The Choroid Plexuses of the Lateral Ventricles, their Anatomy, Functions, and Pathology (in relation specially to Insanity).

John W. Findlay, M.B., C.M.,
Crichton Royal Institution,
Dumfries.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

Contents.

I. Introduction, being a Historical Review of the Literature on the Subject.

Heinrich Heldt in his thesis, "Ueber die Kalkconcretionen in den Plexus chorioides des menschlichen Gehirns", written in 1874, states that before the beginning of the 18th century the literature presents nothing more than a historical interest. "Herophilus, Erasistratus and Rufus had all described them, but", he adds, "anatomists seem to have been more taken up with the enunciation of abstract hypotheses and speculations as to their use and purpose; a more strict anatomy of this formation being looked on as only of secondary consideration. Thus some thought that the choroid plexuses purified the vital spirits, others that they regulated the heat of the body, while others again looked on them as the seat of the imagination or the excitors of phantasy. Of more historic interest is the further fact that to the above investigators only the vascular plexuses of the two lateral ventricles were known, while those of the third and fourth were discovered for the first time in the 17th and 18th centuries."

Coming down to later times we find the first monograph on this subject furnished by a Hollander, Van Gheert, in 1830.

Then, in 1836, Purkinje discovered the epithelial covering of the choroid plexus.

Next comes Bichat who enunciated first the view that, "Ils ne sont autre chose, que la pie mère repliée sur elle même, et non étendue, comme ailleurs sous forme membraneuse," and though this statement, according to Luschka on account of its simplicity and evident harmony with nature, had, till his own monograph appeared, kept the plexuses away from a thorough and independent investigation, the truth of it remains in great part at this present time admitted and uncontested.

In 1854 Luschka's monograph, "Die Adergeflechte des menschlichen Gehirnes" appeared, and may be said to be the first thorough description of the normal anatomy of these structures. Most important of all perhaps, in Luschka's monograph, is the fact, that he not only puts forward the doctrine that the choroid plexuses are actively secreting structures producing the cerebro-spinal fluid, but proves his case from histological observations. Luschka, indeed, though contending for some time (Archiv f. physiol. Heilkunde, Jahrgang XIII.), that the cerebro-spinal fluid was no more transudation, nevertheless, admits in his prefix that he has not been altogether unanticipated in this opinion. Three months before his own

work appeared Faivre in "La Gazette médicale de Paris", had promulgated the idea that "les plexus choroïdes, ont un rapport intime avec la production du liquide céphalo-rhachidien". Moreover, in the same year Lehmann (Handbuch der physiol Chemie.) from a chemical investigation, had arrived at much the same conclusion. But this work of Luschka seems to have passed into obscurity, for in 1897 in his "Text Book of Physiology," Foster, in favouring the secreting function of the choroid plexus, bases his argument on the remarkable absence of albumin and other features of the cerebro-spinal fluid, instead of on the histological facts discovered by Luschka.

As the views and observations of Luschka were in part quite new, and partly stood in direct opposition to the opinions held up till this time, a new investigation was called forth in 1860 under the title, "Beiträge zur normalen und pathologischen Anatomie der Plexus choroides", from the pen of Dr. Haeckel, who, in the main, confirmed the views of Luschka; and while the latter described little else than concretions and cysts, the former gives a full account of the different pathological degenerations met with in the choroid plexuses. Haeckel, however, differs from Luschka in his description of the epithelium, and does not discuss the secreting function of the same.

In 1874 Heldt wrote his thesis, tracing the seat and mode of origin of these bodies more thoroughly than Luschka and Haeckel had done, both of the latter having restricted themselves more to a description of the shape, than the origin of these structures (concretions).

Many different notes and papers have appeared from time to time in our own country on the cysts and concretions so commonly found. The first reference to the former being in 1826 by Hooper, and to the latter, in 1851, by Swain.

In 1854, and evidently quite independent of Luschka, a paper by I. T. Arlidge was produced, entitled, "Observations on Brain Sand and Amyloid Bodies in the Choroid Plexus". Most of his observations were made on plexuses of the insane. He traces the origin of this brain sand and comes very near the actual truth of the matter, while of special interest is the fact that he alludes to the "glomus" (the swelling of the plexus found at the upper end of the descending cornu of the lateral ventricle), the first and only time I have seen it mentioned in English works.

As in Britain, so abroad, random notes and papers have appeared on tumours, cysts, and concretions of the choroid plexus; and except for "Ueber die Innervation des Plexus Ch. inf." by Benedict in 1874, no special article is found till we come down to 1886 when

Albarran published his paper "Sur la structure d'un renflement situé au niveau du bord libre des plexus choroïdes des ventricules latéraux" Bull. Soc. Anat..

Within recent years much work has been done on the histology and pathology of the membranes and vessels of the brain, all of which bears more or less on the subject under consideration. Still more closely related to my theme is the pathology of these structures in the insane. In this department likewise there have been many workers, too numerous to mention, both at home and abroad.

On looking around for a subject on which to construct a thesis, it was suggested to me that the choroid plexus was a structure little written about, and that in all probability it would show important alterations in the insane. The paucity of the literature within recent years seemed to justify my taking this as a field for research.

I have, in the course of my investigation tried to apply the work done on the pia-arachnoid and its vessels to the choroid plexus, and how far I have been successful in corroborating, or refuting the observations and statements of others will be seen in the following pages.

II. Material Examined and Work Done.

The conclusions arrived at in this paper are based upon the microscopic study of the choroid plexuses in 65 cases. Of these Dr. W. J. Robertson Pathologist to the Laboratory of the Scottish Asylums, supplied me with 49, which he had collected ~~which he had collected~~ while acting as pathologist to Morningside Asylum, Edinburgh. Six were from cases examined in the Pathological department of the Glasgow Western Infirmary by Dr. Rutherland. The remainder were from cases examined by myself in the capacity of pathologist and junior assistant to the Crichton Royal Institution, Dumfries.

For the study of the normal structure, I also made preparations from several absolutely fresh choroid plexuses of the sheep, ox, and calf.

The few drawings included are made to no particular scale, the size really depending on the amount of detail I wanted to put in. They were all taken from appearances seen with 1/12 Zeiss oil immersion lens and No. 4 eye-piece, giving a magnification of about one thousand diameters.

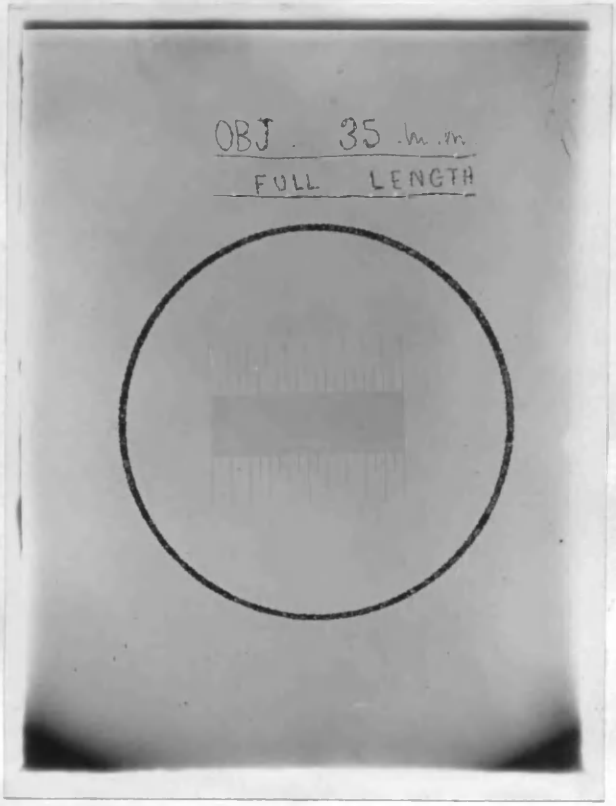
In producing the negatives for the photo-micrographs the lens was frequently used without an eye piece. Some (×36. × 120. and × 130.)

were taken with the ordinary achromatic lenses, others (×26. and ×240.) with apochromatic lenses and compensating eye piece.

A focus electric lamp of one hundred candle power was at first employed as the illuminant, but latterly this was discarded for magnesium ribbon, the flash-light being in every way more serviceable.

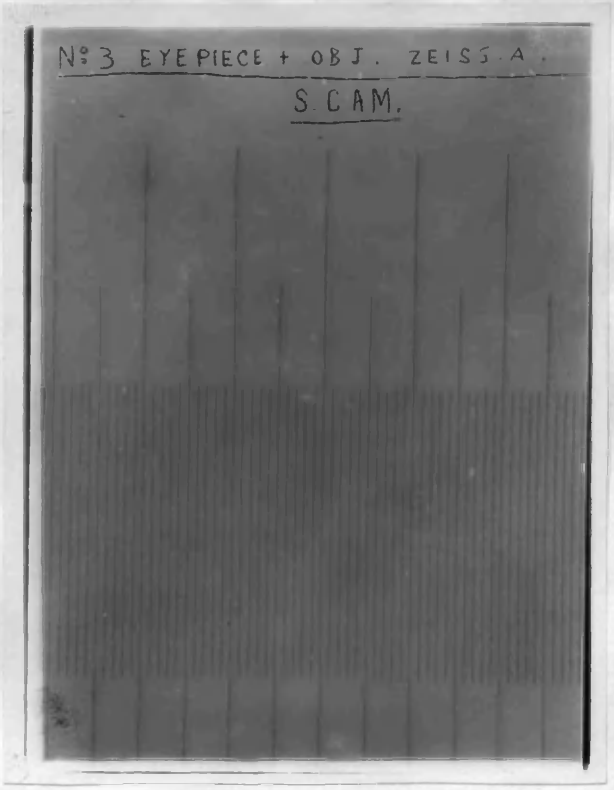
In every case the enlargement attained has been indicated, and I have deemed it advisable to insert photo-micrographs, of a one millimetre stage-micrometer divided into a hundred parts, magnified to the same degree as the sections, for the following reasons, as set down by Dagonet in his "Système Nerveux Central Coupes Histologiques Photographiées".

"This manner of procedure shows that the enlargements obtained are less considerable than one would at first think. In fact one tends to forget in examining a histological preparation by the microscope that it is a question of a virtual image, enlarged by the eye-piece. In this case the role of the eye-piece is preponderant; in the photographic apparatus, on the contrary, it is altogether secondary. These micrometric images not only serve to correct an error of appreciation easily committed; but they have also the other interest of permitting the measurement by the aid of compasses, of the different histological elements."

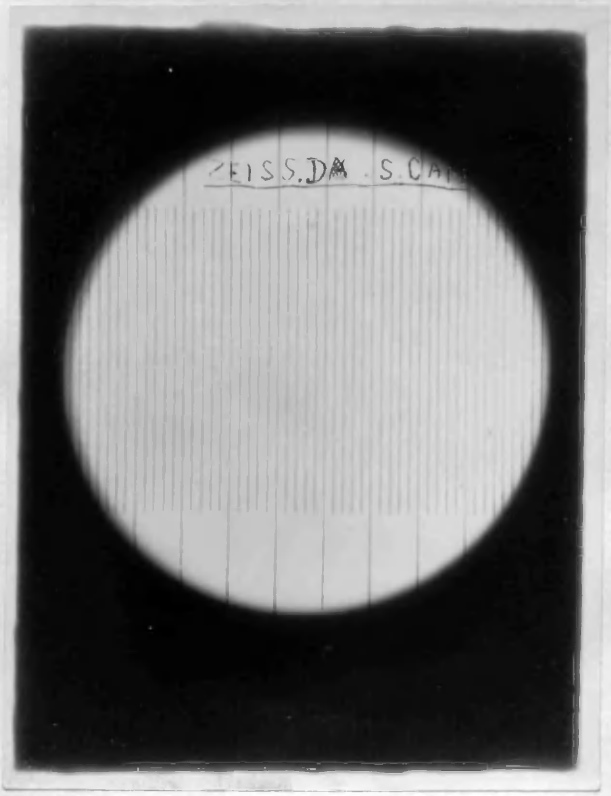


One millimetre stage-micrometer, divided into a hundred parts. (×26).

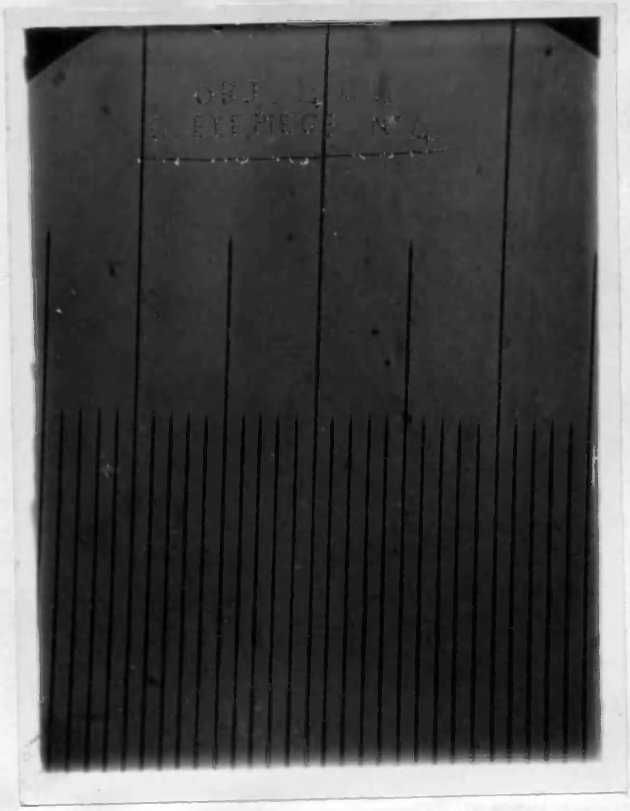
One millimetre stage-micrometer divided into hundredths. (×36).



Portion of one millimetre stage-micrometer, divided into hundredths.
(× 120).



Portion of one millimetre stage-micrometer, divided into hundredths.
(× 130).



Portion of a one-millimetre stage-micrometer divided into hundredths.
(× 240).

In no case were the negatives retouched or altered in any way by local treatment.

I have examined about 600 preparations, from which those accompanying the paper have been selected, in order to illustrate the different points. All the sections are marked and the various appearances alluded to, will be found on focussing immediately beyond the arrow.

The majority of the plexuses were embedded in celloidin, the remainder were frozen in dextrine and then cut.

Haematoxylin and eosine were the stains most commonly used, though the following were also employed viz. osmic acid, picro-carmine, Van Gieson's stain, Weigert's fibrine method, Ehrlich Biondi, Cox Smith modification of Golgi, Heller's method for medullated nerve fibres, and Robertson's methyl-violet method.

III. Anatomical Description.

The choroid plexus of the lateral ventricle is formed by an invagination of the pia-arachnoid from the outer surface of the hemisphere. "Along the free edge of the velum interpositum the plexus projects into the lateral ventricle from beneath the margin of the fornix, in the form of a vascular fringe, which extends from the foramen of Monro over the surface of the optic thalamus, as far as the descending cornu, into which it projects along the whole length of its mesial border. Here (in the descending cornu) it is continuous with the external pia mater, and when the plexuses are dragged away an actual fissure is formed in the hemisphere wall, between the fornix and fimbria on the one side and the optic thalamus on the other. This cleft-like opening is the inferior fissure of the cerebrum, and forms the lower part of the so-called transverse fissure, which follows the plane of the velum interpositum over the optic thalamus and third ventricle, and emerges over the corpora quadrigemina. It is along this fissure that the choroid plexuses of the pia mater are invaginated into the ventricles, covered by the ventricular epithelium, which is pushed in before them. Only however when the choroid plexuses are dragged away is an

achial fissure formed, but with the choroid plexus in situ it is a deep sulcus, i.e., an invagination of the thin hemisphere wall (here formed of the ventricular epithelium alone). This known as the choroidal fissure and appears at an early period of embryonic life." ①

This vascular fringe as it is called has a highly characteristic appearance. It lies like a worm along the cavity of the lateral ventricle, is of a blood red colour, and presents a very shaggy surface, due to the enormous numbers of villi which cover it.

At the junction of the body of the cavity with the descending horn a distinct fusiform or oval swelling of the plexus is seen. This enlargement — called by the brothers Wenzel ② "glomérule choröidien" — is always present, but more marked in some cases than in others, and seems specially liable to the cystic and other degenerations met with in the choroid plexus.

The choroid plexus is a very vascular structure. The large choroidal vein and the principal arteries run longitudinally along its base, and the former joins with the vein from the corpus striatum, at the foramen of Monro,

① This description is adapted from that of Schäfer, Quain's Anat., 1893. Vol III. - Part 1, pp 122-126. but I have confirmed all the anatomical points.

② "Anatomie des centres nerveux", Wejrrine 1895. Tome 1st. p. 361.

to form the vein of Galen. Arteries and veins are exceedingly tortuous and showing up on the surface between the villi may be seen vessel loops, covered by little more than epithelium, and attached to the general body of the plexus by a mesentery. The majority of these loops belong to a remarkably tortuous vein, which runs along the free border of the plexus, and to the more than usual windings of this vein, at the upper end of the descending cornu, Albarran[1] attributes the formation of the glomus.

Two arteries ramify in the plexus. The anterior choroid branch of the internal carotid artery supplies the anterior two thirds of the plexus, while the postero-lateral choroid artery, a branch of the posterior cerebral, supplies the remaining posterior third.

The two plexuses of the lateral ventricles become continuous with one another at the back of the foramen of Monro, as well as with those of the third ventricle.

It is interesting further to note that the choroid plexus of the third ventricle is supplied by the postero-mesial branch of the posterior cerebral, while the velum interpositum derives its nourishment from the postero-lateral and the postero-mesial. The lateral choroidal branch of the posterior cerebral goes to the upper surface of the caudate nucleus.

[1] Dejerine, Tome 1er. p. 361.

Thus we see that the choroid plexuses of the large brain and velum interpositum possess a very rich blood supply, coming, with the exception of the anterior choroid branch of the internal carotid, from a parent trunk — the posterior cerebral. Further we learn that the different plexuses are freely connected with one another, and that the vessels of the plexus of the lateral ventricle communicate with those of the corpus striatum.

"Merkel and Mierzejewsky[1] have described an actual cleft in the pia mater along the descending horn which effects a communication between the ventricle and the subarachnoid space, analogous to the foramen of Magendie and the lateral apertures in the fourth ventricle. This observation has not hitherto been confirmed," and I have never seen any appearances to suggest that such a cleft exists.

[1] Schäfer: - "Quain's Anat.," 1893. Vol III. Pt. I p. 126.

IV. Normal Histology of the Choroid Plexus.

It is generally accepted that the choroid plexus is formed of pia mater, while it is held that the velum interpositum is composed of two layers of pia mater, between which are contained arachnoidal tissue and blood vessels.[1]

As the choroid plexuses are only fringes of the velum interpositum, one would expect to find arachnoidal tissue here also, but such is not described, the generally accepted view being, that they are composed of pia mater alone.

Lately however W. F. Robertson[2] has formulated the doctrine that in the soft coverings of the brain two distinct membranes do not exist. He holds that there is essentially only one structure throughout, and, therefore, only one membrane, which he calls pia-arachnoid. By means of horizontal sections he has demonstrated that the so-called sub-arachnoid spaces may be seen in miniature, from immediately under the endothelial covering on the outer surface, right down to the inner surface immediately external

① Schäfer:- "Quain's Anat." Vol III Pt 1. p. 185.

② Middlemas and Robertson:- "Edin Med. Journ." April & May 1895.
W. F. Robertson:- "The Pathology of Milkiness, Thickness, and Opacity of the Pia-Arachnoid in the Insane". Journ. Mental Science. Oct. 1895.

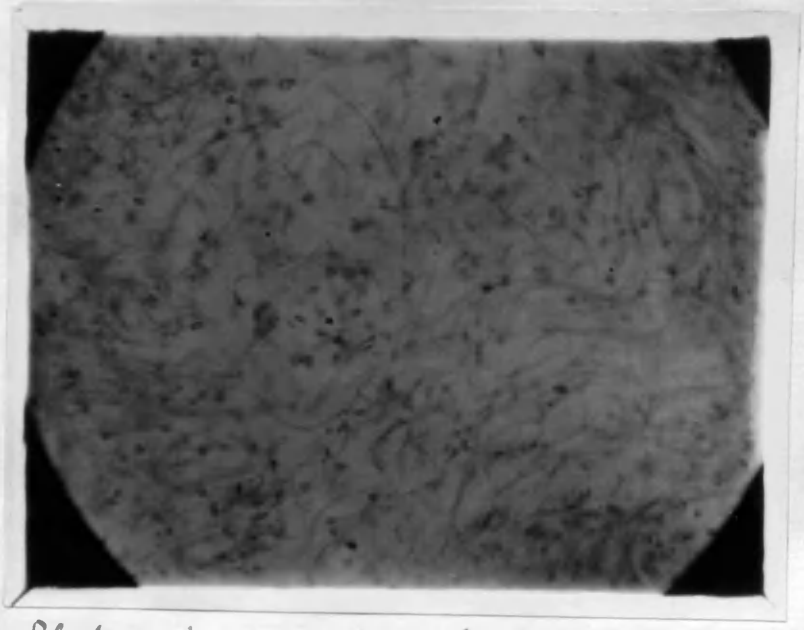


Photo. 1. Section 1. (×240). From a case of early general paralysis.
Loose areolar tissue from near the surface of the gumma, showing very wavy connective tissue fibres and endothelial cells. Here and there distinct spaces seen.

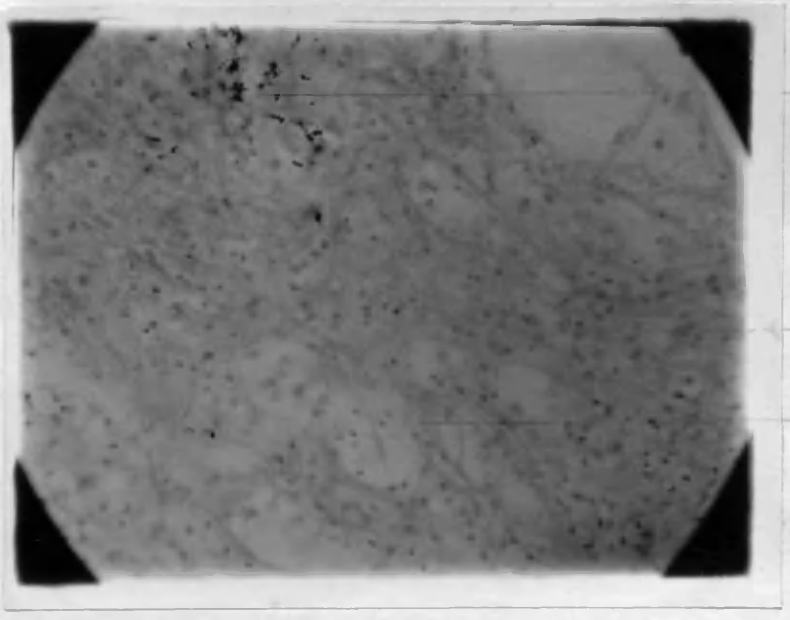


Photo 2. Section 1. (×240). From a case of early general paralysis. Tissue of the gumma a little deeper than Photo. 1.
a. Distinct spaces lined by endothelial cells.
b. Arrangement of spaces not so marked but still evident.
c. Haematoidin granules.

to the cortical tissues.

To my mind, after an examination of Dr. Robertson's sections, his contention of the oneness of structure of the pia mater and arachnoid has been proved, and it seems to me that the basis of the choroid plexus consists essentially of the same structure as the pia-arachnoid covering the surface of the brain, and likewise resembles a spongy lymph sac.

The basis of the choroid plexus is delicate white fibrous tissue. The white fibres are gathered together into bundles or trabeculae of varying thickness and length. These bundles interlace with and cross over one another, after the manner of a network forming numerous spaces of all shapes. These spaces inaccurately placed above and alongside of one another, form freely communicating cavities containing fluid, and are lined throughout by a single layer of flattened endothelial cells with large oval nuclei. The meshes of these networks are larger and smaller, the largest being quite microscopic in size, and the smallest showing only a solitary endothelial cell. (Photos. 1 & 2 Section 1.).

In the pia-arachnoid itself these spaces are largest in the centre of the membrane, where they form the so-called "subarachnoid spaces", or about the base of the brain the "arachnoid cisterns".

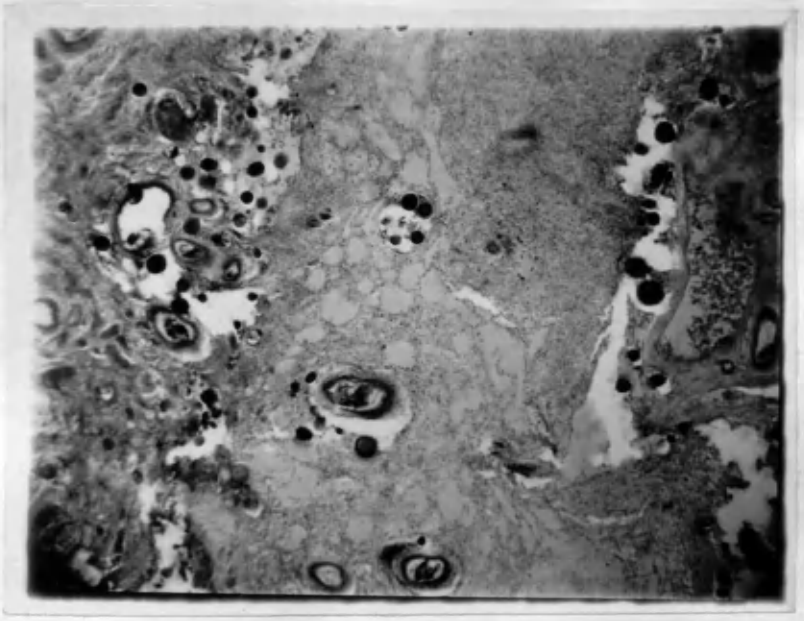


Photo. 2 A. Section 16. Central part of the glomus. (× 26). From a case of puerperal insanity.
In centre large well marked spaces, lined by endothelial cells.

Much the same condition may be seen in the more central parts of the glomus of the choroid plexus, where these cavities often attain a considerable size. (Photo. 2A. Section 16). This might be taken as evidence that the choroid plexus consists of two distinct structures viz. an external layer of pia mater and a central mass of arachnoidal tissue. Such, however, I cannot believe. It seems to me that, as in the case of the pia-arachnoid on the surface of the brain, here is only one structure throughout. Much marked in the centre of the glomus, the lymph spaces get smaller and smaller as we pass towards the surface, till it becomes difficult to make them out. But even here in many cases it is possible to do so, and at most these relatively dense portions of the plexus are but loose areolar tissue lying alongside of distinct and easily recognised sinuses.

The choroid plexus then may be said to be composed of a duplication of the external pia-arachnoid, since the basis of the plexus resembles it in every way.

There is also a small quantity of elastic tissue in the form of fine threads or filaments. These elastic filaments may be seen lying longitudinally on the surface of a connective tissue bundle, and also winding round and encircling it with several spiral turns. This is brought out by treating a portion of teased choroid plexus with acetic acid. The

Photo. 3. — Portion of choroid plexus torn out, and treated with acetic acid. (× 120.)
a. Connective tissue bundle swollen, and showing annular constrictions and markings.

Photo. 4. — Surface view of part of the choroid plexus of a sheep, showing very numerous vessels of an undulating character. (× 26.)

connective tissue trabeculae then swell up, and show circular or spiral markings, with a distinct dark thread at the point of constriction. A continuous spiral may be traced here and there around the bundle, but the appearance of separate rings is more commonly observed. (Photo. 3). areolar tissue,

This arrangement of the elastic fibres, in was pointed out by Henle; but where only separate rings are observed, it has been suggested by Schäfer that this reaction is not due to the presence of elastic fibres, but that "the bundles in question are naturally invested with a delicate sheath, which like the elastic tissue resists acetic acid, but on the swelling up of the bundle under the operation of that agent, is rent into shreds or segments, mostly annular or spiral, which cause the constrictions. In other cases the union of branches of the cells around a bundle may be the cause of the appearance." ①

Connective tissue cells are also found on the surface of the bundles or lying between them, and most frequently assume the spindle or branching form.

Pigmented cells may here and there be seen but their number is never large.

① Schäfer:— "Quains Anat.," Vol I. Part II pp. 229 and 230.

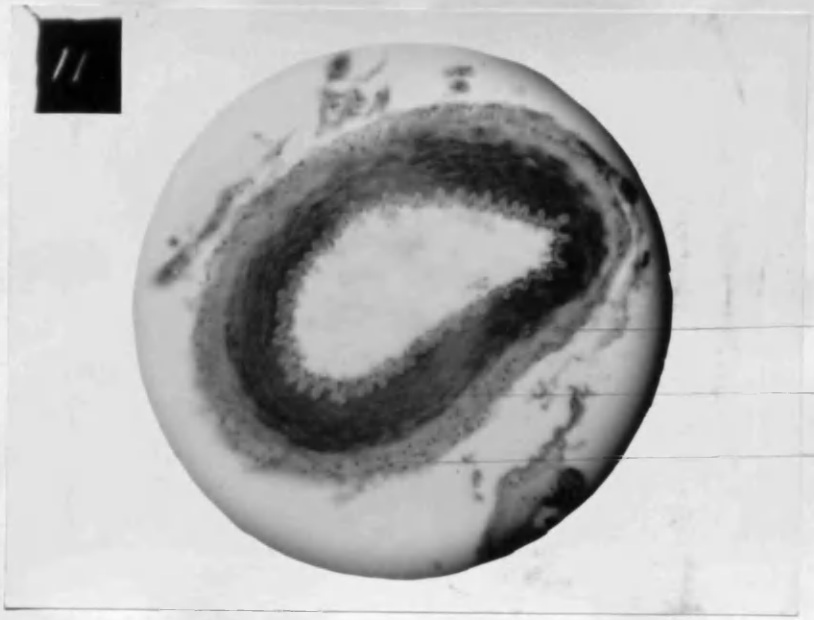


Photo. 5. Section 2. Small artery from the choroid plexus of a ~~retarded~~ ox.
(× 36.)

a. Well marked elastic lamina.
b. Media.
c. Adventitia.

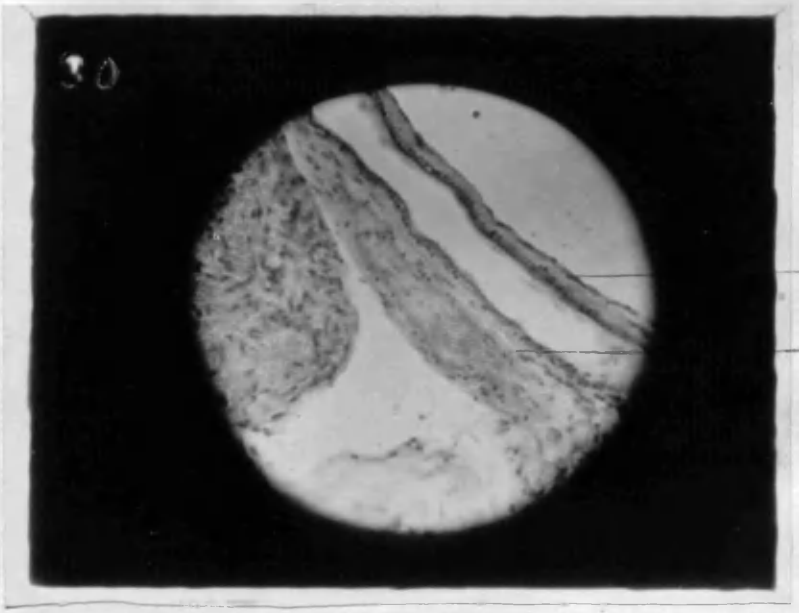


Photo. 6. Section 3. Two small hyaline arterioles from a case of senile insanity.
(× 130.)

a. Layer of endothelial cells immediately beyond hyaline adventitia.
b. Longitudinal channel between the two arterioles, lined by endothelial cells.

Vessels of the Choroid Plexus.

The choroid plexus is a very vascular structure and its vessels are exceedingly tortuous. (Photo. 4). The large choroidal vein and the principal arteries run longitudinally along its base. The branches of the latter pass mainly upwards and go on dividing till eventually a very close capillary network is formed.

Arteries.

The larger arteries in the plexus contain several layers of muscular tissue, and a well marked adventitial coat composed of wavy connective tissue fibres running parallel to the course of the vessel. Outside this adventitial coat, and flattened along it, are the lymph spaces of the pia-arachnoid; indeed the connective tissues of the two structures gradually merge into one another. The elastic lamina too seems to be well developed in these arteries. (Photo. 5, Section 2).

Before describing the arterioles as normally met with in the choroid plexus, let me quote from W. F. Roberton's description of them as found in the pia-arachnoid.

"There is a fact regarding the arterioles of the pia-arachnoid that, I think, helps us to understand the true constitution of the membrane. It is that they have no proper adventitial coat.

Immediately outside of the muscular wall there is a single layer of endothelium, which is continued down to the capillaries, as pointed out by Klein. Obersteiner believes that this layer forms the outer wall of a lymph sac, a point that must be regarded, I think, as doubtful. Beyond this endothelial layer lying on the muscular coat, the vessels, with the exception of some of the very largest of them, have no special investment of longitudinally disposed fibrous tissue, such as is found in the vessels elsewhere. They are, as it were, naked vessels surrounded by trabeculae and lymph spaces. The trabecular tissue, however practically forms for them a common adventitia. From a consideration of these features of structure, Dr. Middlemass and I have advocated the view that the whole extra-vascular structure of the soft membranes may be looked upon as the enjoined and hypertrophied adventitial coats of the pial vessels, the lymphatic spaces of which have undergone a special development so as to form a spongy lymph sac." ①

In many cases it is impossible to make out any adventitial layer; and immediately under the muscular coat appear round, oval or spindle shaped spaces of small size and lined by an endothelium. In other cases again a very thin layer of longitudinally disposed fibres of

① D. W. F. Robertson:- "The Pia-Arachnoid in the Insane", "Journ. Mental Science," Oct 1895.

connective tissue may be seen, and I feel assured that an adventitial coat exists, though in places so thin as to be discerned only with difficulty or not at all. The presence, moreover, of such is further proved, when thickened by hyaline degeneration, the adventitia appears as a well marked regular band beyond the muscular coat, even in arterioles with only one layer of muscular cells.

Beyond the adventitia, now and then, appearances, as of a continuous layer of endothelial cells, may be made out; and in Photo. 6 and section 3, a longitudinal channel lined by such cells seems to exist between two small arterioles. Such a condition, however, does not appear to me to imply the existence of a special lymph sheath, but is most probably produced by one of the spaces of the "spongy lymph sac", altered in shape to suit the exigencies of the case. Albarran[D.] considers the vessels of the choroid plexus as destitute of a lymphatic sheath. Moreover one can see no necessity for such if the contention of Middleton and Robertson be correct — that "the whole pia-arachnoid may be looked upon as the enjoined and hypertrophied adventitial coats of the pial vessels, the lymphatic spaces of which have undergone a special development so as to form a spongy lymph sac."

D. Albarran:— quoted by Weyerine Anatomie des Centres Nerveux," 1895. Tome I. p. 361

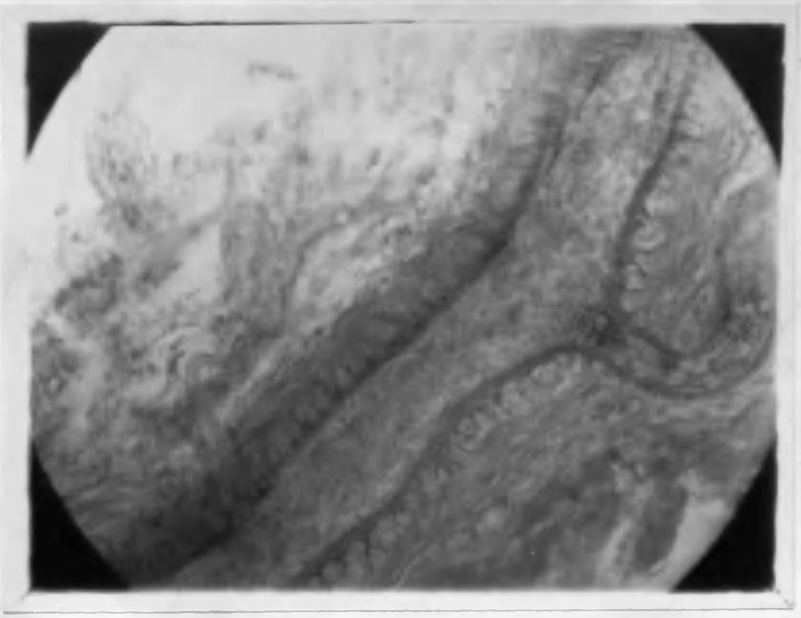


Photo. 7. Section 4. Normal arteriole from the ox. (× 240). The arteriole is widened at points where branch is given off, and near the foot of photo. is an apparent dilatation from unequal muscular contraction.

Photo. 7. Section 4 A. Small arteriole, from a case of senile insanity. (× 240). Only single layer of muscular cells, and a very well marked elastic lamina, in a slightly thickened hyaline intima

I accept this view of Middlemass and Robertson as it stands, and my belief that a delicate adventitial coat is present, does not seem to me to be out of harmony with the general spirit of their doctrine.

The intima of the small arterioles is likewise very thin, the endothelium being separated from the muscular coat by a very delicate layer of tissue.

W. F. Robertson[1] holds that the elastic coat has normally no existence in the small cerebral arterioles. I cannot however agree with him, and it seems to me that even the smallest arterioles possess a fine elastic lamina. Indeed in the normal condition the intima consists of practically nothing else but endothelium and elastic lamina. (Photo. 7, Section 4).

Capillaries.

The capillary network is best marked at the surface of the plexus, immediately under the epithelium and in the villi, but may be traced throughout the greater part of the plexus. The more central parts of the glomus, however, show no such network and the tissues here are practically non-vascular. The capillaries are of large size and are likewise surrounded by the spaces of the pia-arachnoid, and in parts little more than two layers of

[1] W. F. Robertson:- "Edin. Med. Journ." Jan. 1896 p. 630.

endothelial cells — that of the capillary itself and that of the space — seem to separate the cavity of the lymph sinus from the interior of the capillary.

There is no reason to believe that the minute "basal zerosa", described and figured by Luschka[1] in this structure, have any real existence.

The capillaries here, moreover, are remarkable for the fact that they possess a special adventitia in addition to their endothelial intima. There are two forms of nuclei in these capillaries, elongated and rounded. The former belong to the intima, stain faintly and do not project from the capillary wall: the latter on the other hand are adventitial, stain deeply and do project. This adventitial investment must be considered as consisting of two elements, connective tissue cells and exceedingly delicate fibrils, the latter being continuous with the connective tissue of the adventitia of the larger vessels. These fibrils in the capillary walls are of great importance, for it is in them, as Woodhead[2] points out, that the process of waxy degeneration is supposed to occur.

Small capillaries too may be normally seen immediately under the muscular coat of arteries and arterioles and quite close to the intima of veins.

1. Luschka :- "Die Adergeflechte etc" Tafeln I Fig 13
2. Woodhead :- "Practical Pathology", 1885, p. 161.

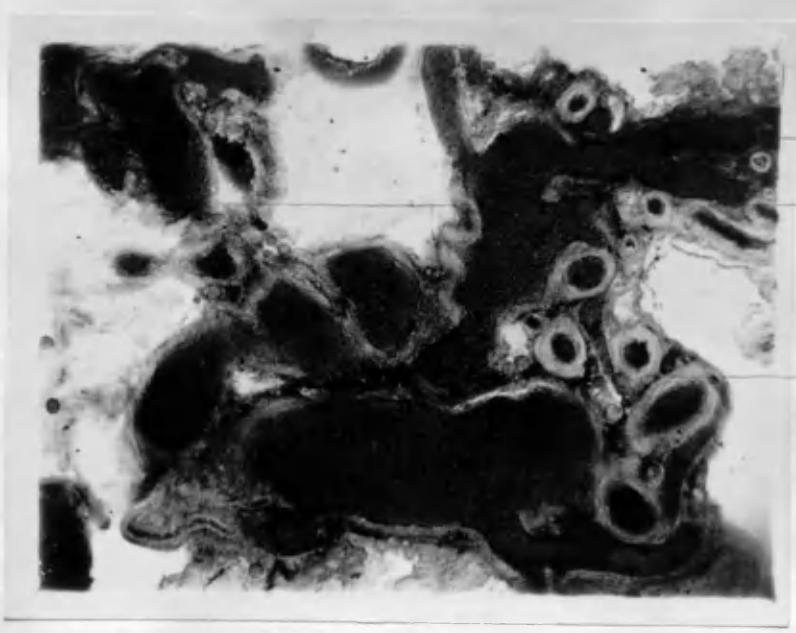


Photo. 8. Section 5. Cavernous-like tissue due to tortuosity of the veins. From a case of melancholia. (×26.)

a. Veins

b. Arterioles with thickened walls.

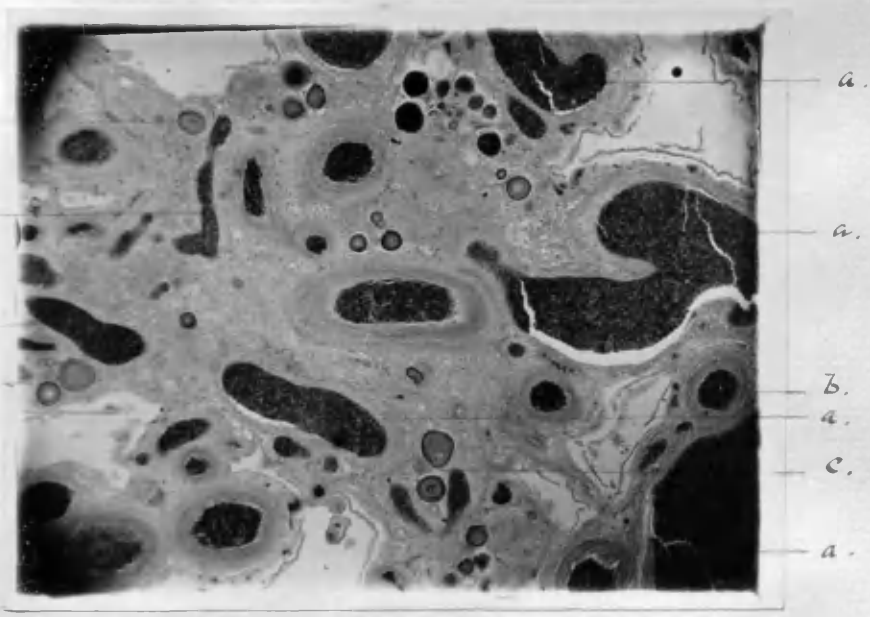


Photo. 9. Section 6. To show more usual arrangement of veins. From a case of alcoholic insanity. (×26.)

a. Veins.

b. Hyaline arterioles.

c. Concentric bodies.

Veins.

The veins are very numerous, and so frequent are their windings and bendings that there almost seems to be in the glomus an arrangement of blood sinuses, approaching the character of cavernous tissue. In sections the blood spaces appear large and very irregular in shape, and I was at first inclined to attribute these to the presence of a cavernous arrangement here, I am now convinced that numerous and very tortuous veins are all we have. (Photos. 8 and 9, sections 5 and 6).

The veins are lined by an endothelium and have remarkably thin walls, which are devoid of muscular tissue. The fibrous tissue of the walls very quickly merges into the surrounding spongy tissue, and spaces lined with an endothelium are seen quite close to the intima. Indeed, the wall of a vein might be said to be composed of only a more compact pia-arachnoid tissue.

The venules have very thin connective tissue walls and an endothelial lining.

Villi.

The surface of the choroid plexus is beset with a large number of highly vascular villous projections. These are of all sizes, and the largest may branch and subdivide many times before the ultimate villi are formed. (Photo. 10

Photo. 10. Section 7. Villi of the choroid plexus. From a case of general paralysis. (× 26.)

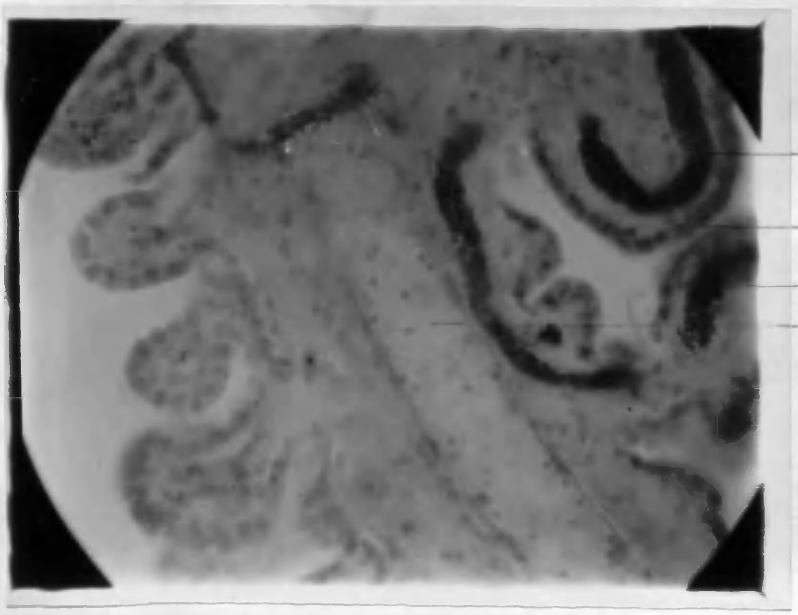


Photo. 11. Section 8. Small villi coming off laterally from a larger villus. From a case of general paralysis. (× 240.)

a. Capillary loop in a villus.
b. Venule
c. Here and elsewhere an appearance as of a single layer of epithelial cells.

(section 7). Where the plexus does not present such a shaggy appearance to the naked eye, small non-branching villi may be seen closely arranged alongside of one another.

Each layer villus has an afferent artery and efferent vein. (section 7). These open into a capillary network lying near the surface, and in the ultimate villi a capillary loop, in the form of a bow may be seen close under the epithelium, which everywhere covers the plexus. (Photo. 11, and section 8). The same capillary may pass through more than one villus. The greater part of the villus structure consists of epithelium and capillary, the smaller remainder being made up of homogeneous connective tissue with a few oval, spindle or ramifying corpuscles. (Photos. 11 + 12). Occasionally however this tissue appears fibrillated, but only in the very largest villi can spaces and trabeculae be made out, a loose areolar tissue being more commonly observed.

Epithelium of the Choroid Plexus.

The free surface of the villi and of the depressions between them is everywhere covered by an epithelium.

Haeckel[1] regards the epithelium as composed of a single layer of cells, but in pathological

[1] Haeckel:— "Schmidt's Jahrbucher" 1860. pp 16+17.

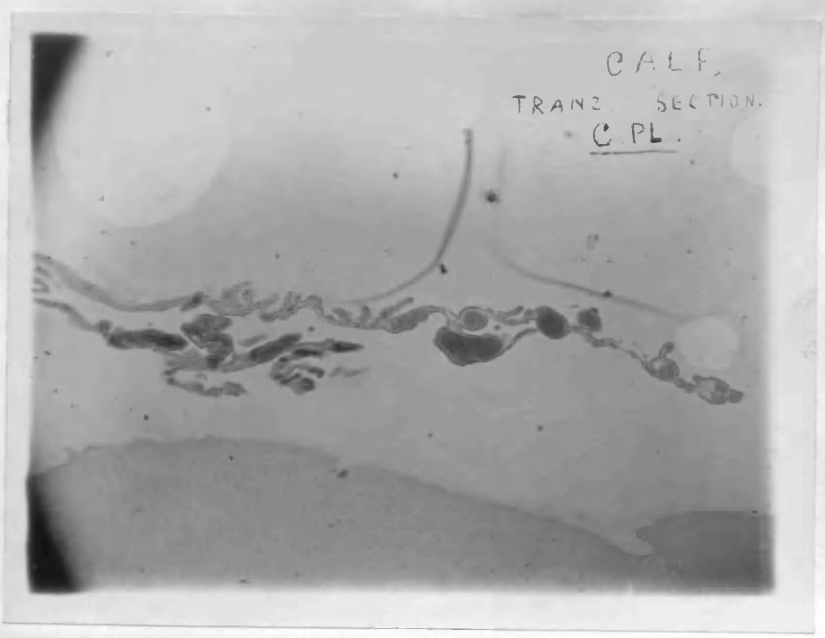


Photo. 12. Transverse section of the choroid plexus of the calf. (x 2.6.)
To show the small amount of connective tissue between the epithelium and blood vessels, even when the latter are of large size.

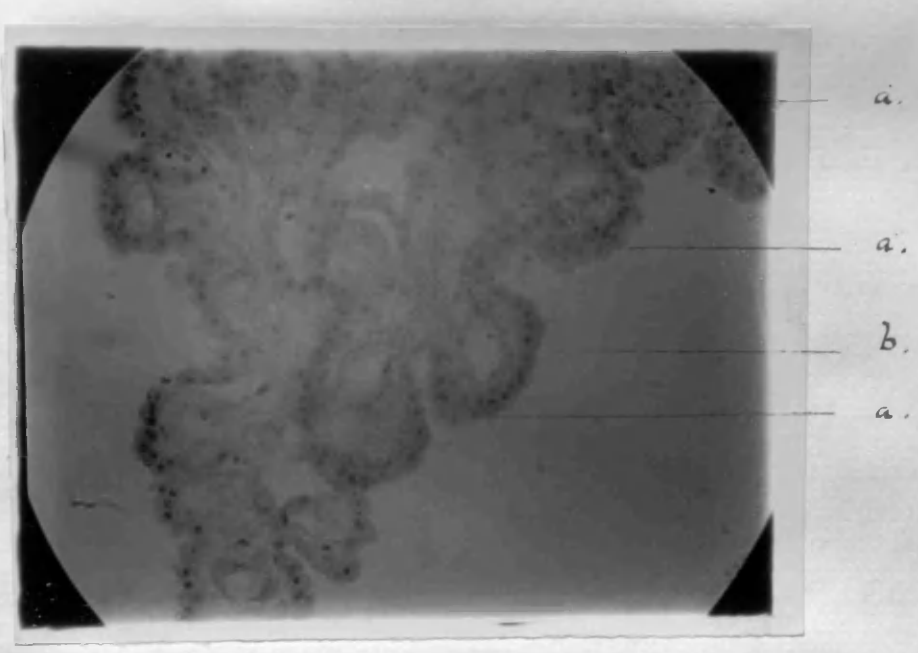


Photo 13. Section of villi. From a case of senile insanity.
(x 240.)
a. Several layers of epithelial cells.
b. Single layer of epithelium.

conditions he has seen these cells greatly increased in number. Heldt[2] likewise describes only a single layer of pavemented epithelium, and denies the existence of several layers. With Haeckel and Heldt may be classed Schäfer,[3] Wejerine,[4] Koelliker[5] and others.

Luschka[6] on the contrary, however, has described this epithelium as approaching the stratified formation, recognising not only two or three layers of cells situated above one another, but also different developmental forms.

In many places it can be demonstrated that only a single layer is present, but then just as often three, four, or more layers may be seen, the two conditions lying alongside of one another. Haeckel, we saw, regards the latter state as due to pathological proliferation of the epithelium. Such, however, I cannot believe. The existence of several layers of cells seems too common to be accounted for in this way, being found in all my cases in parts without exception, and likewise in the choroid plexuses of sheep, calves, and oxen examined. (Photos. 11, 13, 14 and 15, dissections).

Beyond a doubt several layers of cells normally exist, and may be traced through their

② Heldt:- "Ueber die Kalkconcretionen", 1874, p. 6.
③ Schäfer:- "Quains Anat.", Vol III, Part 1, p. 186.
④ Wejerine:- "Anatomie Etc" Tome 1er. p. 362.
⑤ Koelliker:- "Handbuch der Gewebelehre des Menschen", 1896. Zweiter Band, p. 833.
⑥ Luschka:- "Die Adergeflechte etc.", p. 127.

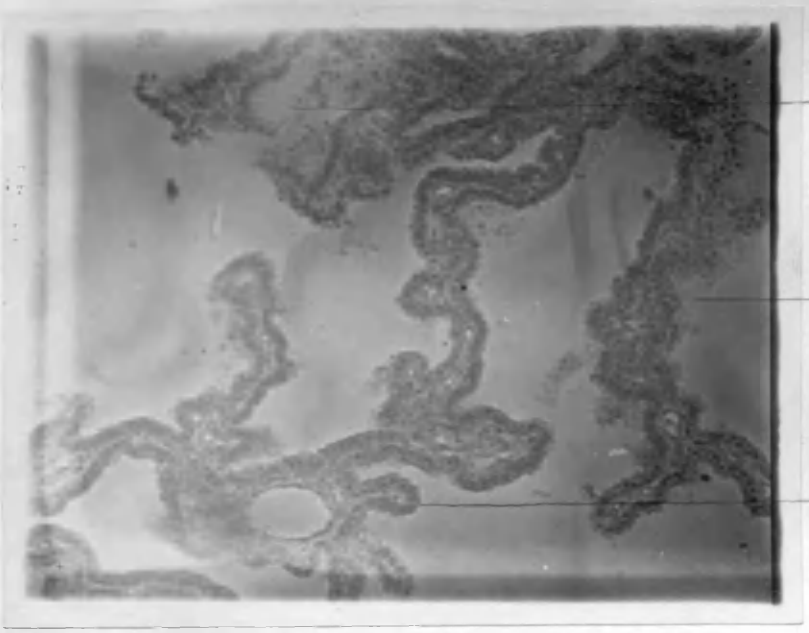


Photo. 14. Section 10. Villi from choroid plexus of the calf. (× 120.)

a. Appearance as of a single layer of epithelial cells.

b. Several layers of epithelial cells, the outermost showing loss of nuclear staining and vacuolation.

c. Many vacuolated cells.

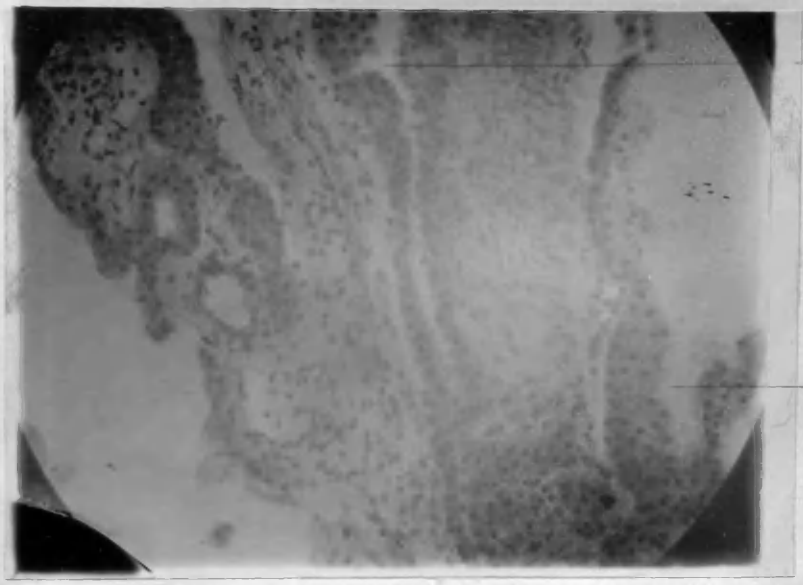


Photo 15. Section 2. Villi from the ox. (× 240.)

Everywhere on surface of villus several layers of epithelial cells are seen; most marked at a.

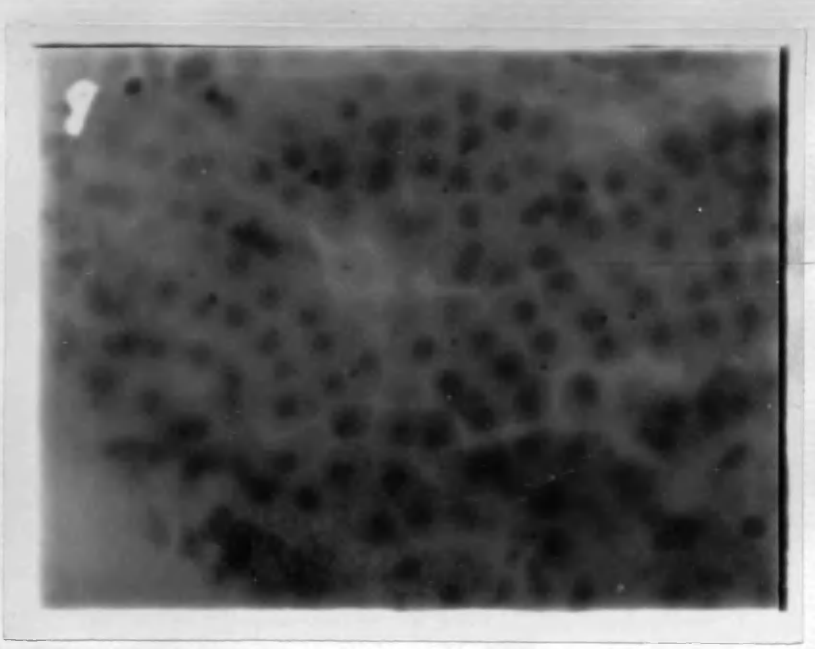


Photo. 16. Section 11A. Surface view of epithelium. (× 500). From a case of insanity, dying of general tuberculosis. Small black dots in cells represent the pigment granules.
a. Cell in process of division.

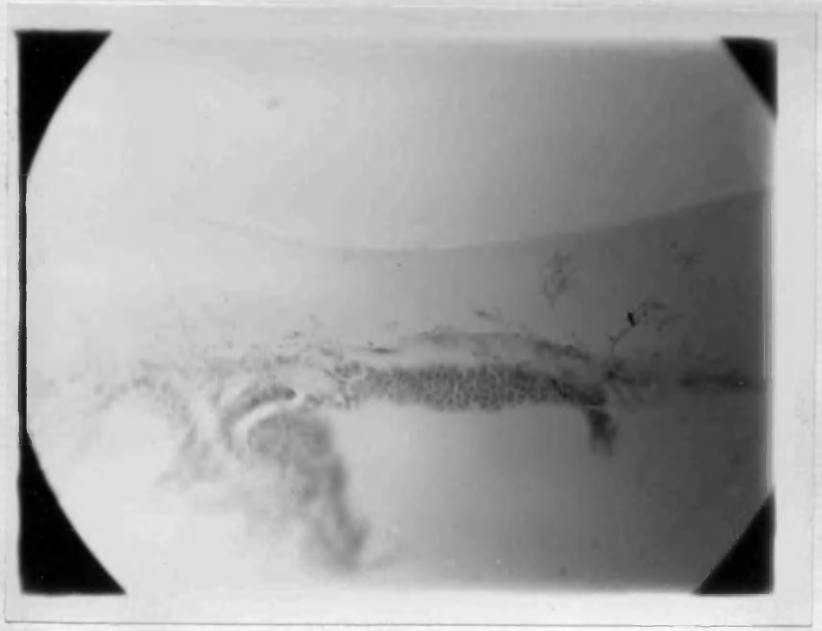


Photo. 17. Surface view of a small portion of epithelium. (× 240). From a calf.

different stages of transition as we pass to the surface However in a few human plexuses I have seen the deeper and more active cells in actual process of division, still further demonstrating, as Luschka held, that there are not only two or three layers of cells situated above one another, but also different developmental forms. (Photo. 16, Section 11A).

Where only one layer of cells exists I must suppose that the others have been brushed off, though I have to admit that narrow spaces covered by, and apparently unable to contain more than, a single layer of epithelial cells are found. It is possible, however, that the contraction of the tissues, in process of hardening, has altered the character, which such a space possessed during life.

These epithelial cells form a transitional rather than a stratified variety of epithelium, for the outermost cells never show any tendency to become flattened.

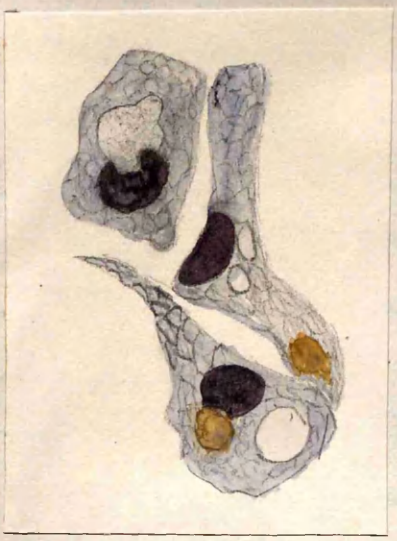
The individual cells vary in size, ranging from a little less than .01 to .015 mm. They are irregularly rounded or polygonal in shape, and when an epithelial surface is seen on the flat, they present an appearance like a piece of mosaic work. (Photos. 16 and 17, Section 11 A). They fit closely by means of delicate processes which interlock between neighbouring cells. Henle, however, has described these processes – which he terms "prickly" –

as locking into suitable cavities in adjacent cells like a wedge. In the deepest layer small and slender processes may be seen coming off from the base of a cell at the angles and penetrating into the subepithelial layer. This last fact was first pointed out by Henle, and is of considerable importance as tending to support the view that the epithelium of the choroid plexus is homologous with the ependymal epithelium, which has such processes even in adult life.

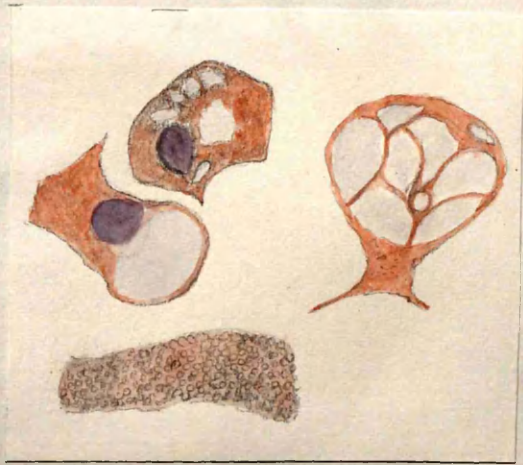
There are no cilia on either the cells lining the plexuses or the ependyma of the ventricles, but such are generally believed to exist in embryonic life.

In the calf, the cells in places tend to be more cylindrical or columnar in form. Each cell contains a large spherical nucleus which lies nearer the base than the summit of the cell.

The protoplasm of the epithelial cell is very granular and contains a large round nucleus, likewise granular, in which a nucleolus can occasionally be distinguished. In addition there is usually present a clear, yellowish, or even brownish coloured, highly refractive globule, sometimes approaching the dimension of the nucleus itself, but as a rule only attaining to a third or less of that size. By means of an oil immersion lens, however, it may be seen that the granular appearance of the protoplasm is in reality due to an



Drawing 1. Normal Epithelial cells, with clear and pigmented globules. (× 1000.)



Drawing 2. Epithelial cells shewing normal process of vacuolation. (× 1000.)

Drawing 3.

Epithelial cells, the nuclei of which are vacuolated, likewise the protoplasm. (× 1000.)

immense number of small globules, which appear of the same nature as the large one. (Drawing 1).

Where there are several layers of cells in situ it may be made out that this vacuolation increases steadily as we pass to the free surface, until cells are reached, entirely transformed into globules and showing no nuclear staining. (Drawings 2 and 3). Beyond this again the cells discharge their contents by breaking up, sometimes leaving an empty cell membrane to indicate where they have been. (Photos. 18 and 19 Section 11). Before the cell actually breaks up the globules may run together to form a single large sphere.

In celloidin preparations where the ventricular fluid has got entangled in the recesses of the plexus, numerous droplets, clear and pigmented, and in every way similar to those met with in the epithelial cells, may be seen lying free on the surface; while here and there these same droplets appear to be running together to form larger drops.

The single globule so often seen in the protoplasm with ordinary powers, almost invariably becomes darkened on being treated with osmic acid, while the granules also are blackened.

This reaction has led Obersteiner[1] and others to regard them as being of a fatty

[1] O. Obersteiner:- "The Anatomy of the Central Nervous Organs", Translated by Hill 1890. p. 388.

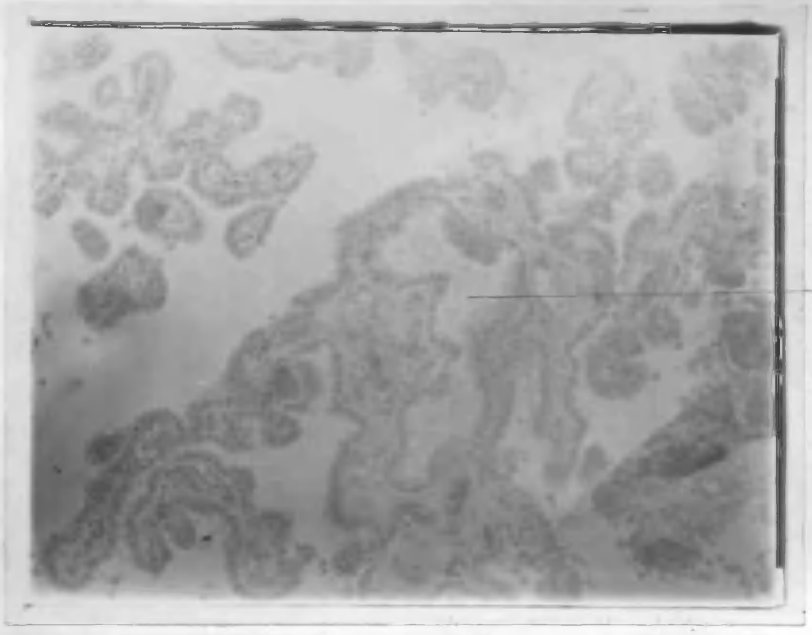


Photo. 18. Section 11. villi. (×120.)
From a case of senile insanity.
a. Appearance of a retention cyst, packed with vacuolated cells. In many cases only cell wall left to show where cells had been. (The same may be seen in the calf.)

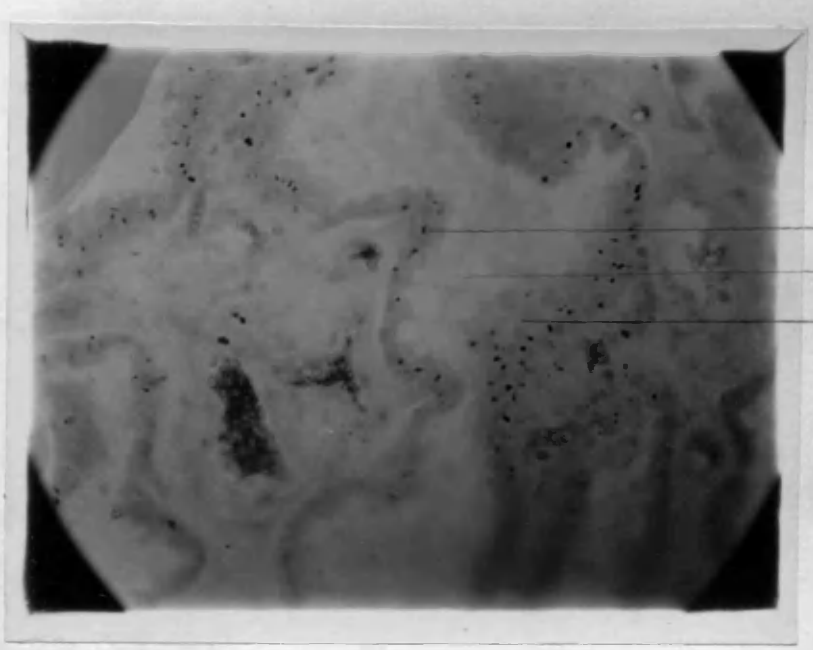


Photo 19. Section 11. Same cyst. like part as in 18. (×240.)
a. Single layer of epithelium at this place.
b. Several layers, no nuclear staining in the outermost.
c. Vacuolated cells and empty cells only represented by a membrane.
Dark dots in epithelial cells due to normal pigment granules.

nature, and its seems to me some relation to a fatty substance may be inferred.

Haeckel① accounts for the presence of the pigment in the epithelial cells by accepting the same view and then supposing a "transformation from fat into pigment, as has been already demonstrated in the case of certain other pigment granules". But there is, to my mind, no reason why we should not accept the pigment colouring the globules — or even the pigmented granules occasionally found — as normal to the epithelial cells, especially in conjunction with the frequency of normal pigmentation in the elemental tissues of the brain and its coverings.

Nerves of the Choroid Plexus.

Purkinje② has described a reticform arrangement of fine nerve fibres in the pia mater. Koelliker③ has found that these nerves always follow the course of the arteries, and though he has never recognised them in their endings, he has traced them into the substance of the brain along with small arterioles. He states, however, that no nerves are to be found

① Haeckel:- "Schmidt's Jahrbücher", 1860, p. 16.
② Purkinje:- "Quains Anat.", Vol III. Pt. 1. p. 187.
③ Koelliker:- "Gewebelehre", 1896, 2ter Band. p. 835.

in the vessel plexuses of the brain, though he mentions that Bochdalek① has seen fine nerve twigs in the choroid plexus of the fourth ventricle, these twigs proceeding from the roots of many cranial nerves.

In 1873 Benedikt② likewise described nerves in the plexus of the fourth ventricle. "From the medulla oblongata and also from the large multipolar cells in the restiform body, a small strap-shaped nerve bundle goes out into the choroid plexus of the fourth ventricle. This bundle consists of doubly contoured fibres, which pass out into the vessels of the plexus for vaso-motor purposes. In gold preparations these nerves may be seen in the neighbourhood of the larger vessels, and in the region of the smaller ones they appear as a terminal network of nerve fibres. Fibres also went out to the epithelial cells, but I can say nothing about the endings of the nerves". In 1874 Benedikt③ has traced these fibres to the vagus nucleus.

Since a nerve plexus has been demonstrated in the pia mater and in the choroid plexus of the fourth ventricle, one would expect by analogy to find a similar condition in the choroid plexuses of the lateral ventricles, but such has not to my knowledge been described.

It may be seen, however, that medullated

① Bochdalek:- Kolliker's "Gewebelehre" p. 836.
② Benedikt:- "Canstatts Jahresbericht" 1873. Band I. p. 44.
③ Benedikt:- "Schmidt's Jahrbücher" 1874, p. 124.

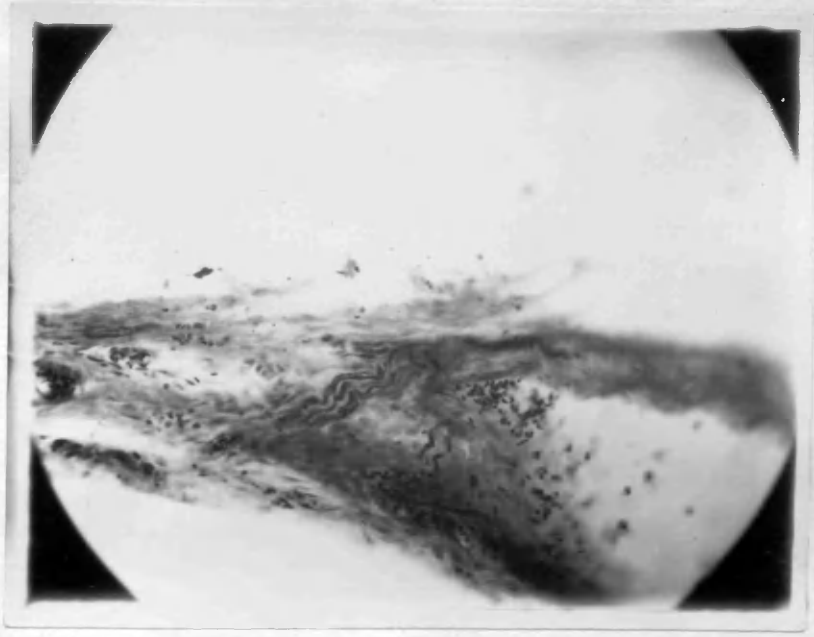


Photo. 19 A. Section 12. Medullated nerve fibres. (× 240). From the choroid plexus of the calf. Prepared by Heller's method. In centre are several nerve fibres with the medullated sheaths stained black.

nerve fibres exist in the plexuses of the lateral ventricles, though they are present in very small numbers. I have not been able to trace them for any distance, and can say nothing as to their relations and distribution, but that they seem to lie in the deeper parts of the plexus and sometimes in the neighbourhood of vessels. They are shown here in specimens from the calf, the fibres being brought into view by Robertson's modification of Heller's method. I have found similar nerves in the human choroid plexus, but never in such perfection as in the calf, probably owing to the freshness of the tissues of the latter. (Photo. 191. Sections 12). I have, nevertheless, been unable to demonstrate the axis cylinders of these nerve fibres, with either Robertson's methyl-violet method, or the Cox Imrie modification of Golgi's method.

It seems not at all improbable that, as in the plexus of the fourth ventricle, these are vaso-motor nerves destined for the blood vessels.

V. Functions of the Choroid Plexus.

Before the anatomy of this structure was known, many and ~~fantastic~~ were the functions attributed to it. In later times, however, there have been two or three theories put forward as to the use of the plexus which deserve mention.

In 1848 Dr. Osborne① made a communication, the object of which was to show that "the choroid plexus is the organ of sleep, that it is an erectile tissue, and in the performance of this function enlarges its dimensions, so as not only to compress the origins of the cerebral nerves and spinal marrow, but to prevent the blood from circulating through the upper regions of the brain."

One can understand a distended choroid plexus acting in a limited space, as in the fourth ventricle, where Dr. Inoscon② considers the lateral strands of the choroid plexus to act precisely like a ball tap, and control the supply of blood to the brain, by pressure on the pneumogastric nucleus. But it seems hard to believe that the choroid plexus of the lateral ventricle, can normally enlarge its dimensions to such an extent, as not only to fill that cavity, but also to so compress

① O. Osborne:- "Lancet", 1848 vol I. p. 351.
② Inoscon:- "Lancet", 1881. vol I. pp. 489 and 545.

the cortex against the bony vault as to prevent the blood from circulating through the upper regions of the brain." The nourishment and activity of the brain depend not so much on the amount of blood in the veins and arteries as on a steady flow through the capillaries, and true anaemia can only be brought about by actual compression of them. An enormous intracranial pressure, and therefore a very great distension of the choroid plexuses, would have to result to bring about such a condition. Moreover, in my opinion, the choroid plexus is not an erectile tissue, though containing a large number of very tortuous arteries and veins.

There seems more likelihood in the view of Müller[1] that the choroid plexuses serve a derivative purpose; a provision against the undue effects of arterial pressure and fulness in the surrounding parts; a ready channel for the transmission of arterial excess into a system of veins, which immediately run into the Vena Galeni and thence into the great sinuses of the occiput." For the above theory Müller finds support in the following facts. "The plexus has numerous vessels which pass to or from it on to the cerebral substance; it is connected on one side with the

[1] D. Müller:— "Die Mechanik der Blut-circulation im Inneren des Schädels," "Zeitschrift für Psychiatrie," 1860.

pia mater, and on the other sends processes to join with the velum interpositum and the choroid prolongations, extending from that structure into the third and fourth ventricles, and into the great vein of Galen. It is further more highly developed in man than in other animals."

There is no doubt to my mind that the choroid plexus is an actively secreting structure, discharging its secretion into the ventricular cavity. This secretion is formed by a constant proliferation of the epithelial cells, which were seen on a few occasions in actual process of division. These elaborate in their interior clear, homogeneous, mucin-like globules. Then the cell wall gives way and these globules are discharged into the ventricular fluid.

Luschka[1] was the first to trace the different steps of this process, and I have been able to confirm his observations.

Such a discharge is continually going on, the life of the individual cells being very short, and a constant change taking place in them. Drops or globules, similar to those met with in the epithelial cells themselves, may be demonstrated in the ventricular fluid. Probably, however, they do not remain as such for any length of time, but break down or become discolored. "We have little or no exact experimental evidence, as to how much fluid is actually secreted by the choroid plexuses"[2]

1. H. Luschka: "Die Adergeflechte etc", p. 127.
2. Foster:- "A Text Book of Physiology", 1897. Part III, p. 1232.

and Luschka[1] attributes this function not only to the epithelial cells of the choroid plexus, but also to those of the ependyma.

Meynert[2] also points out that "in addition to the escape of fluid through the foramen of Magendie, during the first stage of the vascular systole, a certain amount flows into the veins of the choroid plexus"

It is quite possible that such a filtration may occur when the intracranial pressure is increased, and it is important in this connection to note that the vein running along the free border of the plexus is exceedingly tortuous, literally hangs into the ventricular cavity, and is covered by little more than epithelium.

So far I have been unable to detect any difference between the epithelium over this vein and that over the villi, but perhaps such exists.

On the other hand, it seems more than likely that a constant diffusion — independent of the choroid plexus secretion — is going on from the fluid in the villi (blood and lymph) into that in the ventricular cavity (cerebro-spinal fluid), and vice versa. How far this

1. Luschka :- "Die Adergeflechte", p. 165.
2. Meynert :- Hyslop "Mental Physiology," 1895, p. 78.

process is a physical or a vital one, and to what extent it occurs, is hard to say.

It may be that in the choroid plexus we have two kinds of epithelium serving two functions, ejective in the villi and receptive over the exposed veins.

In the intestine such a condition exists. "Over the villi the receptive function, in the glands of Lieberkühn the ejective function is predominant." ①

There is still the other question of inverted secretion to be considered. That such exists in the intestine," is the conclusion towards which observation and experiment seem to be steadily leading us, and all along the intestine the columnar and cubical cells, may perhaps be regarded as engaged in a double function". ②

The mucous membrane of the intestine with its complex processes of secretion and absorption, however, is in no way comparable with the choroid plexus.

More closely related, though still widely separated from the choroid plexus, is a salivary gland. "were the alveolus of a salivary gland habitually filled with a fluid of mixed and varied nature like the contents of the alimentary canal, we should probably in our study of the gland find ourselves compelled to speak of a double current, as existing in the gland, of a current

① and ②. Foster:- "Text Book Physiology", Part II. p. 523.

from the cells to the lumen of the alveolus, and of a current from the lumen to the cells." ①.

In the choroid plexus, however, the secretion is altogether different from that of a salivary gland. The cells — so far as we know — have no sharply divided periods of rest and activity. They are steadily elaborating in their interior peculiar mucin-like globules, and only seem capable of doing so once. The outermost layers of epithelium are practically dead structures: they have fulfilled their purpose, and may be said to have died in doing it. They, therefore, can take no part in inverted secretion. But the cells lying deeper are in an active healthy condition, and while slowly preparing their own special product may quite well be able to extract certain substances from the cerebro-spinal fluid — not a pure choroid plexus secretion, but mixed with lymph and waste products from the brain — and pass them on to the underlying capillaries.

Is it not better to take the analogy of the Kidney where secretion goes on without destruction of epithelium, and where also, according to Newman, Ludwig & others, there is a double current at least in the convoluted tubules?

If such inverted secretion occurs at all, it must be very slight, or else we must attribute to these epithelial cells great powers of selection and discrimination.

Epithelial cells have such powers e.g. renal epithel.

It has been pointed out by Bevan Lewis ②

① Foster: — "Text Book Physiology" Part II. p. 523.

② Lewis, Bevan: — "A Text Book of Mental Diseases", 1889, p. 437.

that in some cases of insanity the cerebro-spinal fluid loses its normal alkaline reaction and becomes acid.

If the epithelial cells bathed in this acrid fluid were absorbing to any extent the morbid waste products contained in it, we would expect to find frequent pathological lesions in the villi — cells and sub-epithelial structures — which expose such an immense surface. But this is not borne out by pathological observations. Indeed, the villi seem to enjoy a comparative immunity, and the majority of the morbid changes are found in the deeps and more central parts of the glomus, on which the action of the epithelial cells can have practically no effect.

VI. Pathology of the Choroid Plexus.

The choroid plexus is liable to be affected by many pathological changes. Each individual tissue may be attacked, or the lesion may be more or less common to the entire plexus.

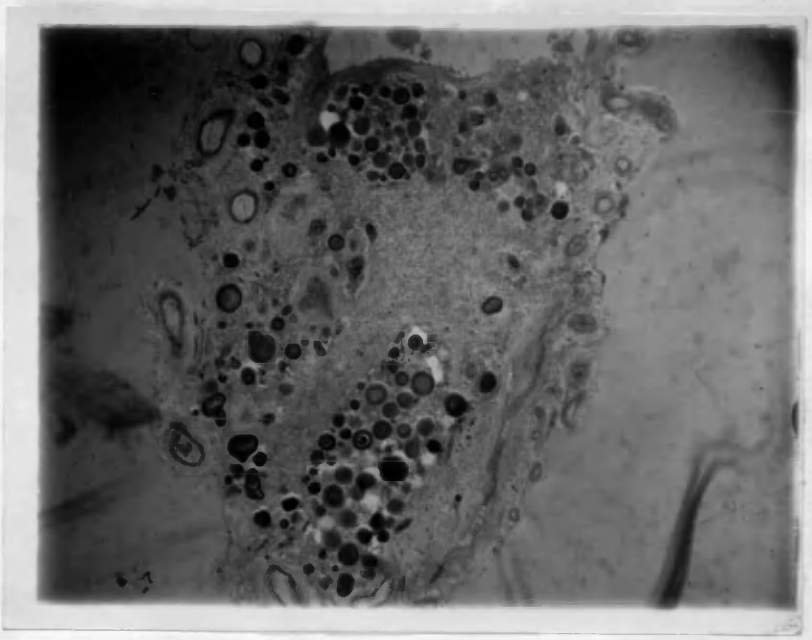
"The tumours are chiefly of the mesoblastic or connective-tissue type, but epithelial or carcinomatous growths are also met with." Among the former Ziegler describes the following, "sarcoma, alveolar sarcoma, endothelioma, myxosarcoma, myxoma, angio-sarcoma, angiomyxoma, angiomyxosarcoma, angioma and psammoma, while more rarely fibroma, lipoma, chondroma, and cystic fibroma are present." ①

Secondary growths of every kind are found, and of animal parasites may be mentioned the Echinococcus and Cysticercus. ②

Cholesteomata are rarely seen in the human subject, but seem to be somewhat common in the horse where they may attain an enormous size.

I have not had an opportunity of examining any of the above mentioned conditions, and will now proceed to describe those changes which I have met with in the course of my investigation.

① & ② Ziegler:- "Text Book of Pathological Anatomy", translated by MacAlister 1886. Section II, pp 317-321.



Section 16. Portion of glomus. (× 26).
From a case of puerperal insanity.
Concentric hyaline bodies of round
and irregular form.

A. Concentric Bodies.

These structures are very common in the choroid plexus. I have found them in every case I have examined. They are often present in enormous numbers, and Heldt[1] has regarded them as being in great part normal and physiological. They have been described under different names, brain sand, acervulus cerebri, concentric concretions, hyaline concentric bodies, etc., and much difference of opinion has existed as to their mode of origin and composition.

In none of the choroid plexuses from the sheep or ox was I fortunate to meet with any of these bodies, though in the calf, I on one occasion found, what I took to be early developmental forms. (Section 14). Luschka[2] has found them in rabbits, dogs, and horses.

Similar concentric bodies are found in all the membranes of the brain and spinal cord, and constitute the chief element in those tumours called psammomata.

Before describing these bodies and their development I will shortly tabulate the views held by others as to their origin and composition.

Luschka[3] considers that they consist of one of the colloid substances, in which a

① Heldt:- "Ueber die Kalkconcretionen etc." p. 14.
② and ③ Luschka:- "Die Adergeflechte etc." p 155, and pp 156 & 157.

gradual deposition of carbonate and phosphate of lime has occurred to form concretions. This sometimes occurs in the connective tissue bundles of the inner coat of the vessels, through which these have acquire an incrusted chalk-like look. He denies most positively any connection of these bodies with cells.

Haeckel[1] states that they are composed of an organic groundwork, which has become impregnated with carbonate and phosphate of lime." These bodies present a variety of nucleus. They may have connective tissue cells, or nuclei of fat or pigment granules, hyaline spheres or shrunken blood corpuscles. It appears, though the almost never failing connective tissue envelope, that the nucleus has been encapsuled first of all like a foreign body, and then secondarily to have become incrusted with lime."

Virchow[2] thinks that a greater part of the chalk formations is devoid of any organic ground layer. Further he asserts that they may be in origin calcified, and their later growth purely mechanical in character, so that one layer becomes impregnated with lime salts around the other layers.

Cornil and Ranvier.[3] "In the physiological

① Haeckel:- "Schmidt's Jahrbücher", 1860, p. 17.
② Virchow:- "Die krankhaften Geschwülste", Tome II p. 111.
③ Cornil and Ranvier:- "Manual of Pathological Histology" Translated by A. M. Hart 1882 vol I. p. 145.

state the blood vessels of the choroid plexus have on their walls buddings or ampullary dilatations, lined by the pavement epithelium of the Ependyma: they are formed of flat connective tissue cells incrusted in the adult so as to form true phleboliths. When the calcified buds have not lost their connections with the vessels from which they emanate, their pedicle and a part of the vessel are often incrusted by calcareous salts, and become homogeneous and vitreous. But if the pedicle has been broken artificially, it may pass unnoticed, and the small rounded mass of the bud resembles then an epidermic globe."

Heldt. D "First of all there is a hyperplasia of the adventitia, consisting of connective tissue and stratified molecular mass. This hyperplasia forms excrescences on the vessel wall. These become gradually larger, take on a spherical form, and then show a tendency to shrink. When the separation of this excrescence has almost resulted, the cells change their appearance, becoming bent and flattened, corresponding to the rounding off of the new formation, and surround themselves then with a thin coat like a mantle, which encapsules and separates them from one another. After this encysting, appears the calcification, which extends from the centre to the periphery."

D. Heldt:- "Ueber die Kalkconcretionen etc.", p. 11.

Koelliker:- ① "Brain sand consists essentially of carbonate of lime, but also of phosphate of lime and magnesium and an organic substance. This brain sand, if it appears in long ramifying or net like masses, develops simply in the connective tissue bundles, or results from calcification of fibrinous coagula."

Robertson ② has found similar bodies on the surface of the pia-arachnoid and dura mater. He has traced the development of these bodies from a degeneration of the endothelial cells. "A single homogeneous globule is developed from an endothelial cell. This may become a concentric body, but more commonly, owing to the circumstance, that several endothelial cells are usually simultaneously affected, the hyaline globules developed from several adjacent endothelial cells coalesce into one large mass. This being apparently of a semi-fluid consistence assumes a spherical form. Concentric rings appear subsequently, evidently owing to shrinkage."

Ziegler ③:- "The organic basis of brain sand consists of flattened cells, which cohere like the coats of an onion, become homogeneous and lose their nuclei, and then are calcified."

① Koelliker:- "Gewebelehre", 1896. Band II. p. 839.

② Robertson, W. F.:- "Researches upon the Pathology of Subdural Membrane Formation" "Journal of Path. & Bacteriology", July 1896. p. 140

③ Ziegler:- "Text Book Path.", 1896 Part II. p. 319.

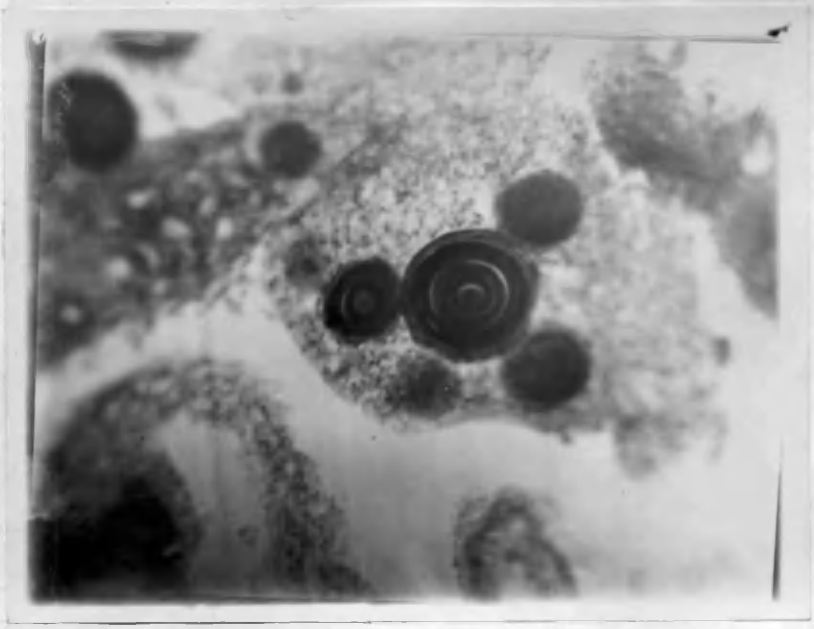


Photo. 20. Section 15. (×120). From a case of phthisical insanity.
Hyaline concentric bodies.

Photo 21. Section 16. (×120). From a case of puerperal insanity.
Hyaline concentric bodies of irregular form.

The usual form of these concentric bodies — as their name would imply — is round, and as a rule they are surrounded by a well marked hyaline capsule, or even a capsule of fibrous tissue with long thin spindle shaped cells. They are marked with numerous concentric rings, these markings varying in intensity and number in individual bodies. (Photo. 20, Section 15 and others). Though the most common this is not the invariable shape, and many different forms may be produced from several spheres coming together. Thus we may have a trefoil-shaped structure, the interior showing distinct concentric bodies with rings of their own, while beyond these the body is surrounded by a common stratification. (Photo. 21, Section 16). Rod shaped bodies are occasionally seen, but they are decidedly rare. (Photo. 22 Section 17).

Irregularly ramifying forms as described by Luschka①, Haeckel② and Koelliker③, I have never seen.

Heldt④, as the result of his observations, states that all these bodies show a thoroughly round shape.

Heldt is, I think, in the main right. All these bodies — with the exception of the rare rod-like forms — show a thoroughly

① Luschka :- "Die Adergeflechte etc." p. 156.
② Haeckel :- "Schmidt's [illegible]" 1860 p. 17.
③ Koelliker :- "Gewebelehre", p. 939.
④ Heldt :- "Ueber die Kalkconcretionen etc." p. 13.

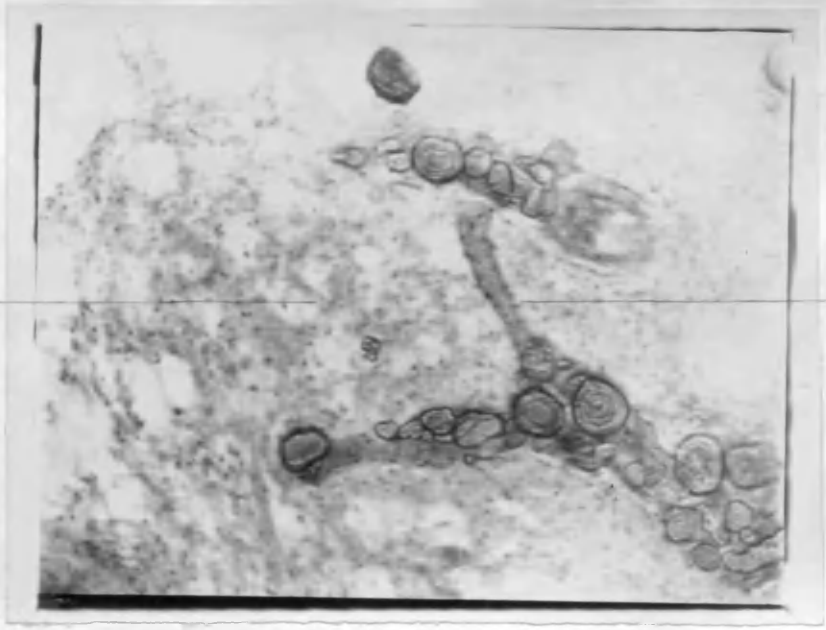


Photo 22. Section 17. (×120). From a case of phthisical insanity.

a. Rod-shaped hyaline body lined externally by a layer of endothelial cells. May represent an occluded hyaline arteriole.

b. Well marked trabecular arrangement, with proliferation of the endothelial cells.

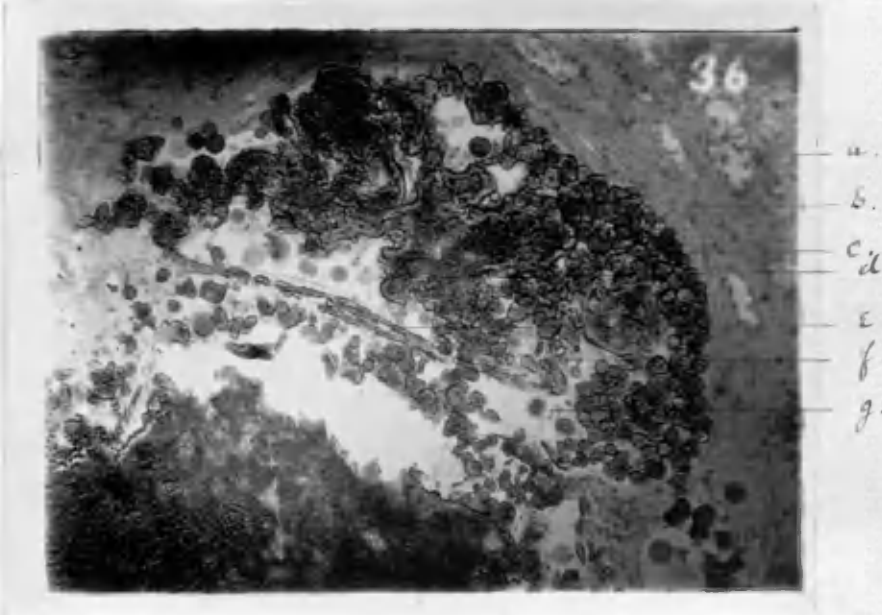


Photo 23. Section 20. Types of hyaline structures in glomus. (×120). From a case of alcoholic insanity.

a. Spaces of the fibro-arachnoid lined by endothelial cells. b. Great thickening of the trabeculae. c. Types of concentric bodies, and doubly contoured spheres. d. Hyaline spheres. e. Hyaline cells running together to form a rod. f. Mulberry body without capsule. g. Mulberry body with distinct capsule.

round shape, or a combination of several such shapes, resulting in a more or less irregular figure, but one, however, which can always be resolved into a collection of spheres. They likewise vary very much in size, and are found in the plexuses ranging from 0·01 to 0·15 mm. in diameter.

Apart from their concentric markings, these bodies are, as a rule, structureless, but now and then, the forms of globes or spheres can be made out in their interior, though in many cases nothing more than a few granules are seen. (Section 18).

Haeckel[1], however, found as the nucleus of such bodies, nucleated cells, fat and pigment-granules, heaps of shrivelled blood corpuscles, and rarely corpora amylacea.

It is often possible to make out cells swollen from hyaline degeneration in the centre of these concentric bodies, but their nuclei are never visible. (Section 18). I have, however never seen any appearances suggesting that blood corpuscles or corpora amylacea might form the nuclei, or beginnings in the development of the same (concentric bodies).

Colour and Chemical Reactions.

In eosin and haematoxylin preparations they usually take on a bright red colour, though sometimes the centre is coloured blue, while the

[1] Haeckel :- "Schmidt's Jahrbücher," 1860, p. 17.

periphery alone shows the eosine staining. In the same body, moreover, the different concentric rings may take up the eosine with different degrees of avidity. (See many sections).

Carmine stains these bodies deeply, though in picro-carmine preparations here and there yellow rings are observed inside the red body, while the very small bodies are alone stained by the picric acid. (Section 16).

Van Gieson's stain colours them a bright-red, due to the fuchsine present in it. In the same way the fuchsine in the Ehrlich-Biondi stain attacks the concentric bodies, making them stand out in a remarkable manner from the surrounding faint red or green coloured tissue. The hyaline droplets, which are found in abundance around the concentric bodies, and which represent a phase in the development of the latter, do not take on the red fuchsine staining, but stain a dirty green colour with the methyl green. (Section 15).

Weigert's fibrine stain occasionally colours these concentric bodies, along with the hyaline connective tissue trabeculae, a deep blue colour, while the surrounding tissue remains unstained.

Another curious staining anomaly is found in some sections which I prepared by Robertson's methyl violet-method. Here the concentric bodies are with very few exceptions

unstained, (in a few cases the capsule is well stained), while the rest of the tissues including the large hyaline droplets, which are present in enormous numbers in this case, have taken on a deep blue colour. (Section 15 A).

These bodies have never shown in any of my cases, a waxy reaction with methyl violet.

Osmic acid distinctly darkens these structures, sometimes bringing out a granularity not before evident, or accentuating the concentric markings. (Section 19).

W. F. Robertson[1], however, has stated that osmic acid has no action on these concentric bodies as found by him in the dura, and he adds that he has never seen any evidence of retrogressive or disintegrative changes in them. On the other hand, it was mentioned above that Haeckel has occasionally seen fatty and pigment granules forming their nuclei.

All the older writers including Obersteiner[2], Haeckel[3], Luschka[4] and Heldt[5] describe these bodies as concretions composed of carbonate of lime, and carbonate and phosphate of magnesium. Heldt, however, lays special emphasis on the fact that there are also hyaline concentric bodies,

① Robertson, W. F.:- "Journal of Path. & Bacteriology" July 1896 p. 140.

②. Obersteiner:- "The Anatomy of the Central Nervous Organs", 1890. p. 388

③. Haeckel:- "Schmidt's Jahrbücher" 1860, p. 17.

④. Luschka:- "Die Adergeflechte etc." p. 157.

⑤. Heldt:- "Ueber die Kalkconcretionen etc." pp 12 & 13.

which have not yet become calcified, present in the choroid plexus

Robertson is of opinion that these concentric bodies found in the dura — similar in every way to those met with in the choroid plexus — are composed simply of hyaline material and contain no lime salts. This he argues from the fact "that they are not readily affected by the action of aqueous solutions of mineral acids."

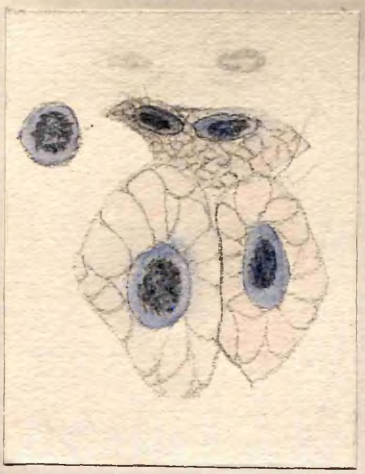
It is true, as Robertson states, that these bodies are not readily affected — I should say are unaffected — by aqueous solutions of mineral acids and acetic acid; but if strong hydrochloric acid be used, a brisk effervescence takes place in many cases. Other concentric bodies, however, give off no gas on being treated with hydrochloric acid.

Development of Concentric Bodies.

After examining my sections I am of opinion, that these bodies are not merely deposited from the tissue fluids, as Virchow and others think, but that here we have an active proliferative process first of all, followed by a degenerative one.

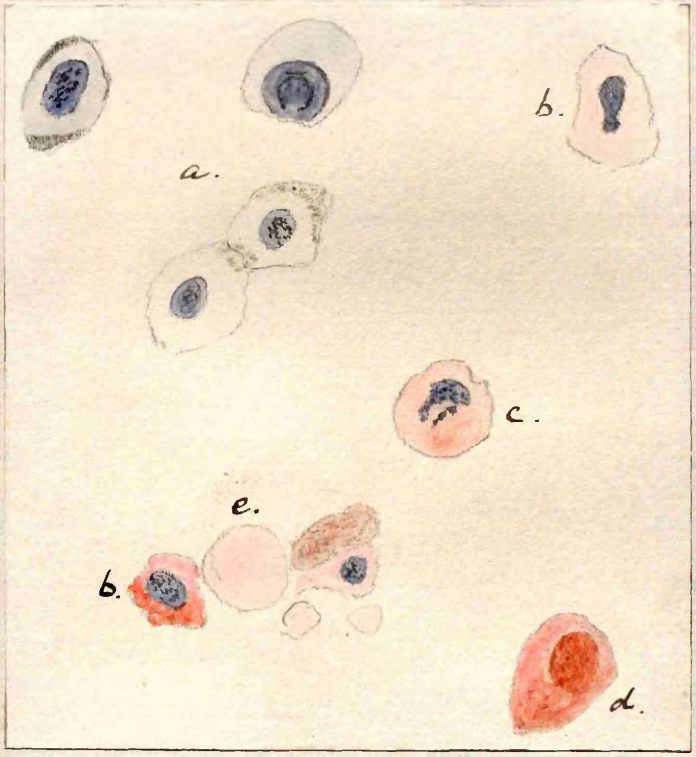
It has been already mentioned that the pia-arachnoid is a spongy lymph sac, made up of trabeculae lined with endothelial cells.

First of all, probably as the result



Drawing 4. Endothelial cells. (× 1000) The protoplasm of the cell breaking up into numerous hyaline globules.

Drawing 5. Developmental form of concentric body. (× 1000).
a. Cells represented by a single homogeneous globule.
b. Mass of nuclei
c. Granular protoplasm + hyaline globules from degenerated cells.



Drawing 6. Cells around concentric body. (× 1000)
a. Cells swelling up + becoming homogeneous.
b. Cells with increased affinity for eosine.
c. Nucleus in parts shows eosine colouration
d. Nucleus stained with eosine
e. Homogeneous hyaline sphere.

of some chronic irritative process, a proliferation of the endothelial cells occurs, and these cells may be seen undergoing division by the process of karyokinesis.

In eosine and haematoxylin preparations the following phases of degeneration may be traced, subsequent to the proliferation. The cell plate first of all swells up and becomes homogeneous, staining a very faint blue, while the nucleus has an increased affinity for haematoxylin. Next the protoplasm of the cell becomes possessed of an increased affinity for eosine, and usually has a somewhat granular appearance. Then the eosine staining becomes fainter and less granular, and, with an oil immersion lens, it can be made out that the protoplasm has formed inside the cell very numerous hyaline globules, which, at first separate, eventually run together. The nucleus now loses its affinity for haematoxylin, stains more faintly and in parts shows the eosine colouration. This progresses gradually, till finally the nucleus is altogether coloured with eosine, being darker than the hyaline cell plate. Afterwards this distinction is lost, and nothing is seen but a homogeneous hyaline sphere staining faintly with eosine, and measuring in diameter .01 to .05 mm. (Drawings 4, 5, & 6. Photo. 26 and Section 22). One of these spheres may form a concentric body, and numbers of such with only one concentric mark — doubly

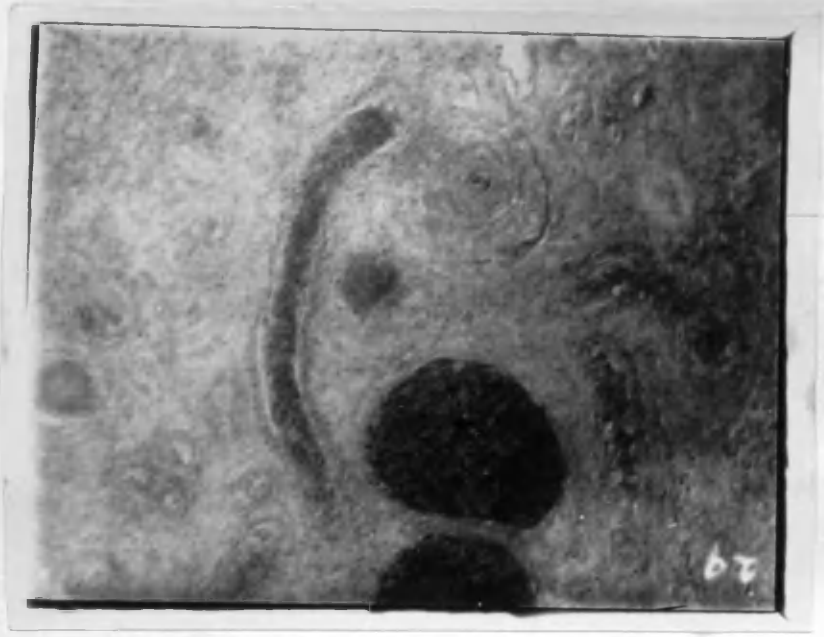


Photo. 24. (× 120). From a case of melancholia.

a. Whorl of cells all showing degenerative changes, the most central being distinctly hyaline.

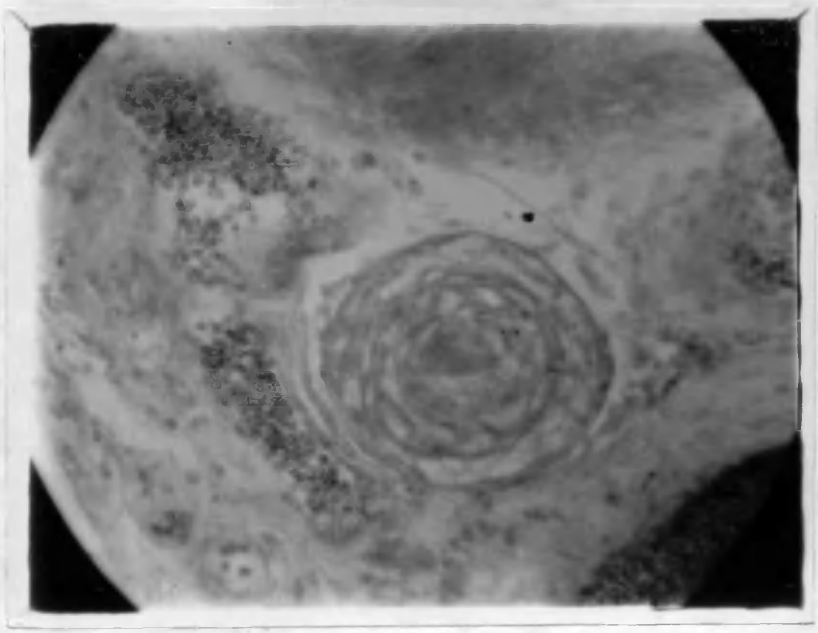


Photo. 25. Section 6. Regular cell nest from the gloma of a case of alcoholic insanity. All the cells show degenerative changes more or less. Most advanced phase seen in centre, getting less marked as we pass towards the periphery. (× 240).

contoured spheres — may be seen in Photo. 23. In this same photograph these bodies may be seen running together to form a rod. As a rule, however, these spheres, probably of a semi-fluid consistence, coalesce to form the more usual concentric body.

In many cases the cells take up this position before degenerating; and in an inter-trabecular space a regular whorl of cells is seen, in appearance like a "cell nest", or as Ziegler puts it, like the skins of an onion. (Photos. 24 & 25, Section 6). All stages of degeneration may be met with in these, from the swollen cell with the dark blue nucleus to the homogeneous hyaline sphere.

Nor does it seem necessary that these hyaline spheres should form concentric bodies in the identical spaces in which they are developed. It appears not at all unlikely that they may be carried along in the lymph stream circulating through these spaces till arrested by some obstruction. Indeed, the position and arrangement of many suggest this. Behind such an obstruction other hyaline spheres will be constantly added, and the never failing pressure applied from behind will be sufficient to weld them into a single large mass, while probably, as W. F. Robertson indicates, the concentric rings appear subsequently owing to shrinkage.

The fibrous capsule so frequently present, is added later, after the manner in which

nature encapsules all foreign bodies; and in all probability the fibrous tissue owes its origin to the still healthy endothelial cells. There is never any round cell infiltration around these bodies, the cellular aggregations in their neighbourhood being endothelial in character. Nor is there any need of such a round cell infiltration to explain the subsequent development of the connective or fibrous tissue capsule, as "the endothelial cells", according to Metchnikoff[1], "are actively engaged in the formation of new connective tissue."

This proliferation and degeneration of the endothelial cells may occur anywhere throughout the plexus, but is most marked in the glomus, where, too, the normal trabecular arrangement of the pia-arachnoid can be most perfectly made out.

In the same way cells may proliferate and degenerate, and concentric bodies may form in the spaces close to the vessel wall, but so far as I can see there is no special tendency to the occurrence of them here. When concentric bodies develop in spaces immediately outside a vessel, they may by pressure seriously obstruct it, or lead to the absorption of a hyaline adventitia, as shown in section 21. These

[1] O. Metchnikoff:- "Lectures on the Comparative Pathology of Inflammation", Translated by F.A. and E.H. Starling 1893. p. 190.

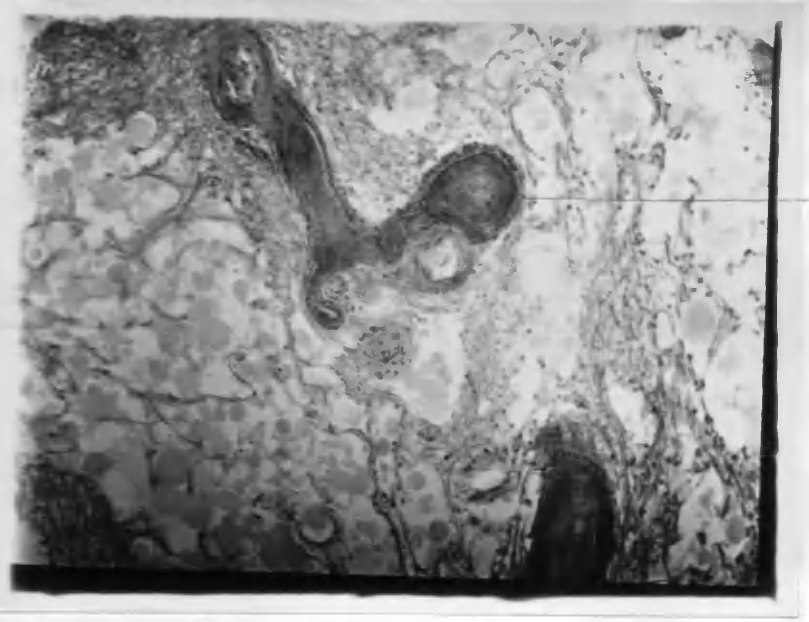


Photo. 26. Section 22. Portion of a cyst, (×120). From a case of senile insanity.
a. Hyaline arteriole obstructed by a clot. The thrombus has likewise become converted into hyaline material, and at one part concentric rings are appearing.
b. Large hyaline spheres and broken down connective tissue trabeculae.

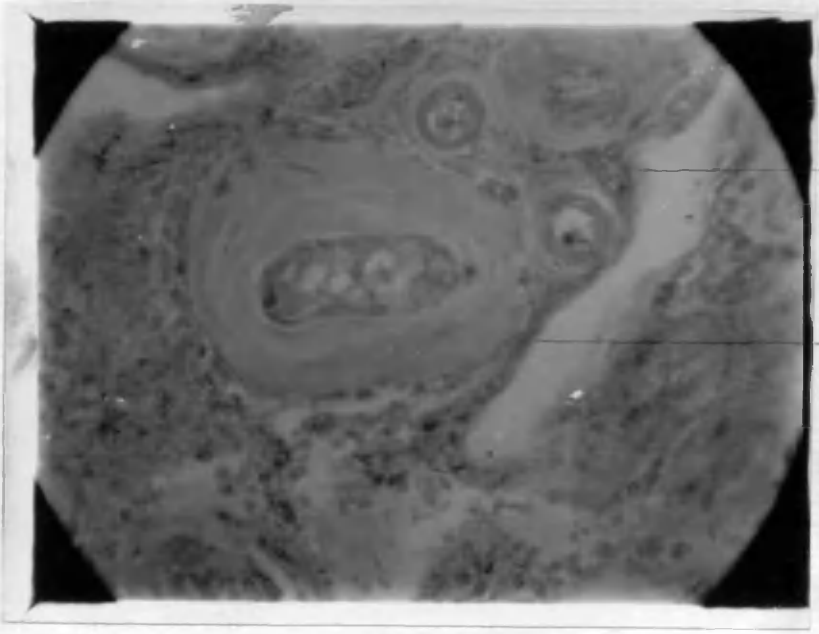


Photo. 27. Section 23. A phase in the formation of concentric bodies. (×240).
a. Thick hyaline ring with spindle cells between the different layers; degenerating cells in interior.
b. Three small vessels, all showing hyaline changes.

facts probably account for the description of buddings or ampullary dilatations of the walls of the blood vessels of the choroid plexus by Cornil and Ranvier, and also for the further idea that the incrustation of these buds by lime salts formed the concentric bodies.

Heldt[1] came nearer the truth, when denying the presence of buds on the vessels, he attributed the formation of these bodies to a hyperplasia of the adventitia, consisting of connective tissue cells and stratified molecular masses, and forming excrescences on the vessel wall.

At no time, however, do these bodies develop in the adventitia, but always in the lymph spaces beyond.

While the above is the most common mode of development of concentric bodies, I do not think that it is the invariable one.

When hyaline degeneration attacks the arteries and capillaries, these sometimes become converted into solid tubes. This condition, though in all likelihood happening often, is but rarely met with, suggesting the idea that some further change occurs in these solid hyaline vessels. (Photo. 26, Section 22). These hyaline cylinders most likely split across, while the segments contract into the form of rounded masses, and in this same photograph such a mass may be seen acquiring concentric markings.

[1] Heldt :- "Ueber die Kalkconcretionen &c," p. 11.

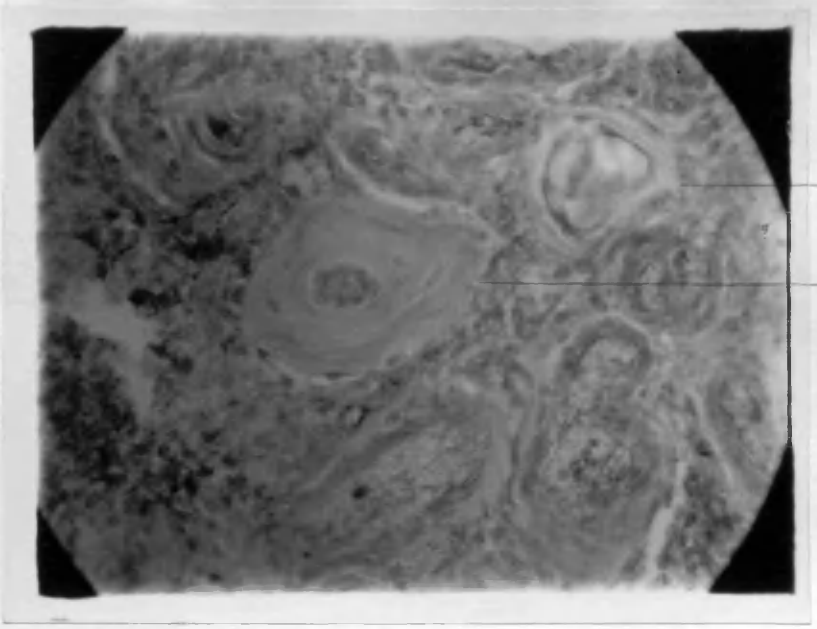


Photo. 28. Section 23. (× 240). From a case of general peritonitis.

a. Thick hyaline ring composed of several layers, between which are spindle cells; degenerating cells in interior.

b. Small hyaline vessels.

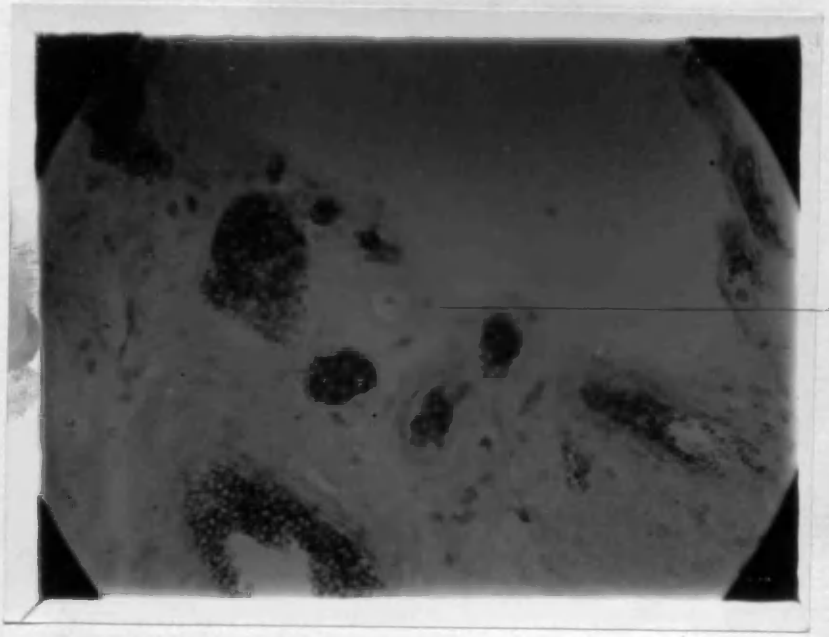


Photo. 29. Section 24. (× 240). From a case of senile insanity.

a. Hyaline ring with a single degenerating cell in interior.

Very frequently, too, in the midst of concentric bodies, hyaline rings are met with containing degenerating cells in their interiors. (Photos. 27 & 28, Section 23). It is impossible to reach the conclusion that these hyaline rings are developmental forms of concentric bodies. The hyaline circle is of varying size and thickness, and may show concentric markings with spindle shaped cells between the different layers. The interior of such a ring may be lined or packed with cells, all more or less showing signs of breaking up, with diminution or loss of nuclear staining.

It is difficult to trace the origin of such a condition, and the different appearances are most conflicting and confusing. In a few cases it has been possible to demonstrate that these are merely depressions from the surface Epithelium — what may be termed acini in transverse section — somewhat similar figures in longitudinal section allowing the continuity of the epithelium to be traced. But this explanation does not satisfy for all. Thus a small hyaline ring with a single degenerating cell in its interior, could not represent a prolongation from the surface, and most probably is a hyaline capillary in transverse section, with a contained endothelial cell. (Photo. 29, Section 24). Others which are larger most likely represent small hyaline arterioles or

venules, with degenerating endothelial cells in their interiors, and in a few cases this can be conclusively proved by the detection of blood corpuscles in the lumen of such a structure. (Photo. 67. Section 25).

Appearances in every way similar to concentric bodies often occur in the smaller villi, and result from hyaline degeneration of the subepithelial tissue, alone or in conjunction with the wall of the capillary (Photo. 30, Section 20). As this is discussed at some length under the connective tissue changes I will say no more here.

To recapitulate, then, I believe that concentric bodies develop in the following ways, and while very doubtful of the last, am perfectly convinced that the first three regularly occur, viz.,

1st – as a result of proliferation and hyaline degeneration of the endothelial cells lining the trabeculae,

2nd – from hyaline obstructed arteries, the hyaline rods splitting across into segments,

3rd – from hyaline venules, arterioles and capillaries, the endothelial cells playing an active part,

4th – from depressions of the surface, the epithelial cells and hyaline connective tissue here sharing in the formation of the concentric body.

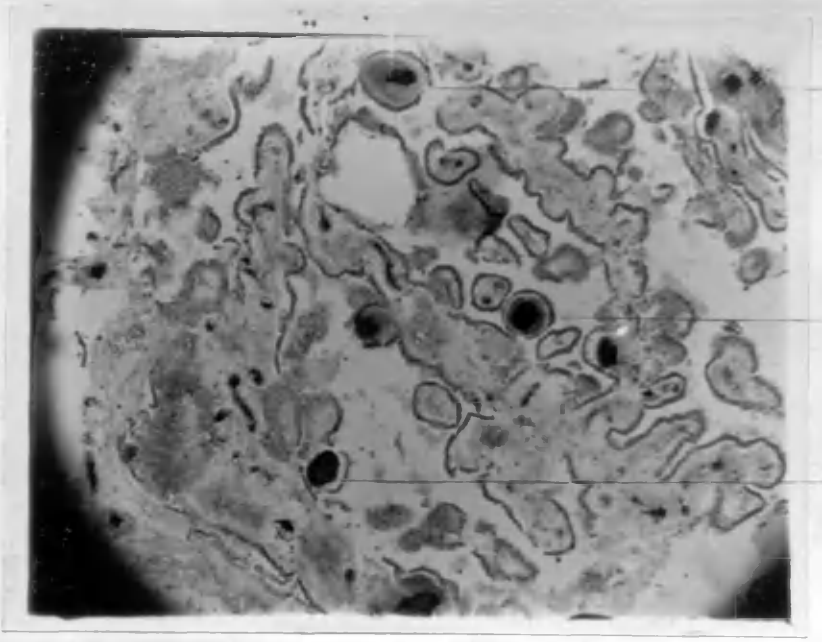


Photo 30. Section 26. (×26). From a case of senile mania.

a. Hyaline villi with more deeply staining hyaline material in the centre, which in a' shows concentric markings.

In conclusion it may be stated that the majority of these concentric bodies are composed of hyaline material, this being more especially brought out by their reactions with eosine and fuchsine. But this hyaline material seems to be an exceedingly unstable substance, leading at times to considerable variations in staining. Thus is the fact explained that in eosine and haematoxylin preparations, these bodies on occasions show a preference for the latter, and take up the former with different degrees of avidity. In the same way the reactions with Ehrlich — Biondi, and the occasional colouring with Weigerts fibrine stain, are accounted for. The conclusion therefore of Alzheimer[1] seems borne out "that the colloid substance — in this case synonymous with hyaline — in the tissues undergoes transpositions and becomes altered in its reaction and chemical property".

But these bodies are not all hyaline, as the effervescence with hydrochloric acid proves. Some of them are concretions, but they are decidedly in the minority, and are only met with in abundance in senile cases. In cutting tissues not previously decalcified, the simply hyaline bodies cut easily, and offer no resistence to the knife, while the concretions will not cut, and tear or break up the tissue.

[1] Alzheimer:— "Die Colloidentartung des Gehirns", "Archiv für Psychiatrie", 1898. Band 30. Heft 1. p. 51.

There is not much, however, in the microscopic appearances, apart from a more or less marked granularity in the latter, to distinguish between them. Both are alike, and the only reliable test is the chemical one with hydrochloric acid.

Moreover, it seems not at all unlikely, from the reaction with osmic acid, that these hyaline concentric bodies preparatory to their calcification, undergo a retrogressive fatty change, as so frequently happens in the case of calcifications elsewhere.

In my experience these bodies are never found in such profusion in the mentally sound, as in the insane.

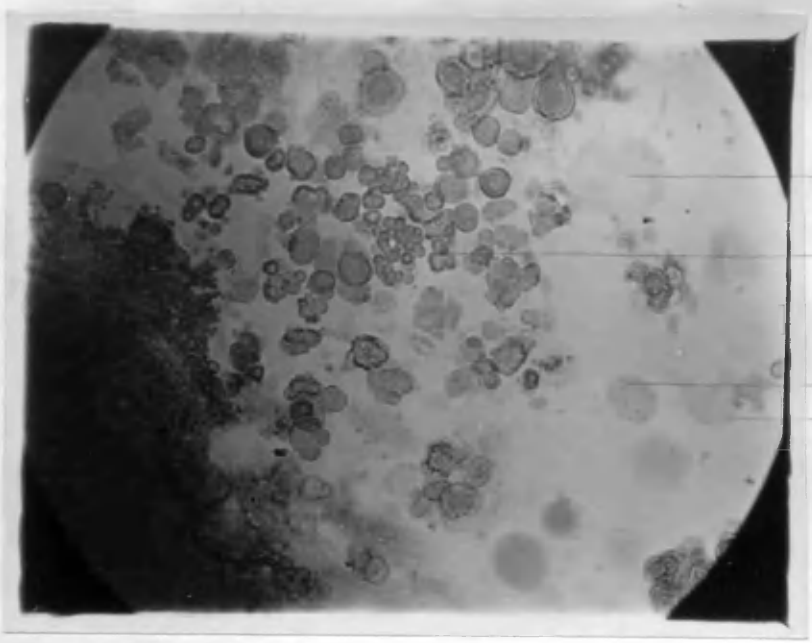


Photo. 31. Section 20. Portion of glomus. (× 240). From a case of alcoholic insanity.

a. Mulberry-like cluster of hyaline cells with indistinct or no capsule.
b. Hyaline spheres swelling up and breaking down.
c. Hyaline sphere with granules or fungous spores?

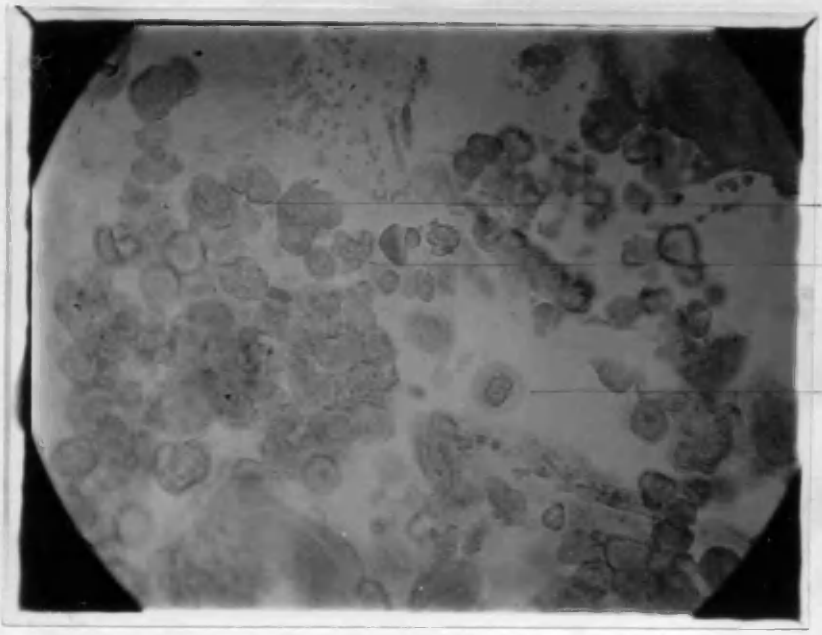


Photo. 32. Section 20. Portion of glomus. (× 240). From a case of alcoholic insanity.

a. Mulberry body with very faint capsule.
b. Mulberry bodies with distinct hyaline capsule.

B. Mulberry Bodies.

Closely allied to concentric bodies are structures, which were first described by W. F. Robertson[1] in the dura mater under the name of "mulberry bodies."

These bodies are also found in the choroid plexus. In comparison with the hyaline concentric bodies they are rare, but when present may occur in enormous numbers. They consist of groups of rounded or oval cells, which stain a deep purple colour in haematoxylin and eosine preparations and are perfectly homogeneous in appearance. (Photo 31, Section 20). The individual cells are pretty uniform in size, possessing a diameter of about .01 mm.. Each group may or may not be surrounded by a capsule. This capsule in some cases is only perceived with difficulty, and, as a rule, is very faintly stained. Occasionally, however, it presents a deeper staining, and when this occurs the cells in the interior are more massed together, and discrimination between them is difficult. (Photo 32. Section 20). Mixed up with these mulberry bodies are isolated cells of the above description, which may or may not have a capsule, while all

[1] Robertson W. F.,:- "Subdural Membrane Formation," "Journal of Path. and Bacter." July 1896. p. 142.

around are fully developed hyaline concentric bodies and pale hyaline spheres.

W. F. Robertson expresses no opinion as to the origin of these bodies, but I think I have traced the process by which they are produced.

Each little oval purple colored body represents a degenerated endothelial cell, and may be seen forming in the spaces around this large collection of hyaline structures in section 20. It is likewise a hyaline degeneration of the endothelial cells, and this anomalous staining, as already seen, is no unusual feature of hyaline material. These little bodies then run together and form a mulberry like mass, which later acquires a capsule. In all probability this capsule or envelope is elaborated not by these cells themselves, but is deposited around them from the fluid in which they are bathed. In their neighborhood are seen large hyaline spheres, staining faintly, irregular in shape and breaking down or gradually merging into the fluid about them. This capsule, at first indistinct, becomes more and more marked, till finally it assumes a very distinct hyaline appearance around the mulberry mass. The oval bodies now begin to merge into one another and become less distinct. Then concentric rings appear in the middle of such a structure, and forms are seen with concentric

markings in their interiors, and still surrounded by the oval purple colored cells. These likewise lose their identity and assist in the formation of a hyaline concentric body, which is the consummation aimed at. (Section 20).

I have gone somewhat fully into the development of these mulberry bodies and their further conversion into hyaline concentric bodies, because W. T. Roberton writes of them as though they were distinct entities. But such I have shown them not to be. They only represent another mode of expression of this hyaline change, which may occur under many different forms, and produce a material having very various staining reactions.

C. Cystic Degeneration of the Choroid Plexus.

This is a very common condition, being found in a large proportion of cases. Indeed so frequently are cysts present, that Faivre[1], writing in 1855, described "choroid vesicles" as normal and peculiar to the human subject. It is interesting on the other hand to note, that as early as 1826 Robert Hooper, M. D., figured these cysts of the choroid plexus in his "Morbid Anatomy of the Human Brain (being illustrations of the most frequent and important organic diseases to which that viscus is liable)."

Of my sixty five cases examined, cysts were present in thirty seven, while Ogston[2] only found them in 19% of the brains of known drunkards.

The glomus is pre-eminently the seat of this cystic degeneration, and cysts, though occurring, are never found to any extent in the other parts of the plexus.

These cysts may be little larger than

1. Faivre :- Review of "Les Plexus Choroïdes" from "Revue Medicale" in "British & Foreign Medico-Chirurgical Review." 1855. Vol I. p. 564.
2. Ogston :- "Pathological Observations on the Bodies of Known Drunkards" "British & Foreign Med. Chir. Rev.", 1854. Vol I. p. 503.

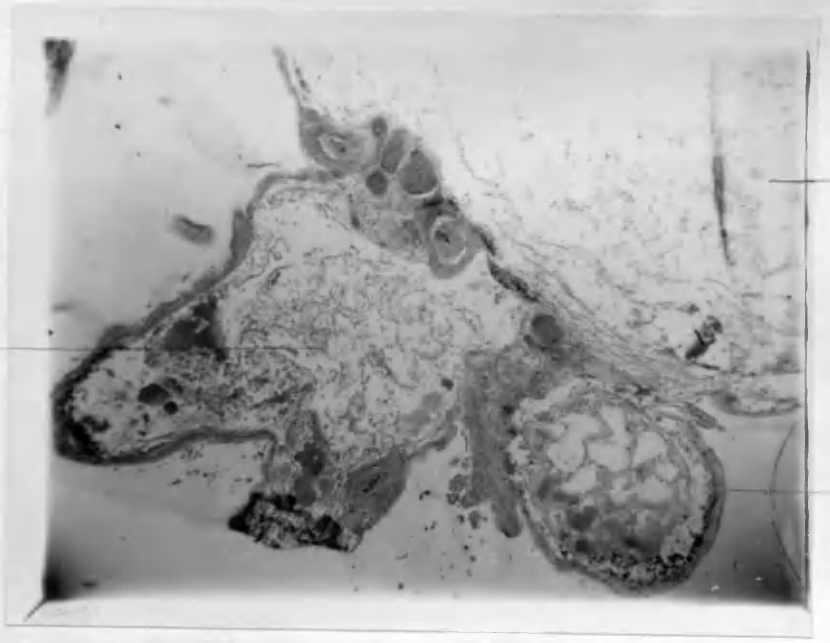


Photo 33. Section 27. Cysts. (× 26). From a case of chronic mania.
a. Well marked connective tissue stroma and loculi.
b. Connective tissue trabeculae breaking down and forming larger spaces.

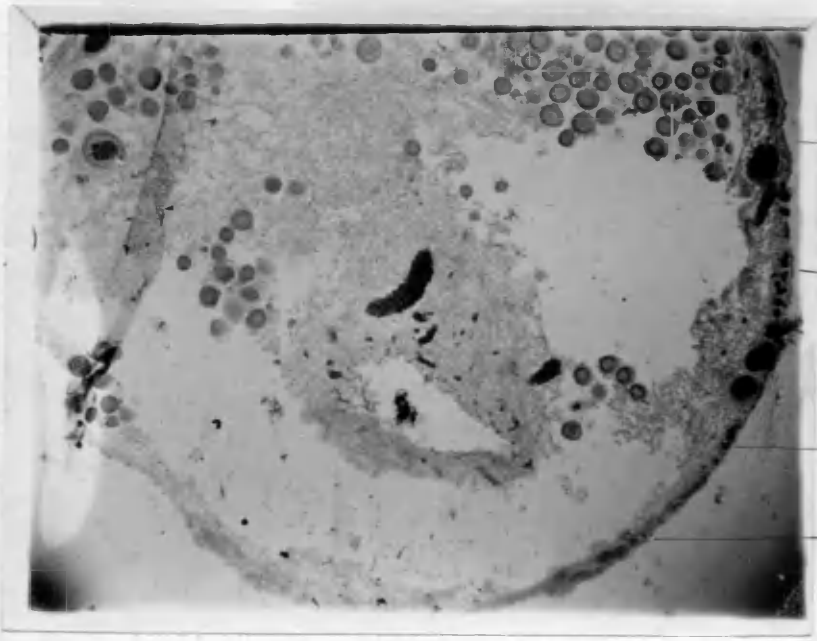


Photo. 34. Section 28. Single large cyst containing numerous concentric bodies, and by the running many spaces together, showing an apparent separation into two layers. (× 26). From a case of delusional insanity. Numerous vessels in cyst wall.
a. Epithelium present.
b. Epithelium absent.

a pin's head or may reach the size of a pea. In some cases they are few in number, in others they are very numerous, the whole glomus being converted into a cluster of cysts like a bunch of grapes in miniature. I have never seen them so large as a hazel nut, as Luschka describes, though the glomus itself may attain such dimensions. Cases are on record where cysts of the choroid plexus have reached an enormous size, distending the ventricles, pressing on the surrounding brain, and eventually causing death. ①

The walls of the cysts are thinner in some places and thicker in others, but everywhere delicate. They are very vascular, and numerous fine vessels may be seen coursing over the surface of the little bladders. (Photos. 33 and 34, sections 2, and 28). The walls are further remarkable for the presence of a fine white dotting, due to concentric bodies embedded in them, or to small aggregations of cells filled with fatty granules. In one case a white patch, about half the size of a split pea, was seen at the apex of a cyst. On microscopic examination this was seen to be composed of large cells filled with fatty granules.

① Brun, G.:- "Cyst of Choroid Plexus of Large Size in an Infant," "Pathological Transactions of London", Vol XXVII. p. 25.

Herringham:- "Tumour of Brain, Cyst of Choroid Plexus", "Illustrated Medical News," 1885 p. 193.

which were darkened on the addition of osmic acid. (Photo. 35, Section 29).

The cysts have a smooth shining surface, and as a rule present no villi. As a result of the distortion caused by this swelling, vessel loops, attached by small mesenteries, are to be seen projecting from the surface of the glomus in greater numbers than they normally do.

The tissue of the walls is composed of a connective tissue stroma in which numerous vessels run, arterioles, venules and capillaries. This connective tissue forms in parts quite thick bands, which are brought about by the obliteration of the normal spaces between the trabeculae. The surface of the cyst, moreover, is very often destitute of an epithelial covering. Near the base of such a cyst the epithelium may be quite distinct, but as the apex is approached the cells become scattered, a bare patch showing up here and there, till finally a portion is reached, where no epithelial cells can be seen. (Photo. 34, Section 28). It is an open question as to how far such a condition is brought about artificially, and there can be no doubt that in the handling of the tissues after death, the epithelium on the most exposed parts will be very liable to be rubbed off; still from the frequency with which it occurs, I am inclined to the opinion that it is not altogether an "artefact."

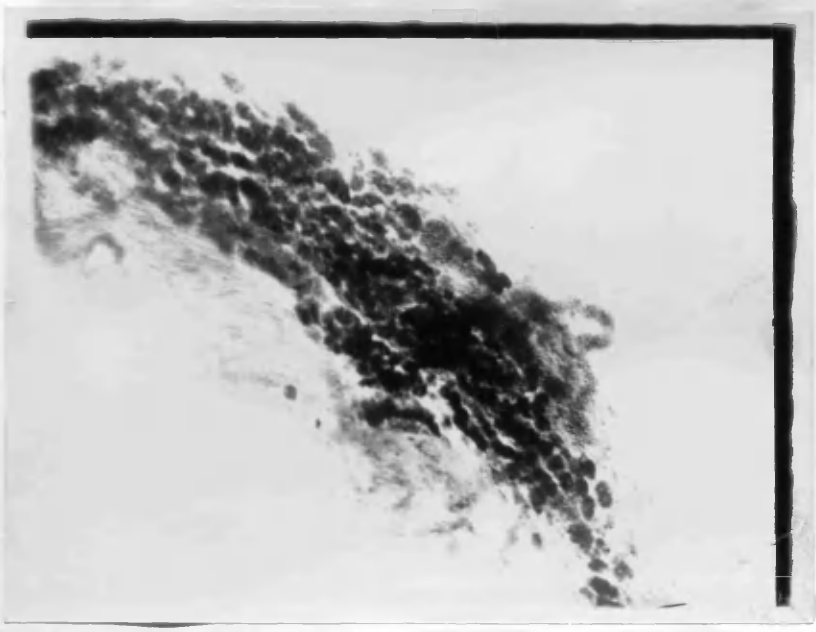


Photo 35. Section 29. Portion of cyst wall. (×120). From a case of chronic mania. Stained with osmic acid. Numerous large cells filled with fatty granules.

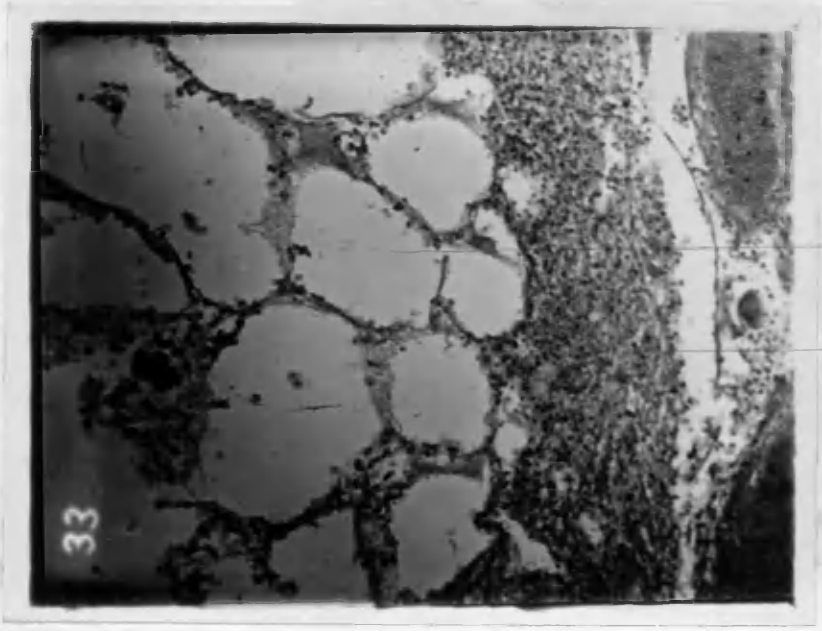
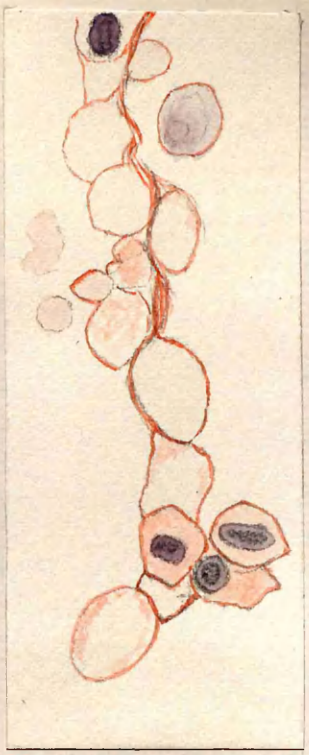


Photo. 36. Section 30. Cystic tissue. (×120). From a case of dementia.
a. Large spaces filled with fluid. The walls of the spaces are lined by cells in all stages of degeneration
b. Dense tissue at margin of cyst composed of proliferating and degenerating cells.

The interior of the cyst is made up of a very open network of connective tissue trabeculae, which are lined by degenerated and degenerating endothelial cells, scarcely one of which presents normal features. (Drawing 7). The spaces are filled with a thin fluid, in which float cells in different degrees of degeneration. Concentric bodies are of very frequent occurrence throughout the cyst, and may be found packed in the meshes, over quite a considerable area. All around this looser and more open network, and gradually blending with it, is a dense tissue, in which there has been very extensive proliferation of the endothelial cells lining the trabeculae; and associated with this usually some thickening of the trabeculae themselves. The proliferated cells, moreover, even in the quite dense portions, usually show early degenerative changes. (Photo. 36, Section 30).

In the fluid which fills the cyst the following formed elements are suspended,

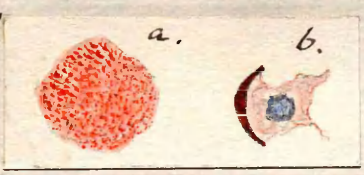
1. Endothelial cells with an increase in the granularity of their protoplasm, the granules staining deeply with Eosine. The large oval nucleus may or may not be obscured.
2. Cells showing one or more vacuoles in the protoplasm, with an occasional cell in which the nucleus is also vacuolated.
3. Large globular cells, whose contents consist



Drawing 7. Trabecula from cyst, lined with degenerated cells. (× 1000). Majority of cells represent No. 4 in list.

Drawing 8. Cells from a cyst. (× 1000).
a. Cells (endothelial) showing vacuolation and granularity of protoplasm.
b. Cells completely transformed into hyaline or colloid material.

Drawing 9. Endothelial cells from cyst. (×1000) Showing sickle-shaped zone of protoplasm, around a large vacuole in which nucleus appears suspended.



Drawing 10. Endothelial Cells from a cyst, (×1000).
a. Cell with very numerous eosinophile granules.
b. Remnants of protoplasm + cell membrane, with the vacuolated nucleus.

almost entirely of a hyaline, perfectly homogeneous and more or less opaque, sphere. This sphere is surrounded by a small circular or sickle shaped zone of granular protoplasm, which contains a nucleus.

4. Large homogeneous globules, in which the appearance of a cell wall may still be traced, but containing no other formed elements.

5. Still larger homogeneous hyaline spheres with no indication of cell membrane.

6. Doubly contoured hyaline spheres. In such the inner sphere probably represents the transformed nucleus, while the outer is derived from the cell protoplasm.

7. Free nuclei, or nuclei with remnants of cell membrane and even protoplasm attached.

8. Irregular masses of hyaline material.

9. Extravasated and disintegrating blood corpuscles, which eventually break down into a granular debris.

10. Hyaline concentric bodies of all sizes.

(Photos 37 and 26. Sections 22, 27, 28 and 30, Drawings 7, 8, 9 & 10).

The above elements (with the exception of the granular debris, which is derived from the blood corpuscles,) arise from the endothelial cells lining the trabeculae, as the result of a degenerative process, and the following sequence of events may be traced.

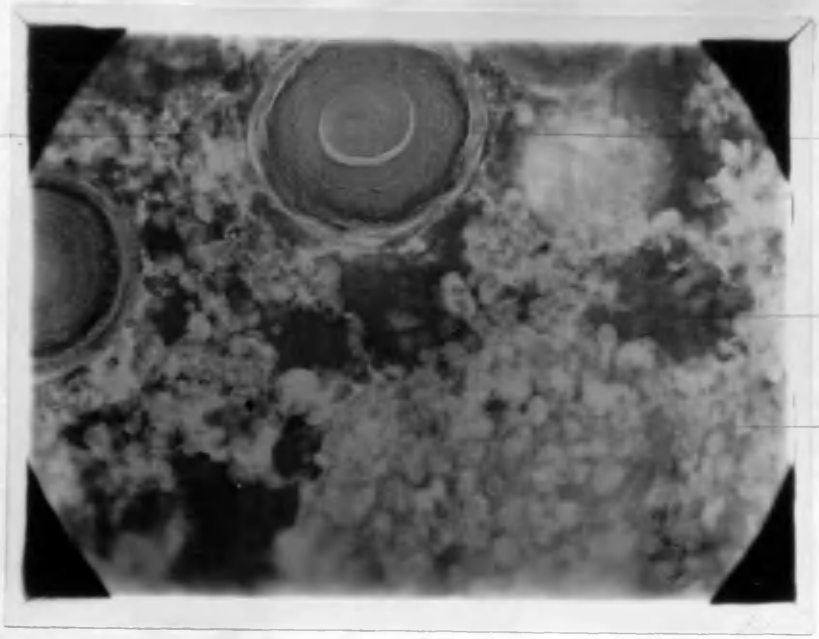


Photo. 37. Section 28. Part of a cyst. (×240).
From a case of delusional insanity
a. Concentric body with well marked hyaline capsule. b. Red blood corpuscles. c. Irregular mass of hyaline material. d. Large number of degenerating and degenerated endothelial cells.

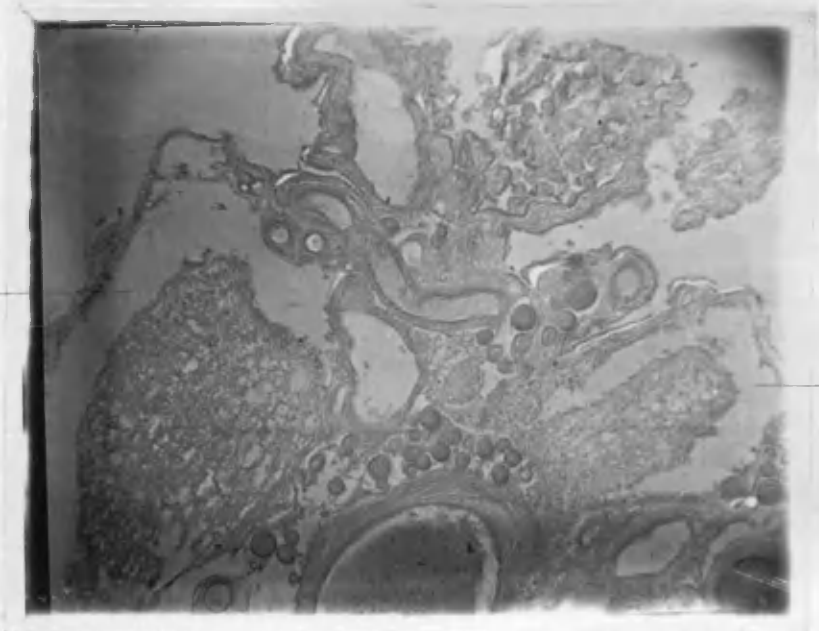


Photo. 38. Two small cysts. (×120).
From a case of senile insanity.
a. Large space in cyst, producing an appearance as of a separation into two layers.

The endothelial cell first of all swells up, and the cell plate becomes coarsely granular, presenting in haematoxylin and eosine preparations numerous eosinophile granules. A vacuole now appears, encroaching more and more on the protoplasm, till the granular contents of the latter are represented only by a circular or sickle-shaped mass at the edge of the cell. A nucleus may or may not be seen, and may appear to float in the vacuole, or remain attached to the cell wall embedded in the granular protoplasm. Then very commonly the cell membrane ruptures and the contents are discharged into the lymph spaces, while in the fluid the free nuclei may be seen. The cell may, however, not rupture at this stage. The nucleus itself may become vacuolated and assist in the general distension of the cell, till nothing is seen but a homogeneous globule with a faint remnant of cell wall and protoplasm. In other cases the whole cell presents a coarsely granular appearance.

These homogeneous globules thus produced may swell up still further till they rival the concentric bodies in size, and could the individual stages not be traced, one would be inclined to think with Alzheimer[1] that these large hyaline spheres are really elaborated from the tissue

[1] Alzheimer:- "Archiv für Psychiatrie", 1898, Band 30. Heft 1. p. 50. "Die Colloidentartung des Gehirns".

fluids, and not, as I believe, actually produced by cell degenerations.

These large hyaline spheres may rupture, perhaps adding to the fluid contents of the cyst. More certainly, however, they run together, forming large irregular masses of hyaline material.

The connective tissue trabeculae may become hypertrophied, and very frequently they undergo hyaline degeneration. Often, however, owing to the pressure of the degenerated cells and fluid these trabeculae become broken down and absorbed, leading to the formation of spaces of large size, while, here and there, lying in the midst of hyaline spheres may be seen free portions of the connective tissue trabeculae. (Photos. 26 and 33, Sections 22 and 27).

The above are the microscopic appearances to be met with in the cysts of the choroid plexus, and before stating more precisely my views as to their formation, I will first briefly mention the opinions entertained by others.

Numerous have been the surmises and opinions as to the cause of these cysts. Apart from the conjectures of the older authors, who designated the cysts, in their opinion, as hydatid, echinococcus cysts, cysticercus cysts, metamorphosed glands, lymphatic effusions, etc., there are five more important views regarding their nature to be considered.

1. Luschka[1], Van Gheuchten and Bruch are of opinion that these cysts are formed by the dropsical separation from one another of the two layers of the pia mater which constitute the tela and choroid plexus. More lately Schnopfhagen[2] has advocated this view.

2. Schrank and Förster[3] believe that they depend on the formation of the normal epithelial cells into numerous large and delicate albuminous cells, which then form colloid cysts and acquire a fibrous envelope from a hypertrophy of the connective tissue.

3. Rokitansky[4] wrongly supposing that the choroid plexus consists of a frequently twisted up, primitive, hyaline, bulb-like cavity, believes that these cysts result simply from widenings of the villi to constitute formed cavities.

4. Haeckel[5] has described the degeneration of cells and the formation of hyaline spheres very completely, and my observations are, in the main, only corroborations of his. He describes what he terms "solid and soft cysts". The solid is the

① Luschka:- "Die Adergeflechte", pp. 157-159.
② Schnopfhagen:- "Die rosen. cystöse Degeneration d. Plexus choroidei d. Grosshirns", 1877.
⑤ Haeckel:- "Schmidt's Jahrbücher", 1860 pp. 18, 19 & 20.
③ Schrank and Förster:- quoted by Haeckel p. 20.
④ Rokitansky:- quoted by Haeckel p. 20

primary condition, and is due to proliferation and degeneration of the connective tissue cells, associated with a hyperplasia of the connective tissue itself. Later on, such a growth may become, through serous infiltration, softer and more watery and eventually form a bladder or cyst.

5. Cysts are frequently found in the arachnoid and pia mater, and Ziegler[1] holds that these are in every way similar to those cysts met with in the choroid plexus. "The cysts are due to oedema of the membranes, with more marked and localised accumulations of fluid in the subarachnoid and pial spaces." Ziegler expresses no opinion as to the manner in which a boundary is formed, in order to enclose the fluid and produce a cyst, apart from the suggestion that, "vesicular oedema or cysts of the pia mater would appear to depend on the presence of closed lymph spaces, congenital or acquired in the pia mater and subarachnoid tissue."

As the result of my own observations I have arrived at the following conclusions as to the origin of these cysts in the choroid plexus.

Hyaline concentric bodies are very commonly found in cysts, likewise the hyaline spheres, which have been shown to take part in the formation of concentric bodies. The degenerative process in the endothelial cells of the trabeculae in cystic formation, is very similar

[1] Ziegler:- "Path. Anat.," Part II. Art. 637, pp. 241 and 243.

to that which precedes the development of encentric bodies. Indeed, so close is the resemblance, that it is very questionable if we are entitled to discriminate between them. Still to my mind, there is no doubt that cells break down into fluid in the cysts in a way that never occurs apart from them. But such degeneration of cells alone does not seem sufficient to account for the development of these cysts, though there is no doubt that the fluid found in them is in part due to this bursting of the endothelial cells, affected with colloid or hyaline degeneration. In all the cysts, I had an opportunity of examining the fluid was quite limpid. Colloid cysts, with gummy viscid contents, have, however, been described by Wallmann[1] and Hoffmann[2].

It seems more than probable that there are two processes here at work, a primary proliferation and degeneration of the endothelial cells, associated frequently with hyaline changes in the trabeculae, and a secondary condition of oedema added thereto.

Still I do not think that Haeckel is accurate in saying that this solid structure — produced by proliferated cells and thickened trabeculae — "may become through serous

[1]. Wallmann:- "Colloidcysts im 3. Hirnventrikel, Lipom im Plexus Choroides," "Virchow's Archiv.", 1860, Vol XIV. p. 385.

[2]. Hoffmann:- "Fall von Epilepsie mit cystoider Entartung der Plexus choroides," "Archiv. für Path. Anat.," 1862, Band 25, p. 184.

infiltration, softer and more watery and eventually form a bladder," for in my opinion the cyst is formed not in, but behind this thickened mass. Moreover, he is wrong in attributing the cell formations to the connective tissue corpuscles.

Through the spaces constituting the pia-arachnoid, of which the choroid plexus is composed, there must be a constant circulation of lymph. This proliferation and degeneration of cells in many cases completely fills up these spaces, and a serious obstacle to the flow of lymph must result. As shown, too, when dealing with the formation of concentric bodies, hyaline spheres may travel till they stick in these spaces or channels, eventually blocking them up. Concentric bodies must have the same effect, and these are never present in any numbers without a concomitant development of cysts. There exist then very numerous points of obstruction, behind which the lymph stream is constantly pressing. There is, in short, an obstructive oedema. The spaces of the pia-arachnoid become more and more distended with the lymphatic fluid, and larger spaces still are produced by the breaking down or absorption of intervening trabeculae, while the cyst itself is produced by a number of such spaces lying adjacent to one another. The degenerated cells add to the fluid their quota, and where the tendency is for the cells to

rupture in the manner described, then are the contents of the cysts colloid. In other cases again where the greater number of the degenerated cells go to the formation of concentric bodies, the cystic fluid tends to be thin and limpid. Finally such a collection of fluid may be shut off from surrounding parts, by the occurrence behind the fluid accumulation of the same changes, which led to the obstruction in front; and the frequency with which dense tissue is found all around the cysts seems to point to such a conclusion.

This is practically in harmony with Ziegler's idea that, "the cysts of the pia mater would appear to depend on the presence of closed lymph spaces, congenital or acquired, in the pia mater or subarachnoid tissue", and, in the case of the choroid plexus, we see very distinctly how such closed lymph spaces may be produced.

So far as I can see, there is nothing in the position of these cysts to bear out the view of Luschka that "they are due to the dropsical separation from one another of the two layers of the pia mater which constitute the tela and choroid plexus. Now and then a separation seems to occur, but can always be explained by the breaking down of trabeculae and the joining together of numerous spaces to form a single large cavity". (Photos. 33 and 38).

With Rokitansky's description of the choroid plexus and his conclusions therefrom I cannot agree.

No more can I concur with the opinion of Schrant and Förster, that "the epithelial cells become converted into large and delicate albuminous cells, which then form colloid cysts." There is a constant change going on in the epithelial cells, and they normally undergo a process of vacuolation, and rupture to form the choroid plexus secretion. With such factors at work, one would expect 'a priori' to find frequent examples of retention cysts.

Appearances suggesting such are frequently seen, both in man and the lower animals. But they never attain any size, and instead of actual retention cysts, we may be seeing only the lower part of the tubular depressions found between the villi, in the base of which tubes, secretion, though not actually held back, would be apt to lodge. (Photo. 18 Section 11).

D. Thickening of the Trabeculae with Proliferation and Degeneration of the Endothelial Cells.

I have described, first of all, the degenerations of the choroid plexuses leading to the formation of hyaline concentric bodies and cysts, as these are the most remarkable, but the endothelial cells and trabeculae proliferate and degenerate to other ends.

"A milky and opaque condition of the pia-arachnoid is very common in the insane. In the majority of cases it is a well developed state, and its absence is quite exceptional." ①

Similar conditions are found in the choroid plexus and are likewise very common. These changes are always more marked in the glomus, where the trabecular arrangement is on a larger scale and unequivocal.

Hyperplasia and Hyaline Degeneration of the Fibrous Tissue Trabeculae.

The fibrous tissue trabeculae undergo a slow hyperplasia and are found in all conditions.

① Robertson, W. F., :- "The Pia-arachnoid in the Insane", "Journal Mental Science", Oct. 1895.

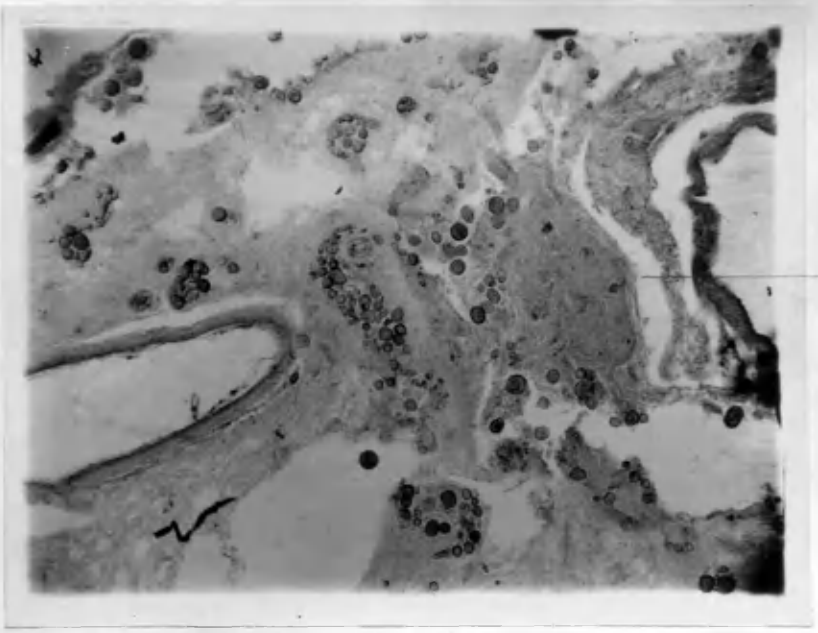


Photo. 39. Section 31. Portion of glomerus. (x 26). From a case of phthisical insanity.
a. Very dense fibrous tissue area.

Photo. 40. Section 32. (x 120). From a case of phthisical insanity.
a. Hyaline thickening of the trabeculae, the endothelium in parts shed. b. Thick hyaline bundles. c. Proliferation of the endothelial cells practically all round the right and lower sides.

In some cases the thickening is slight, the fibres being little more than swollen. In others, again, there is a distinct connective tissue overgrowth, and localised areas of dense fibrous tissue are produced, in which the normal pia-arachnoid spaces are obliterated or merely represented by endothelial cells. (Photo. 39. Section 31).

These altered and new formed fibres are very prone to become affected by hyaline degeneration, and much thickened strands staining very lightly with eosine, and even large hyaline masses may thus result. (Photo. 40, and Section 33).

2. Osteoid Plates.

In section 34 and photo. 41 is seen a small osteoid mass, surrounded by very dense and wavy fibrous tissue, much swollen up from hyaline degeneration. In this hyaline fibrous tissue there are innumerable connective tissue corpuscles of an irregular branching character. Also a few giant cells, and what are very like new vessels, forming and penetrating into this thickened tissue, are seen. Indeed, so closely do the cells in this fibrous area resemble those in the more frankly osteoid mass, that we must presume the existence of a similar though less advanced change. The osteoid plaque is very dense and stains deeply with eosine. About its centre are two more granular areas staining a purplish colour in this

Photo. 41. Section 34. Small osteoid plate. (× 120). From a case of senile insanity.

a. Osteoid structure.
b. Less dense areas containing much granular debris and osteoblasts.
c. Dense hyaline fibrous tissue.

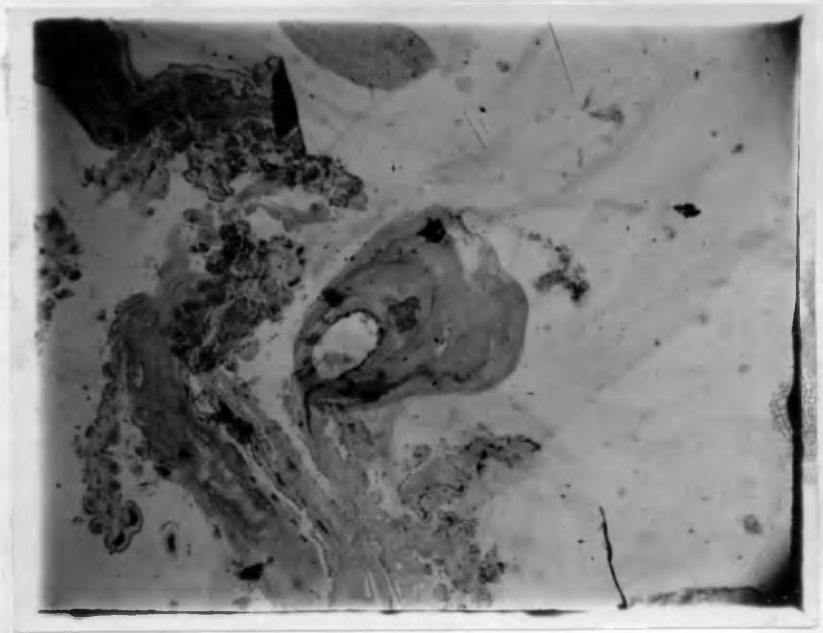


Photo. 42. Section 35. Osteoid plate. (× 26). From a case of senile insanity. Osteoid plate shows well marked lamination and Haversian canals.

haematoxylin and eosine preparation. In these places can be made out well marked osteoblasts, much granular debris and round cells; and in all probability - these are the centres from which the osteoid tissue is being laid down. A considerable number of branching cells are present in this osteoid area, and at one point a cell is seen either undergoing division or but lately divided.

In section 35 and photo. 42 is shown a more perfect example of osteoid tissue. Here the osteoid mass is penetrated by well marked Haversian canals carrying blood vessels and numerous cells. The whole plaque is however very distinctly laminated, and in parts many elongated cells are seen between the lamellae. I have found this condition in three of the cases examined, and in none of them was there any deposition of calcareous salts.

I think there is every reason to conclude that these osteoid plates are produced directly from the connective tissue of the trabeculae by a process of metaplasia or neoplasia, and in this manner Thoma[1] explains their occurrence in the other soft parts of the body.

1. Thoma :- "Text Book of General Pathology", Translated by A. Bruce, 1896, Vol. I. pp. 548 & 549.

3. Hyaline degeneration of the Connective Tissue in the smaller villi.

Before leaving the connective tissue alterations it will be convenient to describe hyaline degeneration of this structure in the smaller villi. Here, as already mentioned, the connective tissue is represented by a homogeneous matrix with very few cells: no trabeculae or spaces can be made out, here and there the tissue is fibrillated, while very occasionally distinct connective tissue fibres are seen.

Hyaline degeneration frequently occurs in this homogeneous connective tissue. The substance between the epithelium and the capillary loop swells up, acquires a more dense appearance, and stains very deeply with eosine. This increase of tissue finds room for itself by encroaching on the lumen of the capillary, which may eventually become obliterated altogether, leaving no trace behind it. Very often associated with this condition is a similar change in the capillary itself; and obstruction of the little vessel may really be brought about by a process of thrombosis. But soon this appearance of thrombus is lost, the clot becomes converted into hyaline material, and may even take part in the formation of a concentric body. (Photo. 30, Section 26).

When the villus becomes thoroughly

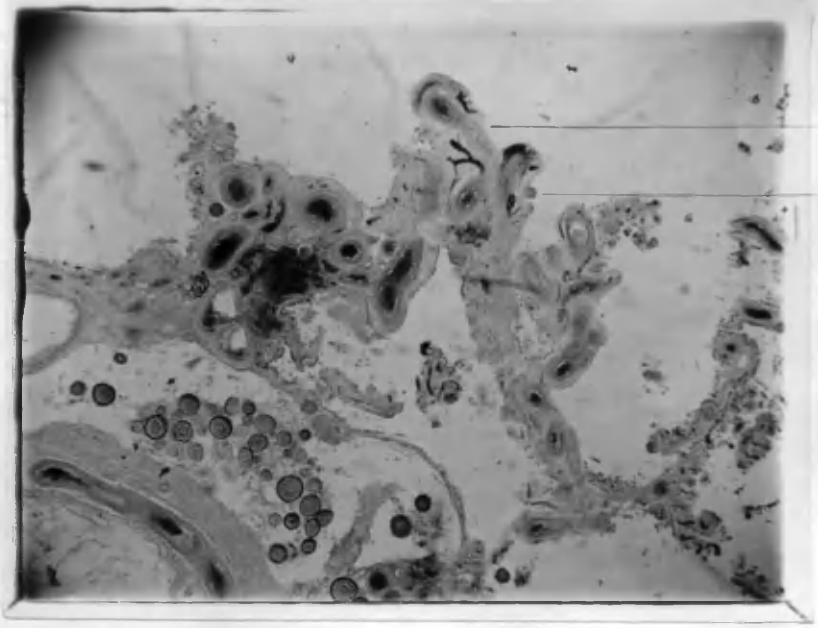


Photo. 43. Section 30. Hyaline villi. (× 26). From a case of Dementia

a. Hyaline villi bereft of their epithelium.
b. Small villus shrunken up, and completely converted into hyaline material. No capillary to be detected in its substance.

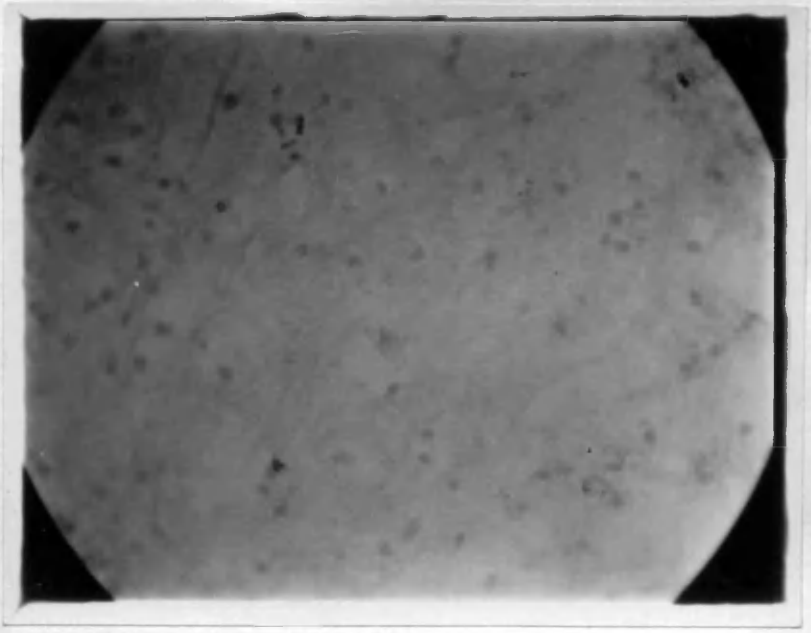


Photo. 44. Section 36. (× 240). From a case of phthisical insanity.

Slight thickening of the fibrous tissue trabeculae with some shedding of the endothelium lining the spaces.

hyaline and is robbed of its blood supply, the epithelium is almost invariably found shed. This desquamation, moreover, may occur while the capillary loop is still present, the intervening hyaline mass cutting off the source of nourishment from the epithelium. Villi over large tracts are found bared of their epithelium, and though at first enlarged, they eventually become much shrunken and distorted. (Photo. 43, Section 30).

This is a very common condition in senile insanity, and I would make the suggestion, that, when spread over a large area, it may account for the atrophy of this organ so frequently seen in these cases.

4. Proliferation of the Endothelial Cells.

Associated with this change in the fibres there is proliferation – and degeneration – of the endothelial cells. When the thickening of the connective tissue trabeculae is extreme, the changes in the endothelial cells are slight, or may be entirely absent. The endothelium is very commonly found shed in cases where the connective tissue fibres are thickened and the arrangement of spaces maintained. (Photos. 44 & 45, Section 36).

The proliferated cells frequently form dense masses in the spaces of the choroid

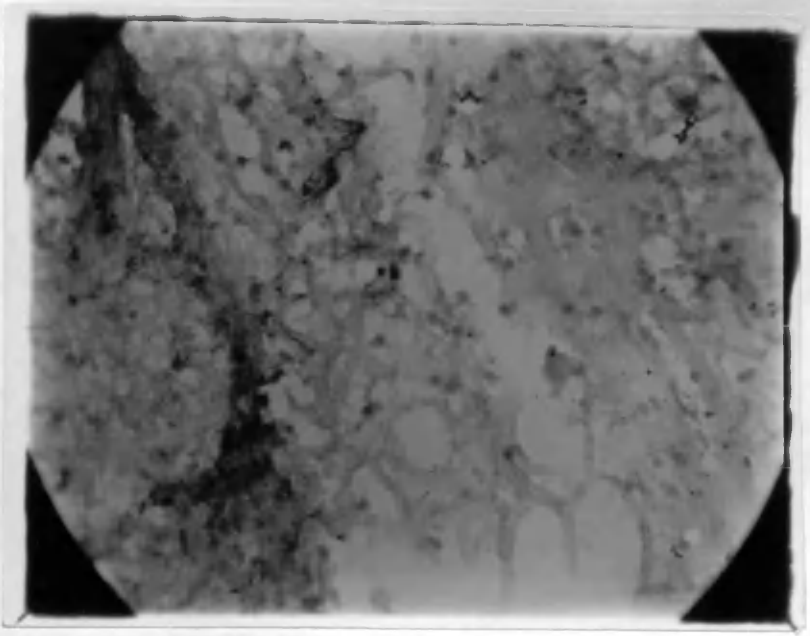


Photo. 45. Section 36. (× 240). From a case of phthisical insanity.
Hyaline thickening of the trabeculae, which, in parts, are completely denuded of their endothelial lining.

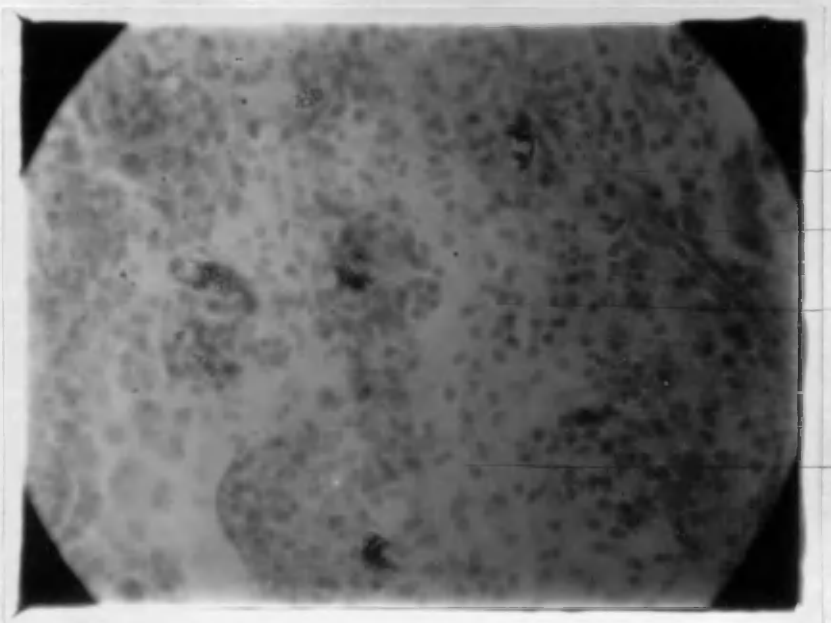


Photo. 46. Section 37. Proliferating endothelial cells. (× 240). From an insane patient, who died of general tuberculosis.
At spots marked 'a' and elsewhere the endothelial cells are seen dividing by the process of karyokinesis.

plexus. This is not a round-cell infiltration, but is caused directly by a multiplication of the endothelial cells lining the trabeculae. These endothelial cells may rarely be seen in actual process of division, and though often the nuclei in these cellular collections are rounder and smaller than those of the ordinary endothelial cells, it can be made out that in the main they resemble the endothelial type. (Photo. 46, Section 37).

In connection with this condition occurring in the arachnoid in certain mental disorders Ziegler[1] states that it is still doubtful whether these "milky thickenings" are always of inflammatory origin. "They are histologically due to fibrous thickening, endothelial hyperplasia, or more rarely to cellular infiltration." In the pia mater itself he holds that these changes, in their later stages at least, are unmistakeably inflammatory and accompanied by accumulations of leucocytes especially around the vessels.

W. T. Robertson,[2] on the other hand, is very definite as to these aggregations being composed of endothelial cells entirely, and is of opinion that areas of small round-cell infiltration

① Ziegler:- "Pathology", Section XI. Art. 656 pp. 293 & 294.

② Robertson, W.T.;- "Pia-arachnoid in the Insane", "Journal Mental Science", Oct. 1895.

upon the vessel walls or elsewhere seldom occur. "It is only," he adds, "in advanced general paralysis, in syphilitic insanity, and in the very rare and still obscure condition, known as purulent infiltration of the pia-arachnoid, that such an aggregation of round cells is added to the other appearances."

I cannot but favour the view of these collections of cells being endothelial in character, and though two syphilitic and seven general paralytic cases were examined, only in one of the latter was I able to detect round cells upon the vessel walls and in the midst of the endothelial proliferations.

5. Degenerative Changes in Endothelial Cells.

These proliferated endothelial cells by and by undergo degenerative changes, and these same changes may be observed without any previous cell multiplication.

a. A very common degenerative process consists in the endothelial cells simply breaking down into granular debris, and spaces are frequently seen crammed with such material.

b. Fatty changes are likewise often observed, and may be present over considerable areas. This condition is shown by the presence in the cell plate of numerous bright and highly refractive little globules or granules, which are darkened by

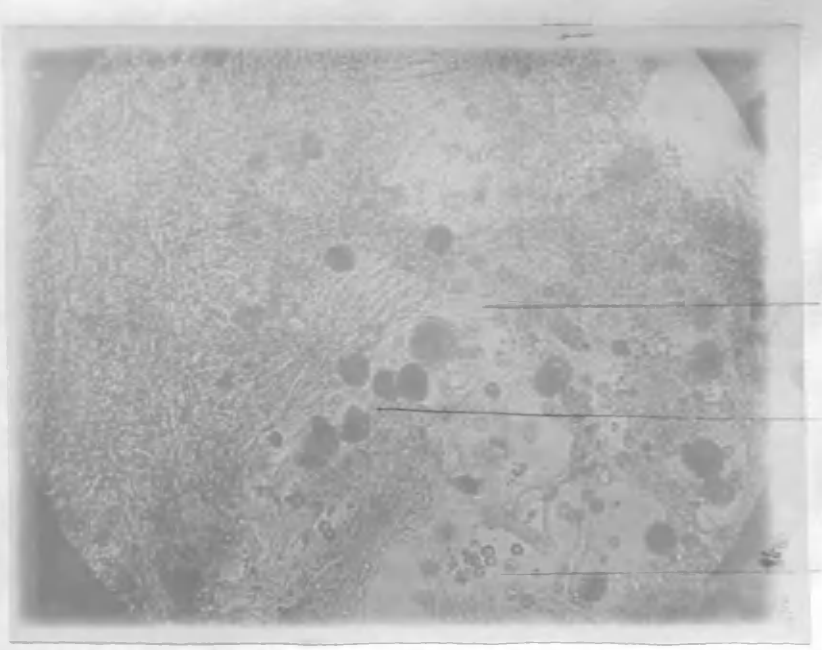


Photo. 47 Section 18. (×240). From a case of senile insanity. Stained with osmic acid. a. Endothelial cells greatly increased in size and containing numerous fatty granules and globules. b. Extravasated red blood corpuscles in a space. c. Thickened tube endothelium.

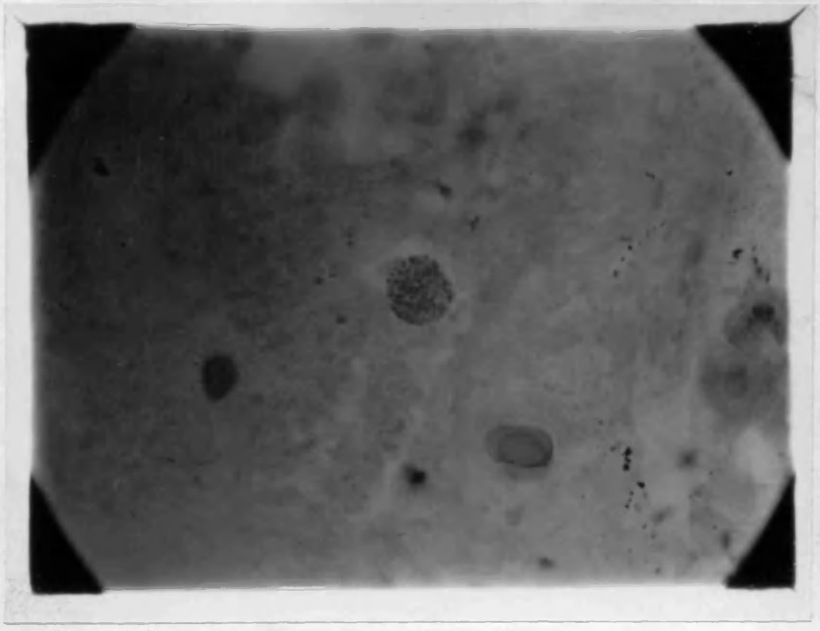


Photo. 48. Section 20. (×240). From a case of alcoholic insanity.
Conidiophore or cell formation?

osmic acid. Sometimes a nucleus can be distinguished amidst these fatty granules, in other cases this impossible to do so. Cells thus affected may attain very considerable dimensions, a diameter of .025 mm. not being at all uncommon. (Photo. 47 and Section 18).

Haeckel[1] describes this as not a rare condition, "especially in association with the proliferating cystoic metamorphosis and hypertrophy of the connective tissue".

I am of the like mind but feel convinced that he is wrong, in saying that this fatty change occurs in the connective tissue corpuscles.

W. F. Robertson[2] and Adler have expressed the opinion that fatty changes do not take place to any great extent in this milky condition of the pia-arachnoid, but an opposite opinion is held by Ziegler.

Whatever may be the actual state of matters in the pia-arachnoid, I feel assured that these conditions met with in the choroid plexuses, and fairly comparable to the milky opacities of the pia-arachnoid, are associated with distinct fatty changes in the endothelial cells, which may be of a wide spread character.

C. In section 20 and photo. 48 is shown another body that is occasionally found either amidst concentric bodies or apart from them.

[1] Haeckel :- "Ueber die Kalkstr", Schmidt's Jahrbucher 1860 p. 17.

[2] Robertson, W. F. :- "The Pia-arachnoid in the Insane", "Journal Mental Science", Oct. 1895.

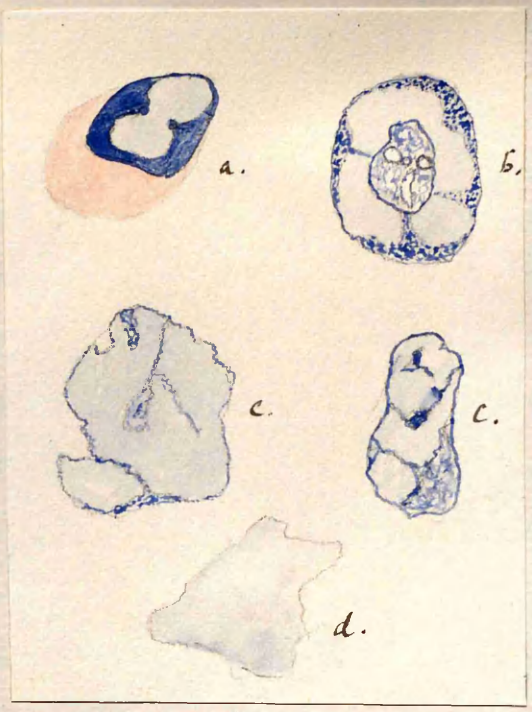
In this haematoxylin and eosine preparation it is seen to consist of a large number of good-sized spherical granules, which stain a deep purple colour and are surrounded by a less deeply-staining capsule. Similar spherical granules may occasionally be seen in the large faintly staining hyaline globules. (Photo. 31).

It is difficult to say what these bodies are or how they originate. It is just possible that they are identical with the large fatty cells just described, though they are larger, measuring in diameter .035 mm.. On the other hand, it is important to note that these sections were made from tissues hardened in solutions of potassium bichromate. They look, moreover, suspiciously like conidiophores, in the one case, and scattered fungous spores, in the other, and such they may really be instead of altered cellular elements.

d. Only on one occasion have I seen an example of what W. T. Robertson (1) calls "vitreous degeneration." This author has described the condition as affecting the endothelium on the surface of the dura, and lining the peri-vascular canals of its substance. "This retrograde change," he adds, "though common and important in the dura mater, is somewhat rare in the pia-arachnoid."

In the early stages there may be vacuolation

(1) Robertson, W. T.:- "Sub-dural Membrane Formation" "Journal Path. and Bacter." July 1896 pp. 133 & 134. "Pia-Arachnoid in the Insane", "Journal Mental Science", Oct. 1895.



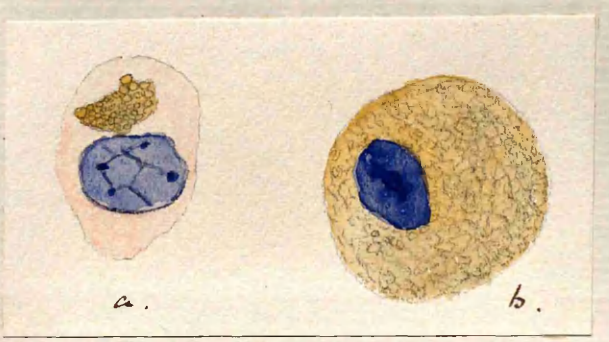
Drawing 11. Endothelial cells showing stages in the process of vitreous degeneration of the nucleus. (×1000). Section 38.

a. Endothelial cell showing large vacuole in the nucleus.

b. Nucleus + protoplasm with vacuoles.

c. Much swollen nuclei, still showing strands of granular protoplasm.

d. Distorted homogeneous mass.



Drawing 12. Endothelial cells showing pigmentary degeneration. (×1000). a. Slight, perhaps normal pigmentation. b. Advanced pigmentary degeneration.

of the cell plate, but the change is essentially in the nucleus, which swells up and becomes vacuolated. These vacuoles, at first small and few, gradually increase in size and number, and run together converting the nucleus into a collection of irregular cavities, staining faintly with haematoxylin. These vacuoles are, to begin with, separated by thin strands of granular protoplasm, staining more deeply with haematoxylin. Eventually, however, even these disappear, and a large distorted form results, of a homogeneous glassy appearance, and staining very faintly with haematoxylin.

This vitreous degeneration is altogether different from the hyaline change which occurs in these same cells. In the first place it is principally nuclear, and secondly the homogeneous substance produced does not stain with eosine. It is, moreover, not a fatty condition, as osmic acid causes no blackening of the vacuoles or the completed homogeneous mass. (Drawing 11. Photo 49. & Section 38).

E. Pigmentary degeneration of the endothelial cells is by no means a rare condition. It consists in an infiltration of the cell plate by numerous little globules of a bright yellow colour. The pigment, at first small in quantity, is gradually added to until no unaltered protoplasm remains, and in this way a very considerable increase in the

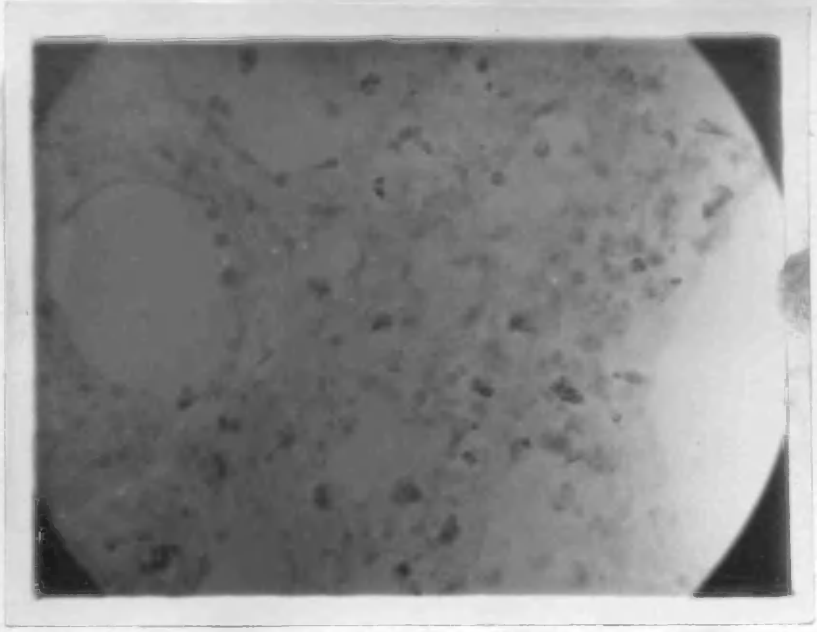


Photo. 49. (× 240) From a case of puerperal insanity. Numerous darkly stained cells showing pigmentary degeneration.

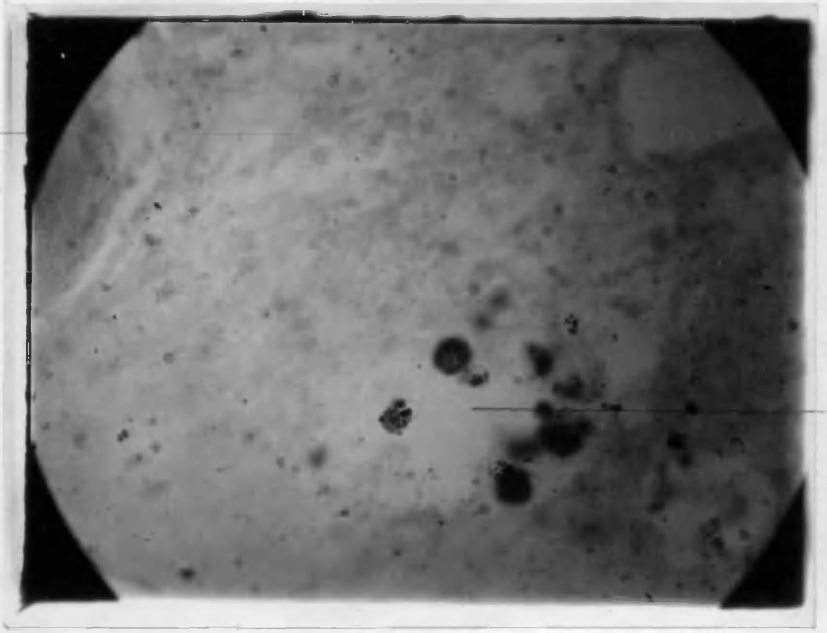


Photo. 49. Section 38. (× 240). From a case of senile insanity.

a. Endothelial cells with swollen and vacuolated nuclei, (vitreous degeneration).

b. Endothelial cells affected with pigmentary degeneration.

size of the cell may result. (Drawing 12. Photo. 49 and Section 38).

This is undoubtedly a morbid change, as evidenced by the fact that almost every cell in a considerable area may be pigmented. (Photo.). Normally cells with pigment do exist, but they are always few in number and far between.

It is however, highly probable, as Robertson[1] suggests for this degenerative process in the pia-arachnoid, that "at the same time it is a change that may have a physiological basis in the normal pigment cells, just as in pigmentary degeneration of nerve cells, the granules that replace the protoplasm are merely an increase in a normal element."

6. Foreign Elements in the Spaces of the Choroid Plexus.

Before passing on to a consideration of the changes in the vessels, it will be convenient to describe here some foreign elements commonly found in the spaces of the choroid plexus.

a. Red blood corpuscles and granular debris, resulting from their disintegration, are frequently found. The occurrence of the former is, I feel sure, not altogether unartificial, for extravasated blood cells more frequently are met with in preparations, which were frozen in dextrine and cut, than in those firmly embedded in celloidin. (Photo 47.)

[1] Robertson, W. F.:- "Pia-arachnoid", "Journal Mental Science", Oct 1895.

b. Haematoidin granules are often present, especially in cases of senile insanity. They are always discovered around vessels, in the spaces just beyond the adventitia. The arteriole surrounded by them may be thickened or even occluded, and their occurrence must indicate a rupture near at hand in the course of the vessel. This pigment is of a dark coppery or old-gold colour, and, moreover, is almost never diffuse, but usually is found in little heaps or aggregations. (Section 34).

I cannot help thinking that these two conditions, viz. pigmentary degeneration of the endothelial cells and the occurrence of haematoidin granules, are closely related to one another. They are frequently associated, and while pigmentary degeneration may occur in the other insanities, it is specially common in that known as senile.

The endothelial cells throughout the body are remarkable for their active phagocytic properties, and in section 40 it is observed that they are playing such a role. It is seen here beyond a doubt that the endothelial cells, in the spaces around a vessel, have actually taken up the haematoidin granules into their own cell-plates. In this particular case also, pigmentary degeneration is a marked feature.

As a rule the haematoidin granules are darker in colour than the pigment found in the interior of degenerated cells. But to this rule there are numerous exceptions, and in many cases

it is difficult to say whether we are dealing with haematoidin granules or cell pigment.

From these facts then, I think we are warranted in concluding that, in senile insanity at least, a great part of the apparent pigmentary degeneration is due to the endothelial cells having englobed these haematoidin granules, and in some cases further altered the colour of them.

That the two pigments are identical with, or closely related to, one another and the blood pigment itself, receives confirmation from photography. Blood offers considerable resistance to the actinic rays, and in the photographic negative is represented by thin clear areas. The same occurs when haematoidin granules or pigmented cells are photographed.

E. Hyaline-fibroid Change in the Vessels.

This change may be found in all the vessels, arteries, arterioles, veins and capillaries, but seems to affect mainly the arteries and capillaries. Of the arteries, the smaller ones and the arterioles show this degeneration to the greatest extent. The adventitia alone, or the intima and media may be affected, but by far the most common condition is to find the whole three coats involved.

Hyaline Degeneration of the Adventitia.

This consists in a homogeneous thickening of the longitudinally running fibrous tissue. The swelling may be slight or considerable, stains a faint pink with eosine, and, as a rule is devoid of granularity. In the smallest arterioles, with only one layer of muscular cells, and in which the adventitia in the normal condition is made out with difficulty and appears no little more than a fine line, the diseased adventitia may form a swelling two or three times the thickness of the original wall. Where two arterioles with thickened adventitiae lie alongside of one another, it may still be possible to make out the presence of a lymph space between them lined with elongated endothelial cells. (Photos. 6 and). In other cases, however, where the swelling has been more

Photo 50. Section 41. (×120). From a case of senile insanity.
Small arteries showing a very thick hyaline adventitia, a.

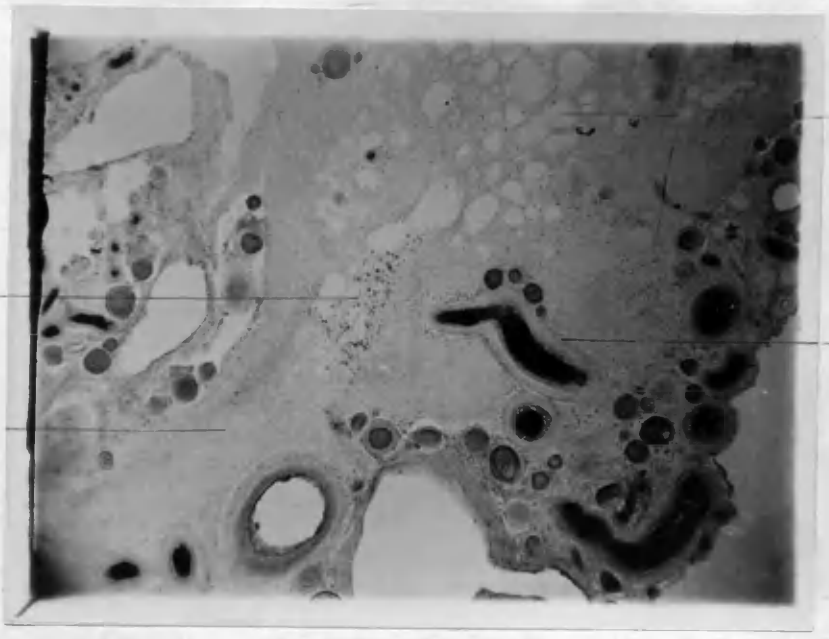


Photo 51. Section 42. (×26). From a case of senile insanity.
a. Very thick hyaline adventitia of a small artery, with marked proliferation of the endothelial cells immediately outside it.
b. Normal arrangement of spaces & trabeculae.
c. Obliteration of spaces from thickening of the trabeculae
d. Very numerous endothelial cells affected with pigmentary degeneration.

extensive, this space becomes quite obliterated by the blending of the two adventitiae, which here and there an elongated cell shows up to indicate where a channel or sinus has been. This thickening is often irregular, and frequently leads to considerable distortions of the vessels. When the hyaline swelling is regular there is very little alteration in the calibre of the vessel, but irregular and nodular swellings invariably lead to serious narrowing of the vessel tubes. The adventitia never becomes much thickened, without the muscular coat showing similar degenerative changes; indeed the whole three coats are frequently more or less involved. (Photos. 50 & 51, Sections 41 & 42).

Hyaline Degeneration of the Muscular Coat.

The muscular coat, as a rule, is only involved secondarily to a hyaline degeneration of the intima, the explanation of this being that the media derives its nourishment from the interior of the vessel, and not from without as in the case of the adventitia. This sequence of events may be traced very frequently, though here and there the media appears to degenerate without any previous hyaline thickening of the intima. (Section 43). In such cases, however, it is frequently found that in adjoining parts of the same vessel or in neighbouring vessels,

the intima is thickened and hyaline. Probably in all cases of hyaline degeneration of the media, there is first of all a similar change in the intima. In cases where such a change cannot be demonstrated, we are warranted in assuming the presence of a chemical alteration in the constitution of the connective tissue fibres. Such chemical change in all probability precedes the more evident structural one, and this is all that is required to interfere with the normal process of osmosis. A chemical barrier of hyaline structure is interposed between the media and its nutritive supply, and thus is brought about a starvation of the muscular fibres, leading to a subsequent degeneration.

The degeneration consists firstly in a swelling up of the muscular fibres, and in Eosine and haematoxylin preparations the nucleus is well stained and is surrounded by clear swollen protoplasm with no affinity for Eosine. Then the nucleus gradually loses its tendency to stain deeply with haematoxylin, while the muscular protoplasm shows an increased affinity for Eosine. By degrees the outlines of the muscle cells are lost, and a homogeneous mass results staining faintly with Eosine. Frequently instead of this homogeneous layer, a finely granular appearance is produced from the presence of numerous Eosinophile granules in the muscle cell plasma, and this may occur before total

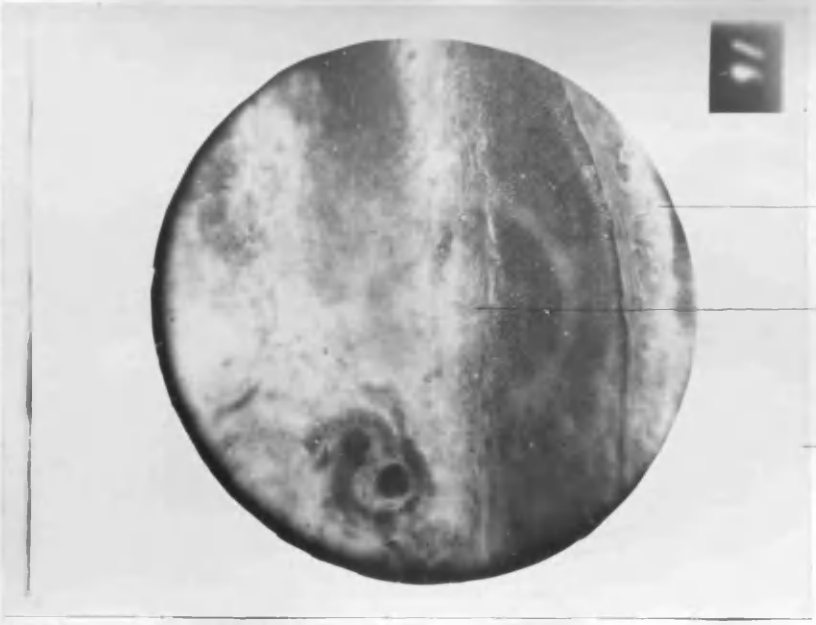


Photo. 52. Section 44. Small artery, the internal and middle coats of which are affected with hyaline degeneration. From case of senile ins.,
a. Intact elastic lamina, underneath which is seen the thickened hyaline intima finely fibrillated.
b. Elastic lamina forming loops extending into and beyond the adventitia; no muscle nuclei are seen here.
c. A few muscle nuclei beyond the hyaline intima. (× 130).

Photo. 53. Section 45. Small hyaline artery. (× 130). From a case of senile insanity.
a. Intima swollen, homogeneous, and staining deeply with eosine. Many of the muscular cells show nuclear staining, but muscle protoplasm contains numerous eosinophile granules.
b. Intima converted into fibrous tissue. Elastic lamina somewhat thickened. No nuclear staining seen in media, which is hyaline and coarsely granular.

disappearance of the nucleus. In osmic acid preparations, it is found that some of these granules are of a fatty nature, for they become distinctly darkened by this reagent. (Photos 52, 53 and others Sections 44, 45 and others).

Hyaline Degeneration of the Intima.

The intima appears normally in the arterioles, when cut longitudinally, as a thin band of tissue covered by endothelium, between the lumen of the vessel and the muscular layer; while close to the latter can be made out, even in the smaller arterioles, a delicate elastic lamina.

The intima rarely becomes so much thickened and swollen up as the adventitia. Such thickening, when it occurs, consists of a homogeneous hyaline mass, which is very irregular on its external surface, dipping down into the degenerated muscular layer, and pushing the elastic lamina before it.

In no case, so far as I have seen, does the elastic lamina itself undergo this hyaline change. When present, it continues to separate the intima from the media, dipping down into the latter, and forming in its numerous loops in order to fulfil its purpose. Wherever the elastic lamina projects into the media, no muscle cells can be seen, though between the loops the muscle may retain its affinity for nuclear stain, and, therefore, its vitality. Into places where the muscle appears healthy,

Photo. 54. Section 42. Small artery in longitudinal section all coats hyaline. (× 240). From a case of senile insanity. a. Several layers of elastic tissue showing increased tortuosity, intima much thickened, the media has disappeared, and elastic lamina projects far into a hyaline adventitia. b. Remnants of muscular coat, showing nuclear staining. c. Recent haemorrhage into thickened hyaline intima.

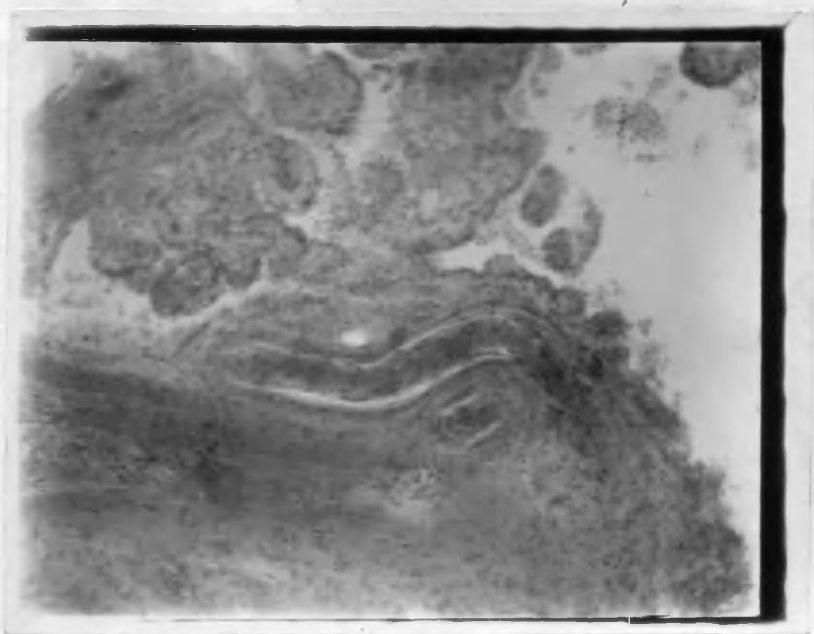


Photo. 55. Section 44 A. Arteriole from a case of senile insanity. (× 120). Well marked space between endothelium and thickened hyaline intima.

the elastic lamina and thickened intima have made no inroads. Therefore it may be assumed that the presence of points of diminished resistance has something to do with this occurrence. (Photos. 52 53, and 54. Sections 44, 45 and 42).

In the intima this hyaline tissue may be invaded by cells and be converted into fibrous tissue, so as to present all the appearances of an endarteritis obliterans. In some cases the cellular infiltration is very abundant, while in others again remarkably few cells are seen, only an odd one here and there showing up between the thick fibrous tissue fibres.

When the hyaline material has been replaced by new formed fibrous tissue, the arterioles show a narrowed and irregular lumen. This narrowing and distortion in some cases is extreme and actual occlusion may be brought about. The latter condition is, however, sometimes due to thrombosis occurring in the altered vessel. In photo. 26 and sections 22 and 43 the occlusion of these hyaline vessels seems to have been brought about in this manner, the thrombus likewise acquiring a homogenous hyaline appearance.

When the intima has been converted into fibrous tissue there is found lining the wall of the vessel next the lumen a single layer of endothelial cells, and lying between this and a more or less degenerated muscular coat, is a certain amount of fibrous tissue, with round, oval, or spindle cells

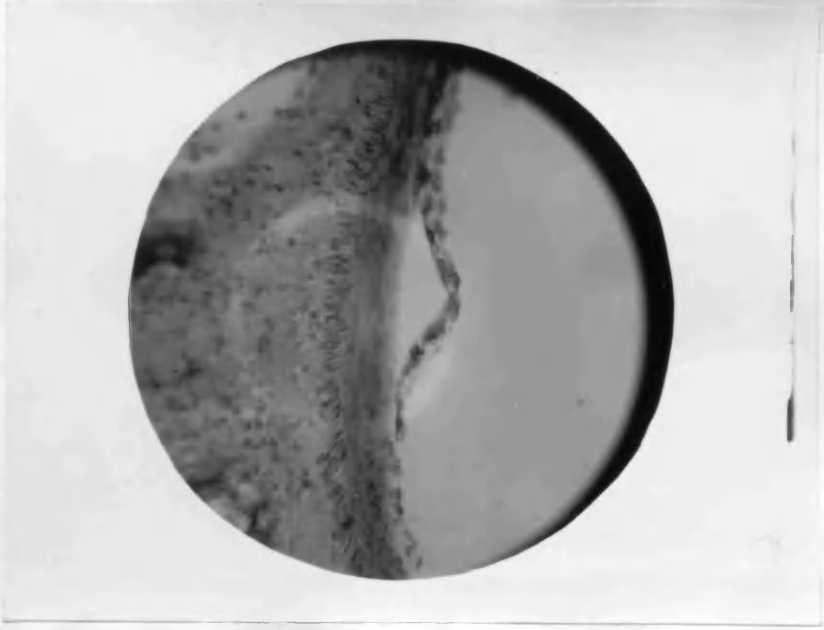


Photo 56. Section 44 B. (×130). From a case of senile insanity. Small artery, showing spaces between endothelium and hyaline-fibroid intima. Elastic lamina in many places dips down into the media. (This is a longitudinal section).

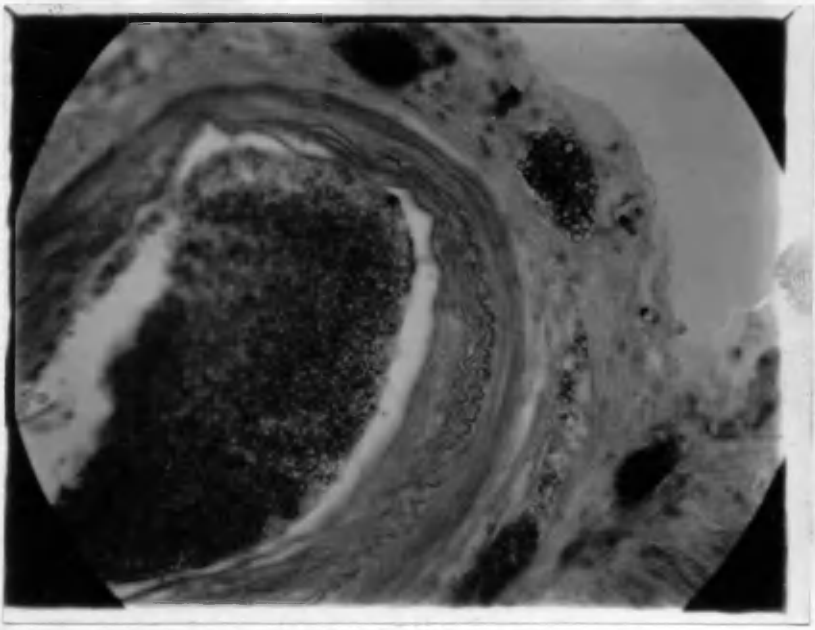


Photo. 57. Section 30. Transverse section of a small artery. (×240). From a case of dementia. Intima is greatly thickened, and contains several layers of elastic tissue. Four layers can be counted almost all round.

between the fibres. Spaces too are often seen in the thickened intima, and these may or may not contain cells.

The endothelium is frequently raised up from the thickened intima, leaving a space which contains no formed elements. Such a separation may also occur between a thickened intima and degenerated muscular coat, and likewise between a degenerated media and thickened adventitia.

W. F. Robertson[D] thinks that these spaces are not altogether artificial, though perhaps exaggerated by bichromate hardening. They are filled with a clear fluid in which Robertson has occasionally seen a few leucocytes.

In my experience these spaces were met with as frequently in celloidin sections, as in those cut by the dextrine freezing method, so they are evidently not produced mechanically. (Photos. 55 and 56, Section 44A and 44).

Mixed up with this fibrous tissue, especially when the thickening of the intima is considerable, may be seen elastic fibres or bundles. In transverse and longitudinal sections of some vessels it is possible to make out two, or three, or more elastic laminae, separated by fibrous tissue and a few cells. (Photos. 54, 57 and 58. Sections 42, 30 and 45). In other cases it looks almost as if the entire thickening was due to a hypertrophy of the elastic lamina, with only a few cellular

D. Robertson, W. F.:- "Edin. Med. Journal", 1896 January.

Photo. 58. Section 45 A. Arteries showing hyaline - fibroid change. (× 120). From a case of mania.

a. Thickened and greatly twisted elastic lamina.

b. Several layers of elastic tissue in the thickened intima.

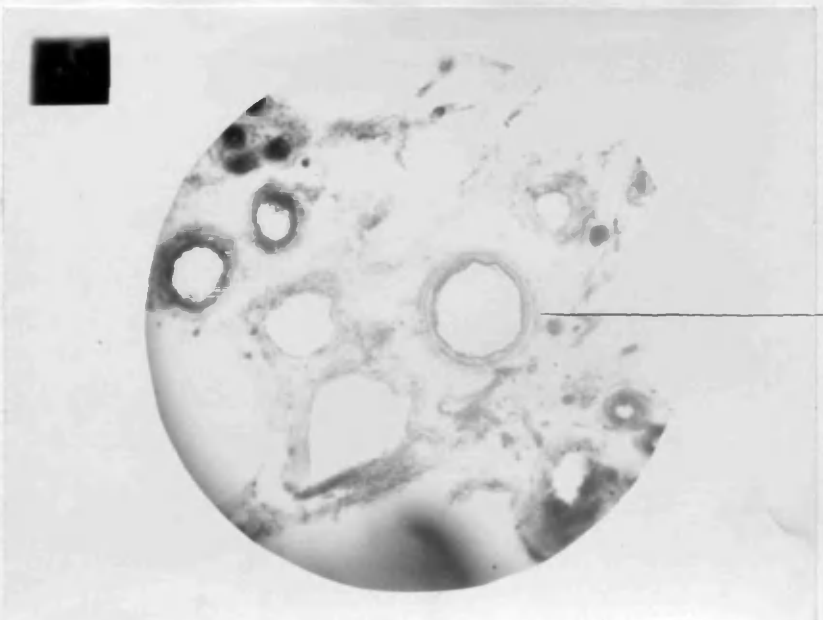


Photo. 59. Section 46. (× 36). From a case of senile insanity.

a. The intimal thickening of this artery consists almost entirely of elastic tissue.

elements separating the different layers. (Photo. 59 section 46). The wavy course of the elastic lamina becomes still more wavy, and, so far as I can see, shows no tendency to become straightened out and to lose its undulations, as Carl v. Rad[1] has found it in syphilitic endarteritis. Its sinuosity is very markedly increased, and in longitudinal sections it loses the character of a straight band, dips into the muscular layer, and may even project far beyond into the adventitia. (Photo. 54 and others).

It is often possible to make out that the several different layers of elastic tissue become continuous with one another, forming eventually, maybaps only at one spot, the single normal elastic lamina. The secondary laminae present the same exaggerated sinuosity of the original one, but are thinner, though by no means invariably so.

In this connection Carl v. Rad[2] states that, "while the original elastic lamina may become straightened out, the secondary elastic lamina shows through normal regular folding, but is in comparison smaller than the old."

I am therefore slightly at variance with the opinion of the above mentioned author.

1. Carl v. Rad :- "Ueber einen Fall von juvenilen Paralyse auf hereditär-luetischen Basis mit specifischen Gefässveränderungen," "Archiv f. Psych. und Nervenkrankheiten." 1898. Band 30. Heft. 1. p. 86.
2. Carl v. Rad :- same paper p. 97.

The elastic lamina is described by Schäfer[1] as formed of elastic tissue, which occurs in longitudinal networks of fibres, consisting of one or more layers of different degrees of closeness.

Under normal conditions, in any of the arteries in the choroid plexus, the elastic lamina appears as if composed of a single layer of elastic tissue; this layer varying in size with that of the artery. Still, it may be possible that, even here, the elastic lamina is made up of two or three layers, though such cannot be demonstrated.

That the extra elastic laminae owe their origin to a transformation of these layers by new formed tissue, as held by Carl v. Rad[2] and Rumpf[3] seems not at all unlikely. Thus two elastic laminae are explained by the division of the primary layer, and three by a further division of the secondary lamina, and so on.

But it seems to me that the process, though perhaps in part, is not altogether a mechanical one, for there is no doubt that in many cases the elastic lamina is very distinctly hypertrophied. It becomes thickened and lengthened, so that its normal sinuosity is much increased. This great sinuosity, moreover, is not produced after death.

1. Schäfer:- "Quain's Anat.", 1896. Vol I, Part III. p. 363.
2. Carl v. Rad:- "Archiv für Psychiatrie", 1898. p. 97.
3. Rumpf:- "Die syphilit. Erkrankungen des Nervensystems". 1887.

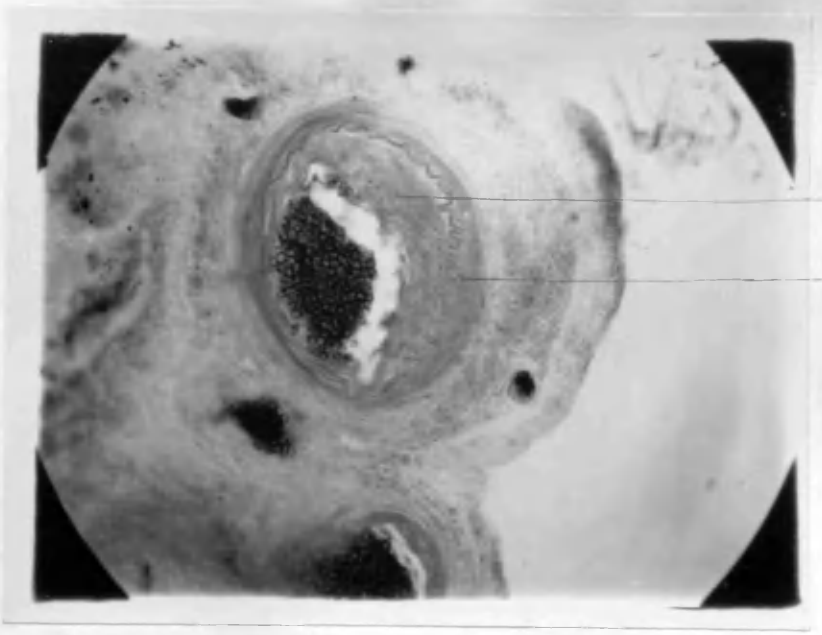


Photo. 60. Section 47. Hyaline-fibroid artery. (× 240). From a case of senile insanity.

a. New-formed elastic lamina under the endothelium of this greatly thickened intima.

b. Thickened elastic lamina.

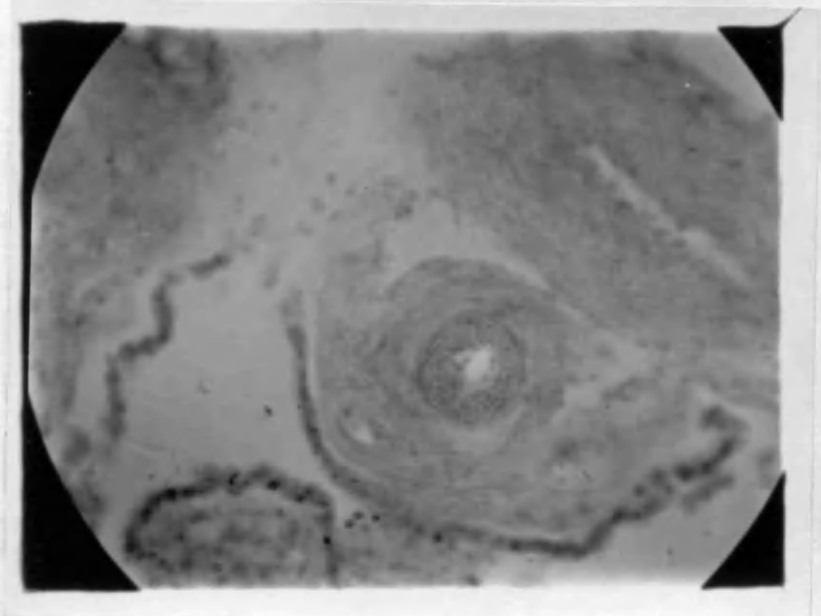


Photo. 61. Section 48. (× 240). From a case of senile insanity.

Arteriole with a very much hypertrophied single elastic lamina. Not much else besides this greatly twisted elastic lamina in the thickened intima. Endothelial layer is nowise distorted.

for there is no associated distortion of the intima or endothelium. If the elastic lamina did not play an active role, the thickened intima would tend to obliterate the normal winding, making it in part quite straight, as Carl v. Rad describes in the basilar arteries of the brain. Such, however, is not the case as found in the smaller vessels of the choroid plexus. Moreover, this view of Rumpf and Carl v. Rad does not explain the fact, that in some cases the new formed elastic lamina lies immediately under the endothelium. (Photo. 60. Section 47).

In reference to this condition Heubner[1] advances quite a different explanation, which is very important and merits consideration. "When the endothelium is no longer caused to proliferate cells from syphilitic irritation, its normal function begins, which it possessed at the time when the artery became thickened: it forms a fenestrated membrane over the new formed tissue, as it formed the same in young organisms over the muscular layer."

This further explanation of Heubner has more lately been supported by Löwenfeld,[2] and appears to me to be in accordance with the facts.

1. Heubner :- quoted by Carl v. Rad in "Archiv f. Psych" 1898. p. 97. "Die luetischen Gefässerkrankungen...", 1874.

2. Löwenfeld :- "Studien über Ätiologie und Pathogenese der spontanen Hirnblutungen", 1886. p. 47

Frequently, as already mentioned, a layer of elastic tissue may be seen immediately under the endothelium, and separated a considerable distance by new formed tissue from the original elastic lamina. Moreover, though sometimes the continuity of this superficial layer with the deeper one can be made out, in other cases no such connection can be traced. The only way to account for its presence then, is to assume, as Heubner does, that the endothelial cells may again become possessed of that power of forming elastic tissue, which they had in the embryo.

Though Heubner is only writing of syphilitic disease of the vessels there is no reason why we should not apply his arguments to the vessel change under consideration, more especially, in the light of the opinion expressed by him in this same work, that "there are no certain histological criteria for deciding on the presence of syphilis."① Both are chronic processes and present a more than close resemblance in their later histological details, while it is more than likely that here also there is some chronic irritant at work.

While hypertrophy of the elastic lamina is the condition most frequently associated with the hyaline-fibroid change, it is not invariably the case. The elastic lamina may be broken through in parts or even be absent altogether.

① Heubner:- quoted by Ziegler "Pathology", 1884, Section II Art. 295. p. 69.

while explaining the increase of the elastic lamina in some, do not do so in all cases. There occurs now and then a very distinct hypertrophy of the fenestrated membrane with little or no proliferation of the endothelial cells, and Löwenfeld[1] describes one such case

In photo. 61 and section 48 is a small arteriole with a greatly thickened intima and narrowed lumen. This intimal thickening is composed almost entirely of a very tortuous elastic lamina. There is no division of the elastic lamina in this case, and very few cells and a remarkably small amount of fibrous tissue are seen between the different folds. That this appearance has in no way been artificially produced is shown by the even distribution of the endothelial layer.

From a consideration of this and similar cases, I am forced to the conclusion, that there must be some inherent vitality in the elastic lamina itself, and that under certain circumstances it is capable of proliferation and growth.

Dilatations and Aneurysms of the Arterioles.

Narrowing and even occlusion of an artery or arteriole, as shown already, may be brought about, by the hyaline change itself or by the

[1] L. Löwenfeld:- "Spontane Hirnblutungen", p 50

subsequent reparative processes added thereto. But this is not the only alteration that may result. Lacculations and dilatations of the vessels, and even miliary aneurysms, may occur; and, without doubt, are closely related to and dependent on hyaline degeneration in the vessel coats.

Little fusiform dilatations or saccalations are frequently met with, and seem to be as common in the vessels of the choroid plexus as in the meningeal stems, and the little twigs supplying the basal ganglia.

The arteriole shown in photo. 62 and section 49, may be taken as a fairly typical example of what Löwenfeld calls "die Rosenkranzform des Muscularisrohres", from its resemblance to a rosary; and it may be seen that the little saccalations are not unlike a string of beads. As this arteriole, moreover, illustrates most of the points in the production of such a rosary, it may be permissible to describe it somewhat minutely.

There is throughout a mild degree of degeneration and hyaline thickening of the intima, and this, though slight, has been sufficient to interfere with the nutrition of the muscular layer. In parts the muscular cells have lost their affinity for nuclear stains, and present a highly granular appearance, or they are swollen, pale, and homogeneous.

O. Löwenfeld :- "Spontane Hirnblutungen", p. 64.

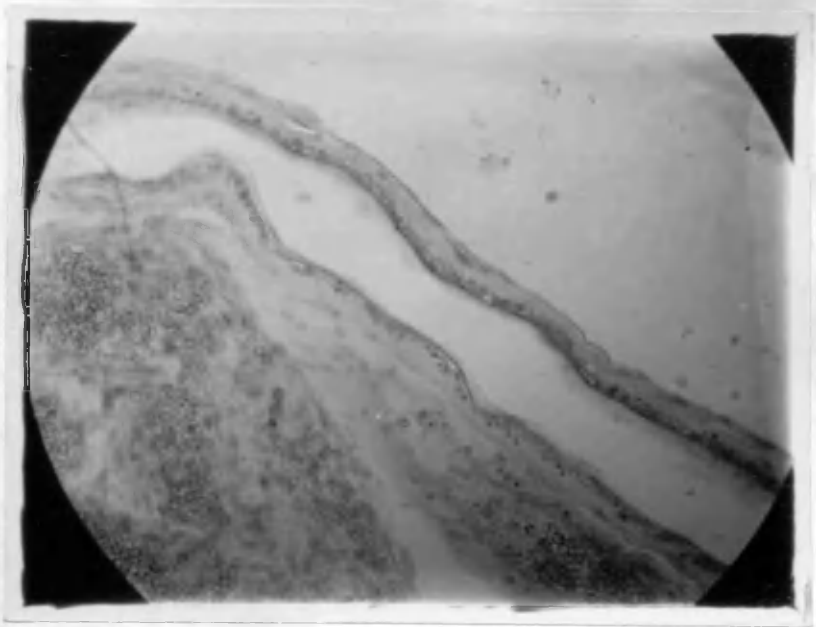


Photo. 62. Section 49. "Rosenkranzform" arteriole. (×240). From a case senile insanity. There is considerable hyaline thickening of the adventitia. Slight hyaline thickening of intima. At points of dilatation the nuclei of the muscular fibres have lost their affinity for haematoxylin.

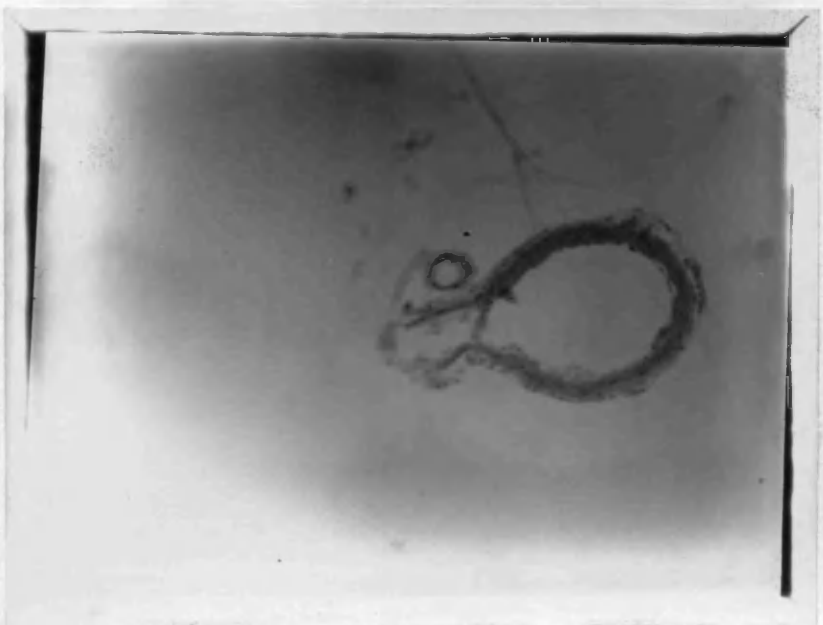


Photo 63. Section 51. Miliary aneurysm. (×120). From a case of senile insanity. In the dense fibrous tissue composing the aneurysmal wall the nuclei of the cells are large in size and oval in shape.

(where this degeneration of the media is most marked the vessel has yielded to the pressure of the blood, leading to the formation of a little fusiform dilatation. Moreover, in those parts where saccculation has occurred, it may be noted that the thickening of the adventitia — likewise hyaline in this case — is less marked, while at the one point where the vessel presents a narrowed lumen this thickening is more extreme.

In the above case there can be no doubt that the dilatations occurred as described, but Löwenfeld [1] states that, "apparent dilatations of the muscular tube not seldom exist in separate tracts of the vessel, through unequal contraction of the muscle fibres." I am in a position to confirm this observation of Löwenfeld, having seen many times, not only in man but also in the sheep and ox, examples of this apparent dilatation, unassociated with degeneration of either the intima or media. (Photo. 7 and Section 4).

In other cases a nodular swelling of the adventitia may produce a localised fusiform swelling of the vessel, and such may be mistaken for a dilatation or an aneurysm. But with this condition there is no increase in the size of the lumen, in fact a narrowing as a rule occurs. These are evidently what

[1] O. Löwenfeld :— "Spontane Hirnblutungen", p. 65.

Kronayer[1] has described as "pseudo-aneurysms". (Section 50).

On reviewing the pathological appearances of this hyaline fibroid change, we may conclude that the greater the amount of hyaline material formed in the intima, the greater is the degeneration of the muscular coat, and the liability to dilatation. On the other hand, however, the facts show that the liability to dilatation is not in direct ratio to the hyaline thickening. Such hyaline material may become so thick and dense — this result may be attained by transformation of the hyaline into fibrous tissue — as to compensate for the loss of the muscular coat, and prevent the occurrence of dilatation. This thickening, when carried beyond a certain point, leads to narrowing and even occlusion of the vessels; in other cases again, pseudo-aneurysms are formed. A very large proportion of the cases examined showed evidence of chronic Bright's disease, and the increased blood pressure in this condition must have been an important factor in the production of these dilatations.

While the small fusiform saculation is the type of dilatation more commonly present, distinct miliary aneurysms, similar to those met with in the meninges are found. In the

[1] Kronayer:- "Ueber miliare Aneurysmen und colloide Degeneration im Gehirn", 1885.

meninges this condition most frequently exists in senile cases, and W. T. Robertson[1] found miliary aneurysms in five out of twenty-five such cases examined.

I have only come across two undoubted examples of miliary aneurysm, but in one other case found appearances, which, though not conclusive, were very suggestive of this condition. I must infer therefore that the occurrence of miliary aneurysms in the choroid plexus is somewhat rare.

I will describe this miliary aneurysm, in section 51, somewhat in detail. It is unfortunately incomplete, the section being such as to show only one vascular tube running into it. At first sight it might be taken for a larger vessel giving off a smaller branch, but, on examining it more closely, there is no doubt as to its aneurysmal nature. The small arteriole entering it is cut longitudinally. It is composed of an endothelial layer, a slightly thickened hyaline intima, and a single layer of muscular cells, beyond which is a loose areolar tissue with a few round cells. On one side of the arteriole the muscle nuclei stain well, while on the other side no nuclear staining is seen, and the muscle protoplasm appears degenerated and coarsely granular.

[1] Robertson, W. T.:- "Pathology of the Nervous System in Relation to Mental Disease," "Edin. Med. Journal", 1896. p. 630.

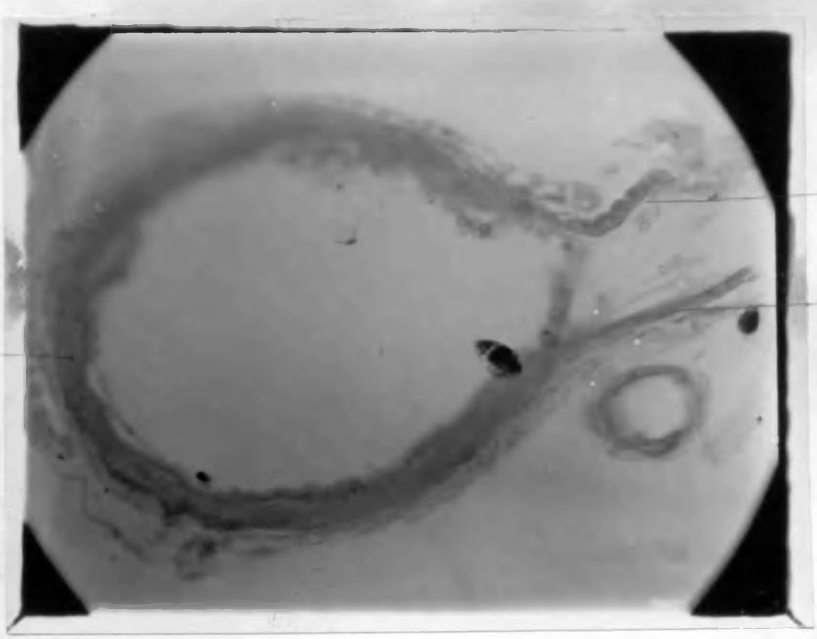


Photo. 64. Section 51. Miliary aneurysm. (× 240). From a case of senile insanity. a. Slight hyaline thickening of intima, media is fairly healthy. b. Media here is degenerated and hyaline. c. Dense fibrous tissue wall. Endothelium separated up from underlying fibrous tissue. Few round cells in loose tissue beyond.

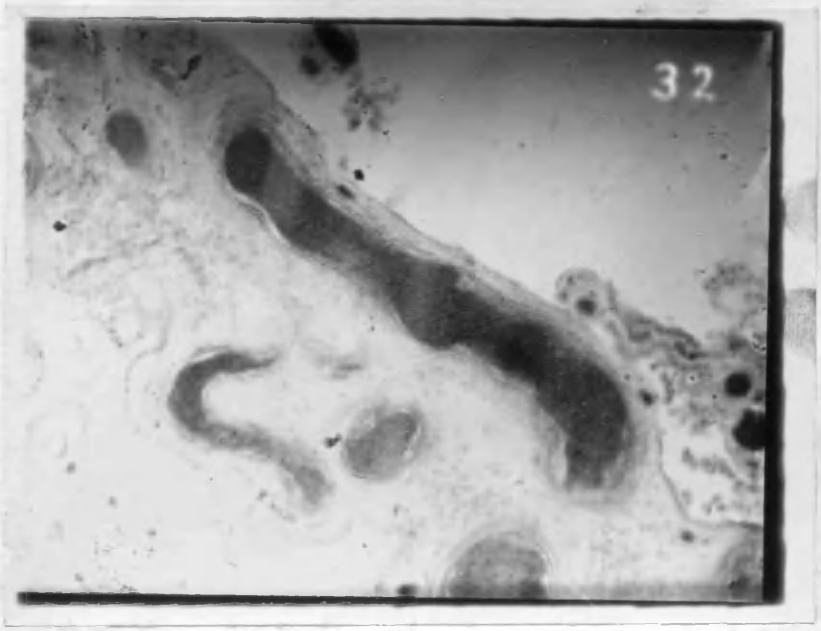


Photo. 65. Section 51. "Rosenkranzform" arteriole. (× 120). From a case of senile insanity.

This hyaline media and slightly thickened intima run into and are continuous with a dense layer of fibrous tissue, which constitutes the greater part of the aneurysmal wall. Scattered through this thick fibrous tissue are a few cells, round and spindle-shaped — mainly the latter — but nothing is seen to suggest the presence of muscular tissue. The endothelial layer may be traced practically all round the aneurysm, and is separated up at one point from the underlying tissue forming a space. No distinct elastic lamina can be seen. Beyond the dense fibrous tissue is a looser areolar layer, studded comparatively richly with round cells. (Photos. 63 and 64).

The course of events has evidently been as follows. In the first place a slight hyaline degeneration of the intima has occurred. So minute is the thickening in the arteriole, that we must infer the nature of the change to have probably been more of a chemical than a textural one. This would bring about hyaline degeneration of the media, and such is noted in the arteriole itself. In this way the very best conditions for dilatation would be provided, viz. degeneration of the media and an almost total absence of any compensatory intima-thickening. A "Rosenkranzform" dilatation would be first of all produced, and an example of this is seen

in the same section close by. (Photo. 65. Section 51). Following on this the development of such an aneurysm must have been gradual, allowing sufficient time for a reparative process to take place in its wall. This would be brought about first of all by the proliferated endothelial cells invading the hyaline mass, till a condition of endarteritis would be produced. Probably a round-cell infiltration also took place from without, as is evidenced by the remains of such beyond the fibrous tissue. But the growth of the aneurysm would not be arrested here. As long as the tissue was incompletely formed dilatation would go on, and would only cease with the complete conversion of the granulation into fibrous tissue.

This case proves conclusively that these miliary aneurysms are true aneurysms, and not merely, as Eppinger[1] holds, examples of ectasis or dilatation in which all the coats of the vessel are present.

Charcot and Bouchard[2] say that miliary aneurysms are the result of a diffuse periarteritis, the first stage of which is characterised by a multiplication of nuclei in the outer coat of the vessel. This inflammatory condition causes atrophy of the muscular layer, and so renders the vessel wall liable to yield to

1. Eppinger:- "Archiv f. ~~Klinische Med~~ Path. Anat." Bd. CXI. 1888.

2. Charcot and Bouchard:- "Arch. de phys", 1868.

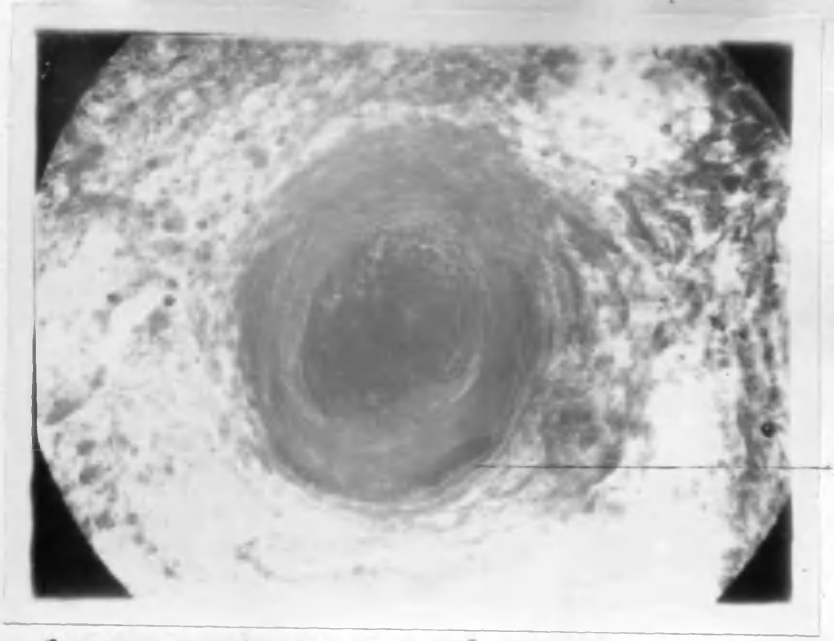


Photo 66. Section 52. (× 240). From a case of senile insanity.
Small artery in which all the coats are hyaline, and at 'a' in a very thick hyaline adventitia is seen a capillary.

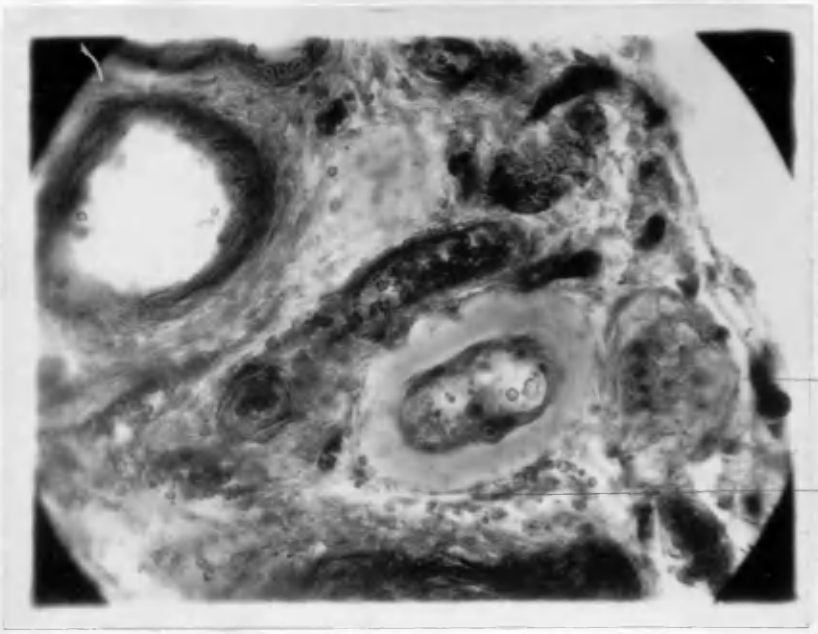


Photo. 67. Section 25. (× 240). From a case of alcoholic insanity.
a. Vessels with very thick hyaline walls.
b. Hyaline vessels occluded by a proliferation of its endothelial cells.

the blood pressure. In the later stages the excess of nuclei disappeared, and the vessel became thickened and fibrous. It was in the early stage alone that it tended to dilate.

I do not think that this view of Charcot and Bouchard can be borne out, and Robertson[1] and Löwenfeld[2] are of like opinion. Around the "rosary form" of artery (undoubtedly the precursor of miliary aneurysm) there is always a complete absence of periarteritis.

So far as my experience goes, vascularisation of either the hyaline or fibrous thickenings does not occur to any extent. In photo. 67 and section 52 a new formed capillary is seen in the thickened adventitia. Such a condition is found not infrequently, but never have I seen new vessels in the thickened intima of the arteries and arterioles found in the choroid plexus.

Such narrowing and obstruction of vessels always lead to the compensatory formation of new vessels or capillaries, and such in all probability exist here. But on this point one cannot dogmatise, for the vessels of the plexus are everywhere very numerous, and, unless in the villi, present no regular sort of arrangement. Thus aberrations from the normal type could not easily be detected; and, moreover, there is nothing

① Robertson, W. F.:- "Edin. Med. Journal," 1896, p. 629.
② Löwenfeld:- "Spontane Hirnblutungen," p. 65.

in the minute structure to distinguish the original capillaries from those more newly formed.

Haemorrhages are occasionally found, and more frequently haematoidin granules. The former are never large in size and occur in cases presenting well marked hyaline changes. These are the cases, besides, in which new formation of vessels would be most likely to occur — and it has been shown that this new formation regularly occurs in the dura mater and pia-arachnoid — and in all probability a rupture of one of these accounts in many instances for the haemorrhage. In photo. 54 and section 42 there is seen a haemorrhage occurring in a hyaline vessel. The extravasated blood is small in amount, and in this particular section, though invading the intima, has not yet penetrated beyond the hypertrophied elastic lamina.

Hyaline Degeneration of Veins and Capillaries.

This hyaline change may also attack the veins and venules. Their fibrous tissue walls become swollen up and eventually replaced by a layer of hyaline material. This is frequently associated with a well marked hyaline degeneration of the connective tissue fibres in the neighbourhood of the vein. The thickening is never very extensive, but the spaces so frequently

seen in their walls become obliterated. The endothelium remains intact on the inner surface. (Section 53).

More serious are the results of this condition when the venules and capillaries are affected. Their delicate walls become thickened and stain a faint pink colour with Eosine.

Oeller [1] describes a preliminary proliferation of the endothelial cells, subsequent to which the hyaline thickening occurs.

Whether such is really the case I cannot say, but there is no doubt that an increase of the endothelial cells is frequently found along with the hyaline thickening; and these two conditions very often lead to obliteration of the capillaries and venules. Probably in some cases, though by no means in the majority, this obliteration is actually brought about by thrombi forming in the altered vessel, these thrombi after a time likewise assuming a hyaline appearance. Cells on the hyaline cords may lose their homogeneous character and become distinctly fibrillated. In the villi too, either alone or associated with hyaline degeneration of the homogeneous tissue around, they may form what are remarkably like hyaline concentric bodies, which structures, as already shown, frequently owe their origin to hyaline venules also. Dilatation of hyaline capillaries is said by Robertson to occur very rarely, and such

[1] Oeller:- Ziegler's "Path. Anat.", Sect II. Art 288.

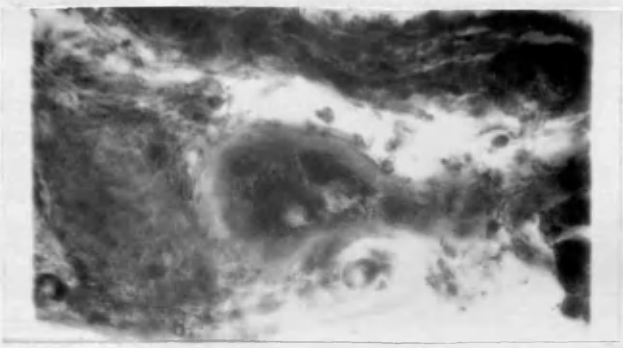


Photo. 68. Section 54. Small dilatation on a hyaline capillary. (× 240). From a case of phthisical insanity.

There is some proliferation of the endothelial cells in the little dilatation.

I have seen on only a very few occasions. (Photos. 67, 30 and 68. Sections 25, 26 and 54).

Pathological Considerations.

This condition of hyaline-fibroid change or "arterio-capillary fibrosis" was first described by Gull and Sutton[1] in 1872 in cases of "chronic Bright's disease"; these authors making use of the results of the former for their researches. "But," as Professor Coats[2] informs us in his "Manual of Pathology," "there are many very competent observers who, after careful investigation, have denied its existence altogether." As many or more authorities on the other hand, have demonstrated that such a change affecting all the vessel coats does exist, either with or apart from chronic kidney trouble. Further the appearances described are not sufficiently explained by the theory that they are produced by the action of certain reagents.

What then is the actual nature of this hyaline-fibroid change when occurring in the intima. Zenker[3], Eichler[4] and I. I Brown[5].

1. Gull and Sutton:- "On the Pathology of the Morbid State commonly called Chronic Bright's Disease", 1872.
2. Coats, J:- "Manual of Pathology", 1883, p. 703.
3. Zenker:- "Tageblatt der Leipziger Naturforscherversammlung" 1872
4. Eichler:- "Archiv f. Klinische Med.", Bd XXII
5. Brown, I. I.:- "Journal Mental Science", 1886 p. 327

are of opinion that it is of an atheromatous character. Robertson[1] holds much the same notion, and states that the hyaline change is merely the first stage of atheromatous disease in these minute arterioles. "This view," he adds, "is indeed strongly supported by the fact that the subsequent formation of fibrous tissue is much greater than one would expect to find in a merely reparative process, and, therefore, distinctly points to the occurrence of a chronic inflammatory one."

When the hyaline intima has been replaced by fibrous tissue, the appearances are such as pathologists would, and have called, endarteritis obliterans. There is, however, no strict distinction between atheroma or endarteritis deformans and endarteritis obliterans. They are more than closely related to one another, and it almost seems as though an endarteritis obliterans was the mode whereby atheroma expressed itself, when it attacked the smaller arteries or rather arterioles. In atheroma, moreover, a hyaline swelling of the connective tissue fibres of the intima constitutes one of the first stages, according to Ziegler.[2] But while fatty degeneration is the rule in atheroma, it is the exception in endarteritis obliterans.

The hyaline degeneration of the intima is the first occurrence in this hyper- - fibroid change. Then this thickened intima becomes

1. Robertson, W. F.:- "Edin. Med. Journal," 1896, p. 619
2. Ziegler:- "Pathology", Section II. Art. 288.

invaded by cells produced by proliferation of the endothelial cells, and an endarteritic appearance is produced. Later these endothelial cells are converted into fibrous tissue.

Robertson's[1] idea is that leucocytes remove the hyaline material slowly, while the connective tissue corpuscles in the immediate vicinity proliferate and form new fibrous tissue, which gradually replaces the hyaline mass. On the other hand, however, Heubner, Löwenfeld and Woodhead[2] are of opinion that the cells, in the thickened intima of an endarteritic vessel, arise from proliferation of the endothelial cells lining the tube, and that these same cells eventually form fibrous tissue.

There seems every reason to suppose that the cells in question are derived from a proliferation of the endothelial cells. The majority of them present nuclei of the same large size and oval shape as those of the endothelial cells. Moreover, there is never any round cell infiltration around hyaline vessels. No more, as Löwenfeld[3] points out, can these thickenings of the intima be attributed in any way to the vasa vasorum: they must be quite independent of them, for these same thickenings are found in vessels which possess no vasa vasorum.

① Robertson, W.F.:- "Edin. Med. Journ." 1896. p. 623.
② Woodhead:- "Practical Pathology", 1885, p. 173.
③ Löwenfeld:- "Spontane Hirnblutungen", p. 47.

Some authors hold that fibrous tissue cannot be formed from endothelial cells, but that such does regularly take place has been conclusively proved by Metchnikoff[1] and others.

Probably, as already stated, even in the miliary aneurysms the cell invasion and fibrous tissue formation are due to the proliferated endothelial cells; and in this connection it was noted that, the majority of the cells between the fibres of connective tissue were of an endothelial like character, while the round cells beyond the fibrous area were not present in great numbers.

In conclusion then I would say, that I am at one with those authors who regard this hyaline-fibroid change of the intima as being of an atheromatous nature.

[1] Metchnikoff:- "Comparative Pathology of Inflammation" Translated by F. A. and E. H. Starling, 1893 pp. 190 and 191.

VII. Conclusion, Pathological Considerations.

I admit that I have not examined a sufficient number of choroid plexuses from the same to justify me in making any sweeping generalisations about their pathology in the insane. Still, it is a very significant fact that, in the six cases examined (apart from cysts, concentric bodies, and hyaline vessel changes in two cases), none of the pathological appearances, so regularly met with in the insane, were developed to any extent.

Before concluding it may not be out of place to try to determine why this disparity should exist, and, if possible, arrive at an explanation for the frequency of these changes in the insane.

The pathological appearances in the pia-arachnoid are attributed by W. F. Robertson[D.] to abnormal, and, perhaps, in some degree irritative qualities of the arachnoid fluid. Continuing he says, "the morbid changes which so commonly occur in the envelopes of the brain in the insane are largely due to an abnormal trophic condition in some way associated with the morbid energizing of the organ which they enclose."

Can such an explanation be applied to the trabecular and endothelial changes in the choroid plexus? I am very decided in my opinion

D. Robertson, W. F.:—"Journal Mental Science", Oct., 1895.

think it can, and adduce the following reasons.

These pathological alterations are always developed to their greatest extent in the deep and more central parts of the glomus, which, though containing many large vessels, has a very poor capillary supply. The trabeculae in these situations are practically non-vascular structures, and must depend for their nourishment upon the fluid which circulates in the spaces between, and formed by them. This fluid is derived from the blood directly entering the choroid plexus, but also to a considerable extent from the lymph which has already supplied nourishment to the nerve cells and fibres and connective tissue elements of the basal ganglia, and more particularly the corpus striatum. At the same time this lymph has received from these structures their waste products, which flow into the spaces of the choroid plexus from the lymphatics around the vein from the corpus striatum and the numerous little vessel twigs connecting the plexus with adjacent structures and neighbouring pia-arachnoid.

"Now in insanity the cortical nerve cells and fibres show profound morbid changes, and it is, therefore, evident that the waste products of their metabolism must be abnormal. These will thus be introduced into the arachnoid fluid substances, which it is easy to understand may seriously affect the nutrition of the arachnoid tissues. We, indeed, need nothing more to

account for the histological changes described," (W. F. Robertson).

The morbid energizing of the cortex is amply proved by the presence of numerous degenerative changes in its different elements, but the same cannot be said of the corpus striatum. There are practically no facts to go on as to the alterations in the basal ganglia in the insane, though Bevan Lewis[1] mentions that atrophy may be general throughout the cerebral hemispheres, whilst the basal ganglia and mesencephalon escape implication; but, occasionally, the whole of the intracranial ganglia are involved.

The physiology of the corpus striatum, moreover, is imperfectly understood, and much difference of opinion exists as to its function, and even its relations to the cortex and the various nerve fibres passing through, or near it. It is, however, proved that, of the fibres passing to and from the cortex, some traverse the corpus striatum: further fibres actually take origin in the lenticular and caudate nucleus and pass down to the cord. On the other hand Wernicke maintains that these two nuclei are independent structures, receiving no fibres from the cortex, to which they are analogous in every way.[2]

1. Lewis, Bevan:- "A Text Book of Mental Diseases", 1889. p. 454.

2. Landois and Stirling:- "A Text Book of Human Physiology", 1888. pp. 650-652.

It is pointed out by Bevan Lewis[1] that there is a considerable proclivity to localised or focal softenings (due either to thrombosis, embolism, or to haemorrhage) in the substance of the basal ganglia in the insane, as well as in the mentally sound. "The caudate nucleus is far the more frequently affected, the optic thalamus comes next in frequency. The lenticular nucleus is somewhat less frequently involved than the optic thalamus, and last of all come the two capsules, and of these the inner shares the greatest immunity."

"Lesions in the nuclei of the corpus striatum only produce paralysis when the fibres of the internal capsule are involved. Sometimes there result vaso-motor paralysis; increased temperature of the paralysed extremities, at least for a certain time; anomalies of the pulse; and very various abnormalities of the cutaneous system."[2]

There is, therefore, nothing here to indicate that these nuclei have to do with the reception or generation of psychical impressions, unless the supposition of Goltz[3] be admitted — that every part of the brain is concerned in the functions of willing, feeling, perception, and thinking. At the same time we have Wernicke's[4] contention that these nuclei are analogous to the cortex and from them fibres proceed.

1. Lewis Bevan :- "Text Book Mental Diseases", p. 453.
2. Landois & Stirling :- "Text Book Physiology", p. 716.
3. Goltz :- Landois & Stirling " " p. 706.
4. Wernicke :- " " " " p. 652.

Granted that Goltz's opinion is correct, or that change in the cortex causes much the same alteration in the corpus striatum by a process of descending degeneration along the lines of function, we have an organ, which, in the insane, must also energize morbidly.

I do not think that this is assuming too much; for in senility there must be serious trophic changes in these nuclei, and when insanity is added to senility, or exists alone, it is hard to understand how the corpus striatum can escape from participating in the serious changes more or less affecting the entire nervous mechanism.

On these grounds, then, I would argue that the proliferative and degenerative changes are due to abnormal, and more than likely irritative, qualities of the fluid in the spaces of the choroid plexus.

That there must be an irritant to account for these numerous lesions seems undoubted, and, if not arising in the manner indicated, could still have another source. The choroid plexuses of the different ventricles are not only connected with one another, but they are directly continuous with the pia-arachnoid on the outer surface of the brain. The fluid in the spaces of the pia-arachnoid and choroid plexuses must thus commingle, and any irritant in the former would spread into and affect the latter.

There are, however, no facts to favour that the circulation of this lymph is from the pia-arachnoid to the choroid plexuses. Indeed, the opinion is that the flow is in a totally different direction, and most authorities agree that the Pacchionian bodies act as the excretory organs for this arachnoid fluid.

How far the vessel changes may be attributed to the same cause is doubtful, and at the same time it is an open question as to what extent they are produced by chronic Bright's disease.

Hyaline degeneration of the vessels is a very common feature in insanity, and though there is much conflicting evidence, the trend of opinion is that chronic Bright's disease is likewise common.

Of the six Western Infirmary cases examined, only two showed hyaline changes in the vessels. One of these was a case of chronic Bright's disease with cerebral haemorrhage and multiple brain softenings, while the other was a case of tubercular kidney in a patient who died under chloroform.

I have found this hyaline-fibroid change of the vessels, in a more or less marked condition in about eighty three per cent of the plexuses from the insane. In these same cases, if cysts and adherent capsule alone or together, be admitted as evidence of cirrhosis of the kidneys, more than half had chronic Bright's disease.

From these facts, then, we must infer the

action of another poison than urea on the vascular tissues of the insane, and much, I think, conclude that the abnormal and irritative fluid bathing these tissues, and produced by the morbid energizing of the subjacent nervous structures, plays a very important role in the causation of the vessel changes.

VIII. Table showing Frequency of Vessel Changes and Cysts.

Class of Cases.	No.	Hyaline fibroid changes.	All Coats	Intima and Media	Adventitia alone.	Dilatation	Cysts
Senile Insanity	17	17	17			7	11
General Paralysis	7	7	5	2		3	4
Phthisical Insanity	7	3	1		2	2	2
Mania	5	5	2	2	1		3
Delusional Insanity	4	3	1	1	1	1	2
Dementia	4	3	1	2			2
Alcoholic Insanity	4	4	4			1	3
Melancholia . .	3	2	2			1	3
Syphilitic Insanity	2	1	1				
Epilepsy	2	1	1				1
Adolescent Insanity	2	2	1		1	1	2
Puerperal Insanity	1						1
Climacteric Insanity	1	1			1		1
Total Number	59	49	36	7	6	16	35
Percentage in Insane		83%	61%	11%	10%	27%	59%
Western Infirmary cases	6	2	1		1	1	2

IX. Bibliography.

A. Literature of the Choroid Plexuses.

*Albarran, . . "Sur la structure d'un renflement situé au niveau du bord libre des plexus choroïdes des ventricules latéraux," 'Bull. Soc. Anat.,' 1886.

Ashby, H. . . "A case of bilious Carcinoma of the Plexus Choroides in a Boy three years of age," 'Medical Times,' vol II. 1884.

Arlidge, J. T., . "Observations on 'Brain Sand' and Amyloid Bodies," 'British and Foreign Med. Chir. Rev.,' 1854.

Benedikt, . . "Über die Innervation des Plexus chorioidens inferior," 'Canstatt's Jahresbericht,' 1873 and 'Schmidt's Jahrbücher,' 1874.

Beigel, ... "Cysts and Concretions of Choroid Plexus," 'Pathological Transactions of London,' vol XX. 1868.

Brown, G., . . . "Cyst of Choroid Plexus of Large Size in an Infant." 'Path. Transactions of London,' vol XXVII. 1876.

Cornil and Ranvier, "Pathological Histology," Translated by A. M. Hart, 1882.

Dejerine, A., . . "Anatomie des Centres Nerveux," 1895.

Faivre, ... "Les Plexus Choroïdes," 'Revue médicale de Paris,' 1854, and 'British and Foreign Med. Chir. Rev.,' 1855.

Foster, M., ... "A Text Book of Physiology," 1891.

Gamgee, ... "Cholesteomata of the Choroid Plexus of the Horse," 'Lancet,' 1859.

Gibson and Stewart, "Thrombosis of the Cerebral Sinuses Extending into the Choroid Plexuses and Cerebral Veins, with Clinical Notes of a case of the Disease," 'Edinburgh Hospital Reports,' Vol III 1895.

Haeckel, ... "Zur normalen und pathologischen Anatomie der Plexus choroides," 'Schmidts Jahrbücher,' 1860.

Nadh, Heinrich, . "Ueber die Kalkconcretionen in den Plexus choroides des menschlichen Gehirns," 1874.

Herringham, . . "Tumour of Brain, Cyst of Choroid Plexus," 'Illustrated medical News' 1888.

Hoffmann, . . . "Fall von Epilepsie mit cystoider Entartung der Plexus chorioicles," 'Archiv f. Path. Anat.' Bd. 25, 1862.

Hooper, R., ... "Morbid Anatomy of the Human Brain, being illustrations of the most frequent and important organic diseases to which that viscus is subject," 1826.

Hyslop, ... "Mental Physiology," 1895.

Koelliker, A., . . "Handbuch der Gewebelehre des Menschen," 1896.

Luschka, ... "Die Adergeflechte des menschlichen Gehirnes," 1855.

Moxon, W., . . . "Influence of the Circulation on the Nervous System," 'Lancet,' 1881.

* Müller, ... "Die Mechanik der Blut-circulation im Inneren des Schädels," 'Zeitschrift f. Psych.' 1860. 'British and Foreign Med. Chir. Rev.' 1860

Obersteiner, . . . "The Anatomy of the Central Nervous Organs", Translated by A. Hill, 1890.

Ogston, F., ... "Pathological Observations on the Bodies of known Drunkards", 'British and Foreign Med. Chir. Review', 1854.

Osborne, ... A communication to the Medical Association of the College of Physicians Dublin, to show that the choroid plexus is the organ of sleep. 'Lancet', 1848. Vol I..

Quain, ... "Calculous Particles from Choroid Plexus", 'Path. Transactions of London,' Vol III. 1851.

Schäfer, ... "Quains Anatomy" 1893. Vol III, Pt. I., and Vol I., Pt. II..

* Schnopfhagen, . "Die sogen cystöse Degeneration d. Plexus chorioidei d. Grosshirns." 1877.

Virchow, ... "Die krankhaften Geschwülste", 2me II.

Wallmann, . . "Colloidcyste im 3. Hirnventrikel, Lipom im Plexus Chorioides", 'Schmidt's Jahrbücher', 1860.

B. Literature dealing with Cerebral and General Pathology.

Alzheimer, . . . "Die Colloidentartung des Gehirns" 'Archiv f. Psychiatrie und Nervenkrankheiten', Bd. 30. Heft 1. 1898.

Carl v. Rad, . . "Ueber einen Fall von juveniler Paralyse auf hereditär-luetischer Basis mit specifischen Gefässveränderungen", Archiv f. Psych." Bd. 30. Heft 1. 1898.

* Charcot & Bouchard, "Arch. de phys." 1868.

Coats, J. . . . "A Manual of Pathology", 1883.

* Eichler, ... 'Archiv f. Klinische Med.', Bd XXII

* Eppinger, ... 'Archiv f. Path. Anat.', Bd CXI, 1888.

Gull and Sutton, . "On the Pathology of the morbid state commonly called Chronic Bright's Disease," 1872.

Heubner, . . . "Die luetischen Gefässerkrankungen", 1874.

*Kronmayer, . . . "Ueber miliare Aneurysmen und colloide Degeneration im Gehirn," Diss. Inaug. Bonn. 1855.

Landois and Stirling, "A Text Book of Human Physiology" 1888.

Lewis, Bevan, "A Text Book of Mental Diseases," 1889.

Löwenfeld, . . "Studien über Ätiologie und Pathogenese der spontanen Hirnblutungen," 1886.

Metchnikoff, . . "Lectures on the Comparative Pathology of Inflammation," Translated by F. A. and E. H. Starling, 1893.

Middlemass & Robertson, "Pathology of the Nervous System in Relation to Mental Diseases" "Edin. Med. Journal," April & May 1895.

Robertson, W. J., "The Pathology of Milkiness, Thickness and Opacity of the Pia-arachnoid in Insane," 'Journal Mental Science,' Oct. 1895.

"Researches upon the Pathology of Sub-dural Membrane Formation," 'Journal Path. and Bacter.' July 1896.

Robertson, W. F., "Morbid Conditions of the Intracranial Blood Vessels," 'Edin. Med. Journ.,' January and March 1896.

* Rumpf, . . . "Die syphilitischen Erkrankungen des Nervensystems", 1887.

Thoma, . . . "Pathology and Pathological Anatomy," Translated by A. Bruce. 1896.

Woodhead, . . "Practical Pathology," 1885.

* Zenker, . . . 'Tageblatt der Leipzigen Naturforscherversammlung', 1872.

Ziegler, . . . "A Text Book of Pathological Anatomy and Pathogenesis", Translated by MacAlister, 1884.

* Those works marked with an asterisk I have not read: I have only had access to quotations from them, made by various authors, British and Foreign.