microcystic cavities commencing as vacuolations in tumour cells. (H.E.) X 125. (27061.)