right eye caused him to return, when the corrected sight was found to be only 20/40. In 1899 it was not quite 20/50, without any change, however, except presbyopia in the left eye. At all these occasions a painstaking ophthalmoscopic examination, however, without dilatation of the pupil, revealed no anomaly. In November, 1901, after an interval of seven years, the sight of the right eye with full (unchanged) correction had sunken to 20/70. On dilating the pupil the only lesions to be seen were slight opacity in the extreme periphery of the lens and two spots each under $\frac{1}{8}$ papillary diameter, one occupying the site of fovea, the other almost adjoining it. The spots were poorly defined, faint yellow in color, with scarcely noticeable increase of retinal pigmentation at the periphery.

There was in this case at no time any sudden disturbance of sight. The lesion was evidently of degenerative character, and of slowly progressive nature.

DISCUSSION.

DR. W. L. DAYTON, Lincoln, Neb.—The first two or three cases mentioned by the essayist simulate the changes at the macula that may occur with senility. The age of his patients, however, would not naturally warrant us in assuming this, yet I do not remember that he spoke of the refraction. It is possible even at that age that a very hyperopic eye might have some influence on this condition inasmuch as the changes in the fovea from senility undoubtedly occur in the nerve and pigment epithelium of the retina, and it appears to me possible for such changes to occur in the cases stated. I had a case somewhat similar to this third one under observation several years ago; a case of pernicious anemia, where the spot appeared to me as if it had been a hemorrhage of long standing—not black, but more of a reddish brown. The patient succumbed to the pernicious anemia. In retinal disease limited to the macula lutea there are a number of conditions that should be carefully studied. There are cases where foreign bodies have entered the vitreous and where some weeks afterwards there appear changes in the macula. This is important, too, because we may have to deal with the condition from a medicolegal standpoint, as bearing on accident insurance, etc. The changes may not appear until some weeks after injury, or extraction of a foreign body. We may find no evidence of foveal disturbance, and then after the eye has assumed its normal condition find changes about the fovea. We may think that we have to deal with a malingering, and then a month or so later these macular changes be very evident. I have in mind a case where such changes about the fovea occurred, yellowish-white in appearance, three months after the injury. Then, as Dr. Gradle has said, there are changes in the macula in retinitis due to the effect of electric light, and there we get a similar condition. There is another condition that I would mention in this connection, and that is where there is but little disturbance of vision and where the ophthalmologic appearance is that of small white dots. This condition may not reduce vision to more than 20/25, and yet present this peculiar appearance. I have never been satisfied as to what the condition is.

DR. LEARTUS CONNOR, Detroit—I have observed a somewhat different case, in a physician 40 years of age. The history showed at a previous examination a healthy eye, until within two weeks of the time I saw him, when suddenly in his left eye central vision disappeared; peripheral vision was normal. A peculiarity he described was this: that this spot which he saw was alive, and he described and drew on paper the various movements observed subjectively; their outline was oval in shape, progressing from the center toward the border in all directions. The drawing I made from the ophthalmic picture corresponded with that made by the patient. Two months later his central vision had become 20/200 and was apparently improving. Evidently it had involved the entire structure of the retina and the cellular elements were in a state of activity during that period. Whether treatment had any effect or not I do not know. He had been a perfectly healthy man with no constitutional taint, but he had overworked while neurasthenic.

DR. C. W. HAWLEY, Chicago—I was much interested in the paper because it calls to mind three cases I had thought of reporting. The conditions about the macula are not exactly like those described by Dr. Gradle, except in one case. The three cases occurred in ladies and came under my observation some two or three months apart. The conditions about the macula were very much like those which occur in albuminuric retinitis less the hemorrhages. I treated the first case for some time and without much improvement. It finally passed into the hands of an irregular practitioner, was treated for constipation and the patient returned home cured, the macula having returned to its normal condition. The next case was similar and I turned it over to a general practitioner, with the same result. He treated the intestinal tract and the condition cleared up. The third case was very much the same, and all three were treated as to the intestinal tract. No investigations were made as to what the nature of the poison was, but I am sure the condition resulted from the intestinal poisoning.

I understand that Moses Gunn has described some cases very similar to these. I am sure Dr. Gradle's success is due to the doses of calomel he gave.

NEUROGLIA TISSUE AND EPENDYMAL EPITHELIUM IN TERATOID TUMORS.*

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In pathology the advances by which our knowledge of any subject is obtained often take the form of a wave. An epidemic occasions renewed interest and furnishes abundant fresh material; a new technical procedure stimulates investigation and invites the reexamination of accumulated material: the result is a series of contributions revealing new facts concerning the subject. Such a period of activity was inaugurated in the study of neuroglia tissue by the publication in 1895 of the staining methods of Weigert¹ and of Mallory.² Since then has come most of our knowledge of this tissue. Many investigators have been engaged on its problems, and other staining methods have been introduced, but none of these differential methods appears to have been applied to any extent in the examination of similar elements in teratoid tumors. In a teratoma of the ovary, some features of which have already been published,³ a large amount of neuroglia tissue was found. This finding occasioned the investigation of other tumors of this class with particular reference to neuroglia elements. As in these tumors structures related to neuroglia occur and by the application of various neuroglia staining methods other elements than neuroglia fibers are brought out, it has seemed well to consider all of these in this study. Hence neuroglia fibers, neuroglia cells, ependyma, dots and fibers which stain by the neuroglia staining methods and retina-like structures will here be described and their significance discussed.

Teratoid tumors have from earliest times received much attention. A great variety of forms has been de-

* Read at the Fifty-fourth Annual Session of the American Medical Association, in the Section on Pathology and Physiology, and approved for publication by the Executive Committee: Drs. L. Hektoen, F. B. Wynn and W. S. Hall.

1. Weigert: Beiträge zur Kenntniss der normalen menschlichen Neuroglia, Frankfurt a. M., 1895.

2. Mallory: Ueber gewisse Färbereaktionen der Neuroglia, Centralbl. f. allgemein. Path., 1895, vi, 753.

3. Christian: Ependymal Epithelium as a Constituent of a Teratoma, Medical Reports of the Boston City Hospital, 1902, xiii, 161; Boston Med. and Surg. Journal, 1902, cxlvii, 873.

scribed and all kinds of tissue, including the elements of the central nervous system, have been found in them. Their rate of growth and the symptoms due to their presence in various regions have been investigated. The contributions made to the various aspects of the subject have been reviewed repeatedly and it is not necessary to do so again at this time when it is our intention to consider mainly the histology of the neuroglia and of the ependymal epithelium in some of these tumors.

There were available for this study twenty teratoid tumors preserved in a way suitable for the application of neuroglia staining methods. Of these, 18 were from the ovary, one from the lung, and one from the anterior mediastinum. The tumors vary much in size and shape. Some consist of a single cyst with a solid ingrowth; some are solid cystic structures; others a combination of the two. All contain islands of bone and cartilage, some teeth. In six neuroglia was found. Of these, tumors 1, 2, 4, 5 and 6 arose in the ovary, tumor 3 in the lung. However, the possible presence of neuroglia in the others can not be denied, as it is manifestly impossible to exclude small areas of neuroglia except by serial examination of the tumor and this for such large tumors would be excessively laborious. For this reason and owing to the comparatively small number examined, these observations have no statistical value as to the frequency of the presence of neuroglia elements in teratoid tumors. They do show, however, that this tissue is of quite frequent occurrence in tumors not specially selected for complexity of structure.

Material from all of these tumors was fixed and preserved in 10 per cent. of formaldehyd. From some material was fixed in Zenker's fluid and preserved in 80 per cent. alcohol. Material fixed in formaldehyd was stained by Mallory's phosphotungstic acid hematoxylin method,⁴ Mallory's modified fibrin method,⁵ and Huber's modification of Benda's method of staining neuroglia.⁶ That fixed in Zenker's fluid was stained by Mallory's anilin blue connective tissue stain⁴ and the acid fuchsin potassium permanganate method very recently introduced by Mallory.⁷ A number of variations and modifications of these methods were also employed and gave some interesting pictures. Besides these, alum hematein and eosin, or eosin and Unna's alkaline methylene blue were used. As many of these methods as possible were utilized in the study of each tumor.*

Neuroglia tissue is most abundant in tumor 1. The tumor consists of a single large cyst, with epidermal lining and an equal amount of tissue containing innumerable cysts, varying in size from very minute ones to those measuring several cm. in diameter. Between the cysts the neuroglia is scattered in masses of varying size and shape. None of these exceeds 1 cm. in greatest diameter. Most are very much smaller. Many of the areas are sharply circumscribed from the surrounding

connective tissue. Into others strands of connective tissue penetrate or, on the other hand, a band of neuroglia makes its way for some distance from an otherwise sharply contoured mass into the surrounding connective tissue. Less often there is so intimate an intermingling along the border of the two tissues that the limits of the neuroglia can with the greatest difficulty

Fig. 1.—Corpora amylacea in neuroglia tissue.

be made out. In some sections single fibers or groups of several parallel fibers which resemble neuroglia fibers are found in the midst of connective tissue. These fibers are either fine or coarse, and have the same general direction as the surrounding connective tissue fibers. They may bear no relation of continuity to any mass of neuroglia tissue, and may be unaccompanied by any cell dif-

Fig. 2.—Meshwork of neuroglia fibers, some coarse, some fine. Four neuroglia nuclei, two of which are eccentrically placed in a distinct cytoplasmic body. In the cytoplasm of one of these is a "dot" near the nucleus.

fering in appearance from the ordinary type of connective tissue cell.

The relation of the neuroglia to the cysts varies. Many neuroglia masses are entirely separated by connective tissue from the cysts. Others abut on or project into cysts. Some cysts are completely surrounded

4. Mallory: A Contribution to Staining Methods, Jour. of Exp. Med., 1900, v, 15.

5. Mallory and Wright: Pathological Technique, Philadelphia, 1901, 328.

6. Huber: Studies on the Neuroglia, Am. Jour. of Anat., 1901, i, 45.

7. Mallory: A Hitherto Undescribed Fibrillar Substance Produced by Connective Tissue Cells, read at a meeting of the Am. Assoc. of Pathologists and Bacteriologists, Washington, D. C., May 14, 1903; to appear in Journal of Medical Research.

* Weigert's method of staining neuroglia was tried, but satisfactory results could not be obtained. This may have been due to the fact that the tumors were not hardened soon enough after removal from the body or that the reagents used by me differed in some way from those originally employed by Weigert. On this account deductions made by me in regard to neuroglia staining methods are not to be taken as applying to the Weigert method.

by neuroglia. There may be a large cyst with a comparatively thin layer of neuroglia about it or cysts of varying size may lie in the midst of large masses of neuroglia. Where the neuroglia is adjacent to a cyst it may be naked or covered by epithelium. The epithelium covering the neuroglia is of two general types. The one is flat cuboidal and lies immediately on neuroglia fibers, though none penetrates between them; the

Fig. 3.—Neuroglia tissue. (a) Band of surrounding connective tissue. (b) Band of quite fine neuroglia fibers in general, running longitudinally and enclosing few cells. Between (a) and (b) there is a space due to shrinkage of tissue. (c) Layer of large neuroglia cells with eccentric nuclei. (d) Loose meshwork of fine neuroglia fibrils enclosing few cells. In this figure the dots represent cross sections of fibers.

other is of high cylindrical type, and between these neuroglia fibers often penetrate to a varying distance. Between these two types of cells are intermediate forms.

Tumor 1 shows greater complexity of neuroglia structure than the others. In tumor 2, with the same division into a large cyst and a solid portion, as in tumor 1, much less neuroglia is present. The solid portion of this tumor consists largely of small irregular cavities

Fig. 4.—Coarse neuroglia fibers ending in an expanded foot adjacent to a hyaline band of connective tissue. From base of so-called rosette.

and spaces, into which project papillary processes covered by high cylindrical epithelium containing goblet-like cells. In this respect it resembles a papillary adenocystoma of the type which is very common in the ovary. Besides this structure, in a few places are small cysts whose walls are lined by neuroglia. Tumor 3 shows numerous cysts, but the neuroglia tissue bears no

close relation to these. It is sparingly present as small, irregular masses lying in connective tissue and sometimes abutting on a cyst.

In tumor 4 the neuroglia is present in relatively large masses. In one of these masses there is a central elongated cavity, which is not lined by epithelium. From this larger mass, bands of neuroglia extend into the surrounding tissue. In many places there is a very intimate intermingling of neuroglia and connective tissue fibers. In other places the two tissues are sharply demarcated. Tumors 4 and 5 each consist of a large

Fig. 5.—Part of a cyst lined by irregular cuboidal cells. In inner border of these are groups of "dots." In vicinity of cyst there is no neuroglia tissue. Section cuts cyst obliquely.

cyst, whose wall is not very thick. In this wall lie small, rounded masses and elongated bands of neuroglia. In one of the tumors numerous corpora amylacea of irregular size and shape are present in the neuroglia tissue (Fig. 1). In tumor 6 a single mass of neuroglia measuring 3 to 4 mm. in diameter is seen.

In the smaller neuroglia masses of all these tumors blood vessels are generally not present. In the larger masses they are found in moderate number and surrounded by a slight amount of connective tissue.

The appearance of the neuroglia in different areas is

Fig. 6.—Groups of "dots" situated in the central end of cells lining a space. Section cut so as to give a view looking down on the top of the cells. Pale halo about some of the groups.

very various. The fibers differ in size and direction, the cells in form and frequency, and these differences are combined in an almost endless variety of ways. On the one hand we have masses of cells with but few fibers, on the other hand masses of fibers with infrequent cells. In neither extreme is the picture similar to that found normally anywhere in the central nervous system,

though both resemble types of gliomata. The most frequent arrangement is a coarse irregular meshwork of fibers, some fine, some coarse, crossing each other in all directions (Fig. 2). Scattered among these fibers cells are rather infrequent.

Instead of this arrangement, in many places, especially at the periphery of neuroglia masses, there is a more regular compressed meshwork of fibers having, in general, a parallel course (Fig. 3, b). Here nuclei are less frequent. Where these fibers are fine, the structure resembles that of the normal subpial and subependymal neuroglia.

A further modification in this direction results in bands of fibers, almost all of which run in the same direction and have practically a parallel course. In one or two instances these fibers are quite coarse and are interspersed with cuboidal cells roughly arranged in columns. This bears a slight resemblance to the arrangement of cells and fibers sometimes seen in tendons.

In places, instead of the interlacing fibers at first described, we have a finer meshwork of more delicate fibers and rather indefinite granular material, with nuclei widely scattered and generally having but little cytoplasm (Fig. 3, d). This arrangement of neuroglia fibers is similar to that found in many parts of the cerebral cortex.

The individual neuroglia fibers do not vary in diameter in different parts of their course and do not branch. Different fibers vary greatly in size. Some are very fine, others coarse, and some appear as narrow bands. In many areas the fibers are of approximately the same size (Fig. 3). In some the fine and coarse are mingled together (Fig. 2). For most fibers no definite method of ending is apparent; they apparently end abruptly or pass from the level of the section. Some, like those in the so-called rosettes, to be described later, end by an expanded foot applied to connective tissue (Fig. 4).

The cells, like the fibers, present a variety of appearances. Many have rather small, deeply staining, round nuclei, about which little or no cytoplasm can be made out (Fig. 3, b). Some, on the other hand, have abundant cytoplasm, though when the cytoplasm is abundant the nucleus is apt to be larger, oval or slightly irregular, and vesicular (Fig. 3, c). The larger nuclei contain a distinct rounded chromatin mass, besides scattered fine granules. Some nuclei are elongated or even spindle-shaped; where they have a narrow cytoplasmic zone around them they resemble the cells of dense connective tissue. A few of the larger cells possess two or three nuclei. Sometimes the smaller cells are closely packed in a rich network of fibers. At other times the large cuboidal or irregular cells lie close together, separated only by an occasional fiber (Fig. 3, c). In some places the picture is one of closely packed polygonal or elongated epithelial-like cells, with very few intervening fibers.

A number of the cells possess protoplasmic processes, but these are not very prominent. The fibers may be widely separated from the cytoplasm of a cell, and their closest relation appears to be one of contact, rather than of continuity. The cells have no cell membrane, and, whether round, oval, cuboidal, or irregular, their cytoplasm is rarely sharply demarcated, but gradually fades out at the periphery.

What is of particular interest is the presence in very many of the cells in the areas of neuroglia tissue of small dots, staining in the same manner as the neuroglia fibers. Often there is but one (Fig. 2). Sometimes there are two lying close together. Very frequently

there are five to fifteen scattered in the cell or grouped together. They may have any position in the cell; sometimes they lie close to the nucleus, sometimes remote. Many times they are surrounded by a halo staining more palely than the general cytoplasm. Very rarely short rods, instead of dots, occur. These same

Fig. 7.—Ependymal epithelium lining a large space. Neuroglia tissue, with many rather coarse fibers perpendicular to ependymal layer and extending a short distance between the ependymal cells. From a preparation not stained by a method suitable for the demonstration of ependymal dots.

dots occur also in the epithelium of the cysts of the first tumor. Here they occur in the inner border or between the nucleus and inner border of the cells (Fig. 5). They can be best seen when the section cuts the cyst so that a view of the top of the cell is obtained (Fig. 6). The cysts which these cells line vary in size. They may be

Fig. 8.—A simple rosette.

minute, representing a small space or lumen in a group of cells, or they may be large. The cysts may have neuroglia in close proximity, or none be adjacent. In some cysts neuroglia fibers penetrate between the lining cells (Fig. 7). Of these cells some are low and cuboidal, and others high and cylindrical. Not infrequently in cili-

ated cells rows of these dots are situated at the base of the cilia. In others they are not present.

In tumor 1 are peculiar structures which deserve attention from their vague resemblance to retina and from their containing fibers which stain like neuroglia fibers. These partially fill some of the cysts. In their simpler form they consist of a rounded mass with a pedicle but little smaller than the mass (Fig. 8). The outer portion of this mass is made up of closely packed round or oval nuclei, sometimes deeply staining, sometimes vesicular with one to three rounded chromatin masses. The cytoplasmic bands of these cells are ill-defined, and be-

Fig. 9.—A more complicated rosette.

tween some of them fibers staining like neuroglia fibers can be traced. As the central and basal portions are approached there are fewer nuclei and more fibers. At the base there are almost no nuclei and many coarse fibers (Fig. 4). Most of these coarse fibers are parallel in direction and end against connective tissue by a fairly definite expanded foot. The connective tissue in this portion is frequently in the form of a hyaline band (Fig. 4), sometimes gently undulating, sometimes quite convoluted. Instead of this band there sometimes is a

mass of indefinitely fibrillar or ill-defined hyaline connective tissue. In the region of the base there is always a layer of high cylindrical epithelium which passes by gradual transition into the epithelium lining the cyst. The ingrowth and fusion of several such masses produce more complicated structures (Fig. 9). The cysts in which they occur are almost always partially or completely lined by epithelial cells, which are filled with fairly coarse granules of brown pigment. This pigment resembles that found in the retina. The structures themselves resemble in many places the rosettes of gliomata retinae, and, for need of a better word, may be called rosettes. They have similar small, round nuclei. The coarse neuroglia fibers ending in apposition to a connective tissue band suggest the fibers of Müller. Their occurrence in cysts lined with pigmented epithelium adds further to the analogy.

The mode of development of the structures described above can apparently be traced. At first there is a proliferation of the epithelium at one point in a cyst, resulting in a thickened layer of cylindrical cells, between which fibers staining like neuroglia appear (Fig. 10). The fibers and cells increase in number, and at the same time the connective tissue proliferates and pushes the mass into the cyst cavity (Figs. 11 and 12). The fibers grow mainly toward the base, while the cellular portion remains toward the center. In some cysts several such ingrowths are found (Fig. 13), and it is probable that in this way the more complicated masses are formed. Many variations in complexity are seen, and forms representing different stages of development appear in the various sections.

Discussion.—Nowhere in the central nervous system do we have such an intimate intermingling of neuroglia and connective tissue as in these teratoid tumors. In the brain and cord the separation between pia and cortex is usually sharp. Gliomata, as a rule, are in juxtaposition to surrounding white or gray matter or to pia, and so do not lie in very intimate contact with mesoblastic tissues. The nearest approach to these conditions is where vascular radicles, accompanied by a small amount of connective tissue, penetrate nerve tissue from the pia, and where the connective tissue of the choroid plexus abuts on neuroglia. In case of the teratoid tumors this mingling of the two tissues often occurs at points where no vascular radicles penetrate, but seems due rather to a coincident growth of adjacent foci of two tissues of different germ layer origin, with an overlapping, due to irregularity in rate of development. Such an explanation seems more plausible than that we have the one tissue invading preformed tissue of the other kind in the way a malignant tumor invades adjacent structures.

Moreover, there are present fibers in connective tissue remote from definite neuroglia masses. These stain in a manner identical with the neuroglia fibers of the larger masses, and in size, absence of branching, and undulating course present no differences from many fibers seen in them and in gliosis and gliomata. Their isolated presence in connective tissue seems difficult of explanation. At first it was assumed from their staining properties that they were to be considered of undoubted neuroglia origin. It was thought that their presence in connective tissue might be explained by their arising as an offshoot from a neuroglia mass, with which they were originally connected, and from which later in the growth of the connective tissue they had become separated. Another possible explanation is that early in the development of the tumor a small group of neu-

roglia cells became separated in the midst of connective tissue elements, formed their specific intercellular substance and then disappeared. Either theory would explain their present position, assuming that they are true neuroglia fibers, that is, fibers formed by neuroglia cells. Of this we have no proof, except the morphology

Fig. 10.—Early stage in formation of so-called rosette—a local thickening of epithelium of a cyst with formation of fibers between cells.

of the cell, the relation of the fiber to the cell and the staining reaction of the fiber. The former, in many cases, is by no means definite, and in this connection no cell resembling neuroglia cells are present. Doubt as to the latter arose from the following: In some of the teratoid tumors, in which no neuroglia occurs, there

Fig. 11.—Beginning of pushing forward of epithelium by connective tissue formation at base.

are present about sweat ducts fibers staining in the same way as neuroglia fibers, with both the phosphotungstic acid hematoxylin and modified fibrin methods (Fig. 14). While these studies were in progress, Dr. Mallory, investigating connective tissue and smooth muscle,

found fine fibers which stain red by the acid fuchsin potassium permanganate method, in sharp contrast to very abundant unstained fibers. This method also stains sharply true neuroglia fibers, and suggests a possible further resemblance in staining reaction between neuroglia and certain connective tissue fibrils.

To test this analogy three specimens of carcinoma of the breast, in whose stroma Dr. Mallory had found the red staining fibrils very abundant, were fixed in either formaldehyd or alcohol. To these were applied the phosphotungstic acid hematoxylin, modified fibrin, Benda's and Huber's methods of staining neuroglia. With all of these fibrils were found, which, from their holding the stain and, to a certain degree, their relation to cells, might be confused with neuroglia. From this it is evident that there are connective tissue fibers which do not readily decolorize after these staining methods and whose identification can not be based solely on staining reaction, since they at times stain in a manner similar to neuroglia fibers.

From this evidence it appears that the fibers scattered in the connective tissue of the teratoid tumor staining

Fig. 12.—More definite pedicle of connective tissue capped by mass composed of cells and fibers.

in the same way as neuroglia are not of necessity of neuroglia origin. Their true nature at present is indeterminate. In some places they are probably neuroglia, in others not.

Dots, staining in the same way as the neuroglia fibers, have been described as occurring in many of the cells of these tumors. The question as to their significance naturally arises. Similar dots or short rods have previously been described by Weigert in the normal ependyma,⁸ by Storch in cells lining small spaces of a glioma,⁹ by Benda,¹⁰ by Mallory,¹¹ and by Lewy,¹² in the neuroglia cells of gliomata and by myself³ in a teratoma (tu-

8. Weigert: Bemerkungen über das Neurogliagerüst des menschlichen Centralnervensystems, *Anat. Anzeiger*, 1890, v, 543.

9. Storch: Ueber die path. anatomischen Vorgänge am Stützgerüst des Centralnervensystems, *Virchow's Arch. f. Path. Anat.*, etc., 1899, clvii, 127 and 197.

10. Benda: Path.-anatomische Bemerkungen zu dem zweiten vorstehenden Fall A. Fraenkel's, *Deutsch. Med. Woch.*, 1898, 476.

11. Mallory: Three Gliomata of Ependymal Origin; Two in the Fourth Ventricle, One Subcutaneous Over the Coccyx, *Jour. of Med. Research*, 1902, viii, 1.

12. Lewy: Ueber Centralkörperchen in Gliomen, *Virchow's Arch. f. Path. Anat.*, etc., 1903, clxxi, 236.

mor 1 of this report), both in the cells lining cysts and those scattered among neuroglia fibers. Various meanings have been attached to them. Weigert in his first paper regarded them as an interrupted cuticular layer. Mallory considered the dots as possible evidence of the ependymal origin of the gliomata studied by him. I,

Fig. 13.—Several ingrowths into a cyst.

concurring in this view, attached a similar import to their presence in a teratoma. Lewy looked on them as centrosomes, but regarded the presence of groups of them in neuroglia cells as an inheritance from ancestral ependymal cells, and the ring or rosette arrangement of some as a probable rudimentary cilia formation. In considering the different views, certain facts have been brought out which do not readily harmonize with them, though at the same time it has not been possible to determine definitely the nature and significance of these

Fig. 14.—Sweat duct in teratoid tumor, showing cross section of coarse longitudinal fibers lying between true basement membrane and epithelial cells. These stain with neuroglia stains.

dots, and the attempt to advance any new hypothesis regarding them will not be made.

The earlier view of Weigert that they are a cuticular arrangement no longer seems tenable since the dots are found irregularly scattered through the cytoplasm of cells lying in the midst of large areas of neuroglia fibers and lining no space or lumen.

Are they centrosomes? They can be stained by methods used for demonstrating centrosomes as the iron hematoxylin method. Multiplicity of centrosomes has been described by Heidenhain in bone marrow giant cells. We have studied these dots in the ependyma of a series of pig fetuses from 18 mm. to 17½ cm. in length, and in several early human fetuses, using the phosphotungstic acid hematoxylin staining method. Here they are almost always present as a row or group adjacent to the spinal canal or ventricle. At this time nuclei are situated generally at some distance from the central space and its bordering dots, and dots are not found except in this arrangement. Mitoses of the cells in this region are common, and the dividing nuclei often approach near the space at whose border the dots are grouped. Yet there is no apparent change in the dots, nor are any dots seen associated with the mitoses. This does not seem to favor the view that the dots are centrosomes.

That they bear no close relation to the formation of neuroglia fibers, whose staining reactions they have, is shown by their presence in the fetuses studied at a time much before the fibers show any evidence of their presence.

The dots are already present in an 18 mm. pig, when, according to Hardesty,¹³ differentially staining neuroglia fibers appear first in pigs from 16 cm. to 21 cm. in length.

The dots do not appear to be closely associated with cilia, since they were absent in some ciliated cells, and occurred in some non-ciliated cells. They are not always present in cells which originate from ciliated cells, as they could not be demonstrated in an adenocarcinoma of the uterus.

Can the presence of these dots be considered evidence of the ependymal character and ancestry of a cell? Dots were not found in most parts of these tumors except in neuroglia cells or cells lining cysts, and presumably of ependymal character. They were not found in several carcinomata of the breast or in a malignant adenoma of the large intestine. Dots very similar were found in the high cylindrical epithelium of that part of one tumor described as resembling a papillary adenocystoma of the ovary. Dots similar, but slightly larger, were found in some sweat ducts in these teratoid tumors and in those of a specimen of normal skin. Larger granules staining similarly with Mallory's phosphotungstic acid hematoxylin were found in the pancreas, but dots were not present in the kidney of this case, nor were they found in the fetal organs of the 18 mm. pig. This shows that dots, if not identical with those occurring in true ependyma, yet staining similarly, occur in cells undoubtedly of different nature, and so the mere presence of such dots in a cell or group of cells can not be considered diagnostic of the ependymal character and origin of these cells. When they do occur in cells which offer other evidence of a central nervous system origin, it seems justifiable to regard their presence as adding evidence in favor of the view that the cells containing them bear a genetic relation to ependyma. This is true for cells which line cysts and are in close relation to neuroglia tissue and for cells which are embedded in neuroglia fibers. Where the cells line cysts and bear no close relation to neuroglia, such a conclusion does not seem justified, and their nature remains undetermined.

13. Hardesty: The Neuroglia of the Spinal Cord of the Elephant with Some Preliminary Observations on the Development of Neuroglia Fibers, *Am. Jour. of Anat.*, 1902, II, 81.

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CONCLUSIONS.

From the preceding work the following conclusions may apparently be drawn:

1. Neuroglia is a common constituent of teratoid tumors.
2. Its structure in them is very varied, simulating many known forms.
3. Neuroglia is more intimately associated with mesoblastic tissues in teratoid tumors than elsewhere.
4. In such tumors occur isolated fibers and groups of fibers which stain like neuroglia, but whose nature can not be determined by the staining reactions of Mallory. Huber and Benda, since these methods may stain other fibers than neuroglia fibers.
5. In many cells of these tumors occur small dots or groups of dots which have similar staining reactions to neuroglia fibers.
6. The presence of these dots in cells, though not absolutely diagnostic, may be considered as evidence in favor of the ependymal origin of the cells in which they occur.

Finally, it is with great pleasure that I acknowledge the very many valuable suggestions made by Dr. F. B. Mallory and his interest in this study. To Dr. J. A. Sampson of the gynecologic department of the Johns Hopkins University I am indebted for a number of these tumors, and to Dr. W. H. Lewis of the anatomic department of the same institution for the series of fetal pigs.

DISCUSSION.

DR. L. HEKTOEN, Chicago—Are the rosette bodies which you have described to be regarded as imperfectly developed eyes?

DR. H. A. CHRISTIAN, Boston—The analogy of these structures to eyes was considered and there is a great deal in favor of this view. The occurrence in many of these cysts of pigmented epithelium, the fibers which suggest Müller's fibers, and the small round nuclei which are very common in imperfectly formed retinae, are all in favor of that theory; but there is no proof of what they are, and this is a mere opinion. However, I regard them as possibly an attempt to form eyes.

HEMOGLOBINURIC FEVER.

ITS CAUSES AND TREATMENT, WITH ESPECIAL REFERENCE TO THE USE OF QUINIA.*

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In presenting this subject for your consideration, we do so because of the diversity of opinion concerning it, hence evident need for more thorough study and discussion. Our consideration must leave out many of the features and characteristics of that arch mimic of all diseases, malaria, and be confined to that disease characterized by hemoglobin in the urine and due to malaria in some of her protean manifestations, discarding for the time Yersin's supposed discovery of a specific cause other than the malarial plasmodium, and all other theories and suppositions born of efforts to account for this peculiar manifestation.

In making an effort to clear up some of the uncertainty enveloping the subject, and to arrive at the truth concerning this disease, it was determined to depend, not alone on the individual conclusions of those who saw the disease, influenced no doubt by former teachings and impressions, but to get as thorough report of cases as possible, and view them, their cause, treatment and results, singly and collectively, drawing conclusions from

recorded facts, and not by one individual or from one point of view, but by men of many localities, teachings and impressions.

Accordingly 2000 blanks for report of cases were printed, which provided for a thorough report of all features that we are to consider here, together with some others that are desired for future consideration, and with a letter requesting a report of cases were mailed to the physicians of southern and eastern Texas and Louisiana, selecting localities where it was presumed the disease most prevailed. Of those requested, 81 replied; 40 of whom could not report cases, while 41 reported 173 cases, to which I added 29 cases of my own, making a total of 202 cases reported by 42 observers. Many of those reporting had treated many times the number of cases reported, but owing to the lamentable fact that no case book was kept, they were unable to make even a partial report on others.

Of those cases reported many features of the disease were unreported on, owing to the fact that in most instances the patient was in the rural districts, so far from the attendant's office that frequent and proper observations could not be made; and when the patient was seen many of the accoutrements necessary for proper observation were not at hand. Therefore, in tabulating and reporting on the different features observed, it will not be of the whole 202 cases, but of that number on which these features were reported.

Of the 202 cases collected there were 61 cases treated without methylene blue or with less quinia than 15 grs. per diem, which is practically no quinia, of which 26.2 per cent. died and 73.8 per cent. recovered; while 112 were treated with 20 grs. or over of quinia, of which 16.9 per cent. died and 83.1 per cent. recovered; 4 were treated with methylene blue, with 1 death and 3 recoveries.

Of the cases treated without methylene blue or quinia 30 per cent. had hemorrhage from other organs than the kidneys, occurring on the second, third and fourth days, evidencing a non-subdued condition of the malaria and its recurrence, involving other organs; of these 50 per cent. died, two during the chill following the hemoglobinuric attack, and one during the second chill thereafter.

Of those treated with quinia, 9.8 per cent. were so affected, with 3.6 per cent. fatality. It thus appears that quinia effects not only a lower death rate, but also lessens the percentage of recurrent paroxysms. In those cases treated with quinia your attention is invited to the following facts which bear on the adequacy of the dosage: Of 50 cases treated with 20 to 30 grs. per os, 22 per cent. died; while of those given 30 grs. or over in the stomach, 16 per cent. of the 43 died; and of those given 40 grs. or over only 8.6 per cent. of the 35 died. Of the 19 cases treated with quinia hypodermically, only one case or 5.26 per cent. died, and that one within 48 hours of the onset, of toxemia, due to the paroxysm had before treatment was begun. There were 12 cases reported where the urine became darker upon the administration of quinia and three where it became darker when quinia was withdrawn. Of the total of the non-quininized patients, 9.8 per cent. died of uremia, while of the 19 deaths among quinia patients, 8.9 per cent. succumbed to uremia. While uremia occurred in 16 per cent. of those treated with less than 30 grs. by the stomach, it occurred in only 2.8 per cent. of those treated with 40 grs. or over by the stomach, and not at all in those treated with quinia hypodermically. The average illness of those treated without quinia was 9.66 days and of those

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