SECTION 2.

PATHOLOGICAL.
SECTION 2. PATHOLOGICAL.

We now come to the consideration of the changes that occur in the lining membrane of the ventricles in diseased conditions of the brain; in other words, to the morbid Anatomy and Pathology of the Ependyma. We shall proceed on much the same lines as in the previous section.

It will be best to arrange this section according to the following scheme, viz:-

1. GENERAL CONDITIONS affecting the ependyma, including tumours, but excluding "granulations".
   a. Naked-eye appearances.
   b. Histological changes.
   c. Pathology.

2. The SPECIAL CONDITION known as the "granular" ventricle.
   Its histology, pathology, &c.

The frequent occurrence of granulations on the ependymal surface, and their close association with one disease in particular, merit their consideration separately and in detail. Clouston says (25.382) that in General Paralysis "there is no single tissue in the brain whose condition is so morbid as the epithelial linings of the ventricles."

1. GENERAL CONDITIONS.

a. Naked-eye appearances.

The ependyma has often a translucent oedematous appearance. This is seen in cases of extensive brain atrophy with enlarged ventricles and great increase of cerebro-spinal fluid. It may be associated with areas of
softening, the brain tissue immediately subjacent being soft, yellow, and disorganised.

Small hollow, puckered patches may be present in the ependyma; due, no doubt, to small soleroses and consequent contraction. They too, are frequently associated with softening, and always with extensive brain wasting elsewhere. This, and the previous condition, are usually seen in the walls of the lateral ventricles; softening in the floor of the fourth ventricle would seem to be somewhat rare, we have only met with it once or twice.

Sometimes in the 4th. ventricle the ependyma looks like a thin stratum of clear white jelly.

The ependyma may be macerated and disorganised. According to Wilks & Moxon (19.211) in acute hydrocephalus the ventricle walls may be quite diffuent and broken down, "shreds of the tissue hanging into the ventricles".

ROKITANSKY, referring (14.351) to the same disease, states that the lateral ventricle walls become "opaque, soft, and dissolved", and shreds appear in the effusion.

We have no experience of the ependymal condition in acute hydrocephalus.

In congenital internal hydrocephalus, according to Ziegler (11.226) the ependyma is "stretched". Whether there is ever any solution of continuity in the epithelium or not, he does not say.

The ependyma may be thickened, and opaque; and is often leathery and may be peeled off. This is often the case in long standing brain disease, in which there is
much wasting, with dilatation of the ventricles and accumulation of fluid. According to Flaggge (20.652), in chronic hydrocephalus, the "ependyma is generally thick, tougher than natural, and of an opaque white or grey colour." Rokitansky (14.965) says it is thicker than natural in old age. A.W. Campbell (40. Oct. 1894 633) refers to the membrane as being "generally thick" in the aged insane. It has been found thickened, in long standing cases of syphilis, by Barlow and Bury, (30. Syphilitic disease. 1261). In general Paralysis, Mickle says (30. General Paralysis 530), that it is "often thickened, opaque, or of swollen gelatinoid appearance, or congested, or tough." In cases of general Paralysis we have seen the ependyma shewing all the conditions described by Mickle. In epilepsy &c, where death is due to repeated congestive attacks, the membrane has often a pinkish appearance, due, no doubt, to the congested state of the vessels below it. Very often these vessels shew up dark and prominent through the ependyma in congested conditions.

In the lateral ventricles it is common to find adhesions between small portions of the adjacent walls where they come in contact. These adhesions vary usually from two millimetres to one centimetre in length, and are most frequently seen in the anterior part of the ventricle. They point to a probable localised inflammatory condition, which has resulted in a small area of union between two surfaces which are nominally normally very close together. It does not seem to be peculiar to any particular form of brain disease. Sometimes the choroid plexus in the lateral
ventricles becomes adherent to the ependyma over a small part of the surface, and forms a little vascular tumour. It is not a common condition; we have seen it several times. Sections of it, which we have examined, shew merely the structure of the choroid plexus.

Tumours of considerable size— as large as a pea, or larger — are sometimes seen growing from the ependyma. They do not seem to be of common occurrence. We only recollect having met with one, which was of a fibroid nature; it will be described later. Rokitansky (14.866) says "a few cases have been noticed in which flat, or rounded, or irregular modulated tumours of fibroid structure were developed in the lining membrane, independently, so far as could be traced, of any inflammatory process." Cornil and Ranvier (17.378) describe a papilloma situated upon the ependyma of the 3rd. ventricle and projecting into the lateral ventricle through the foramen of Monro; "a cauliflower-like growth formed of vessels more or less dilated" and covered with pavement cells desquamating. Moxon (27.1881.Vol. 528) describes a papilloma starting from the floor of the 4th. ventricle near its apex, and running upwards to touch the roof, almost completely closing the opening of the ventricle, and preventing the escape of the ventricular fluid.

Bristow states (21.1022) that "gliomatous tumours of minute size sometimes stud the ependyma of the ventricles. According to E. B. Fox (28.157), glioma of the floor of the 4th. ventricle may grow to the size of a cherry. We have
never met with gliomatæ in the ependyma. "Concretions which may occasionally form small psammomata are not rare on the ventricular ependyma", according to Obersteiner, (3.376). Similar conditions are certainly frequent in the choroid plexus. We have seen them occasionally in the lateral ventricle walls, forming small, hard, whitish, gritty masses. Rokitansky (14.366) says "In some few cases I have noticed here and there traces of a formation of bone in the fibroid products of inflammation attached to the ependyma; and in one well marked case delicate plates of bone were formed so extensively in a knitted (areolar) false membrane of that kind, that the lining membrane seemed to be encrusted with them." He further states (ibid) that "growths of a cancerous nature" occur on the ependyma but are "extremely unfrequent". We have seen malignant growths in the brain, which have spread to and involved the ependyma, but there was no indication that they had originated from that structure. Rokitansky (14.367) states that he has met with "encephaloid degeneration diffused over the lining membrane of the cerebral ventricles". Cysts are very common in the choroid plexus; occasionally they adhere to the ependyma. The so-called "granulations" may be looked on as small tumours; they, however, come up for special consideration later.

b. Histological changes.

We have now to examine briefly the minuter changes which the microscope reveals in the Ependyma. First, as regards the Epithelium.
The cells forming the single layer of epithelium may become proliferated. The condition apparently is not a common one pathologically. It is most frequently seen at the bottom of the central furrow in the 4th. ventricle—See micro-sketch 11—at the lower ends of the sulci bounding what we have termed the ependymal convolutions; round the central canal in the spinal cord; and at the points where the choroid plexus joins the 4th. ventricle—we have seen it in all these cases, and believe the condition to be, probably, more or less a normal one. It is also present in "included" portions of the epithelium, and in this case is undoubtedly pathological; this will be referred to later on under the subject of granulations, see micro-sketches 25, 26, 35, 46. The epithelial cells become increased in number and heaped together in more or less shapeless masses. Batty Tuke (40. Oct 1878) mentions two cases of epileptic insanity in which the central canal of the cord was occluded by growths of columnar epithelium. We are inclined to think this is hardly pathological. Proliferation is also frequently seen on the tips of the granulations.

The epithelial cells may become shrunken. Their regular columnar like arrangement is lost, and they have a shrivelled appearance. This condition has been seen occasionally over small areas in the 4th. ventricle. It is doubtful whether the nuclei participate or not. We have often seen large oval nuclei with their contents—nuclear chromoplasm—contracted to the centre of the nucleus.

The regular contour of the epithelial layer may be
lost by the growth of a tumour or a sclerosed patch, or by the bursting through of a "granulation"; in this case the cells are thrown out of place, or crowded together by pressure.

There is a condition which may be referred to here. Very frequently the layer of cells on the free surface of the ventricle stains badly with haematoxylin or alum-carmine, the nucleus being faint and often quite indistinct; while, in the same section, at the bottom and down the sides of the central furrow in the 4th ventricle, or in portions of "included" epithelium, the nuclei are deeply stained, and show up sharply and distinctly.

Whether this has any pathological significance or not, it is different difficult to say ; it, however, very frequently occurs.

2. **Subepithelial neuroglia.** There may be an increase in its nuclei; this will be referred to later. The chief change in it is an increase in density; its fibres become coarser and more definite, it loses in fact its fine granular reticulated appearance and becomes a dense feltwork. We have seen all degrees of it, from a slight coarseness of the fibrils to a coarse and dense fibrous layer. It is generally associated with some fibrous tissue formation or sclerosis, is frequently present in connection with granulations, and is often seen in long-standing epileptics and dementes. Very often it shows an outer portion which is dense and coarse, and an inner which is more finely reticular.

3. **Ependyma as a whole.** We have frequently seen
a clear space, crossed only by a few fine interlacing fibrils, separating the epithelium from the rest of the ependyma. This had not the appearance of a localised separation of the epithelial layer, but looked like a permanent condition. It might possibly be the result of an oedema of the ependyma in the particular cases in which we saw it—see micro-sketch 47. We have seen a similar appearance in the 4th ventricle of the kitten.

Tubercular deposits. We have never met with these in the ependyma. It is questionable whether they are ever found in this situation.

Reference may here be made to "heterotopic" grey matter. According to Ziegler (11.232) this is a condition in which masses of grey matter, 1 to 10 millimetres across, in the form of grey nodules, are found in the ependyma of the ventricles. We have never met with them. It would, at any rate, be rather a case of abnormal development, than a pathological condition. Obersteiner says (3.376) that these "heterotopes" are "always to be traced to abnormalities in development."

Sclerosis. According to Obersteiner (3.206) the ependyma of the lateral ventricles is often the starting point of large lesions. He says (3.375) "patches of disseminated Sclerosis" are "not so common or so extensive elsewhere as they are in the walls of the lateral ventricles.

Sometimes the brownish gelatinous degeneration is seen to surround the whole ependyma of the ventricle of so far as it rests on white substance." We have frequently
seen small patches both in the floor of the 4th ventricle and in the lateral ventricle walls. One or two very minute patches were seen in association with the foldings shewn in micro-sketch 15.

**Haemorrhage.** Small haemorrhages may occur in the ependyma, due to rupture of a small vessel in the subependymal vascular line. These vessels are frequently seen with thickened walls, and engorged with blood; and minute haemorrhages into the ependyma are not uncommon.

**Adventitious products.** Amyloid bodies are frequently met with in the ependyma, and according to Obersteiner (3.156) indicate a "retrogressive atrophic process," and are found especially on the mesial wall of the optic thalamus. As far back as 1858, Buckwill and Tuke (28.431) referred to the ependyma as "the seat of those puzzling bodies the amylaceous corpuscles". They occur in a variety of diseases. Kölliker (4.242) says they are very frequent in dropsy of the ventricles, and in old age.

Fagge (20. Vol.1.652) mentions them in hydrocephalus. Maudsley (13.506), quoting Dr Lockhart Clarke, refers to them as occurring in general Paralysis. Woodhead (16.393) mentions them in a case of epilepsy. Ziegler (10.91) says they are found under "normal conditions" in the central nervous system, especially in the ventricular ependyma. There is no doubt that they are closely associated with brain atrophy in dementia, and we have frequently seen them in the granulations in the ventricles of general paralytics, especially near the tips or older portions of the tumours.
Ziegler says (10.91) that they are specially apt to "follow in the wake of inflammation", either early in the process of granulation, or later when cicatricial tissue has been formed. They are, as a rule, strongly refracting, round or oval, bodies, with a concentric striation.

The concretions, already mentioned under tumours, may be looked on as adventitious products.

We have not found any condition of a syphilitic or gummatous character in the ependyma. We have seen granulations in cases where there was a history of Syphilis; there was no evidence, however, to point to the latter being the cause of them.

C. Pathology: causation.

It is impossible in the present state of our knowledge of brain pathology, and especially of that of the ependyma, to say anything very definite with regard to the cause of the conditions we have just been describing. Many of them, no doubt, are degenerative in character and are associated with degenerations going on elsewhere. In the atrophied brains of old demented we find examples of the majority of these conditions, thickening of the ependyma, sclerosed patches in its substance, even gritty modules or calcareous plates, or softening disorganisation of the membrane.* These conditions may be the result of previous active congestions of the brain, or they may be consequent on general vascular disease. We frequently find much thickening of the walls of the vessels below the ependyma in these cases. In epilepsy the membrane is often thickened and the vessels engorged;
this we should expect as a result of the frequent congested states of the brain in that disease. B. Lewis states (24.525) in "epileptic insanity we find a special freedom from nuclear proliferation, from vascular degeneration, and from hypertrophic states of the lymph-connective system, which obtrude themselves in alcoholic" and general paralytic cases. Unless the case is a long-standing one, with much brain atrophy, the ependyma in the epileptic, in our experience, is not markedly pathological. In alcoholism and general paralysis, perhaps, the ependyma may suffer most. The latter disease we shall consider after dealing with the granulations. Apparently in alcoholic cases there is hyperplasia of the connective tissue elements. Andriezen says (36: Vol.2.1893.230), the protoplasmic glia cells are the elements with which show morbid hypertrophy in alcoholic cases; in the final stage of their morbid activity, their protoplasm will deposit numerous organised fibrillae, in the act of doing which their proper protoplasm will be used up.

Since this hyperplasia will tend to be general throughout the brain in these cases, we may assume that the frequent small sclerosed patches in the ependyma have an intimate connection with it.

Inflammatory states of the ependyma must be common; in association with general inflammation of the brain substance we should expect to find them. That they occur in connection with general Paralysis there can be little doubt, and we see the results of their activity in the granular condition. Probably many of the degenerative
appearances we have been considering were primarily due to acute or subacute inflammatory processes in the brain, involving the ependymal membrane.

Chronic hydrocephalus is said to result from repeated and continued active congestions of the ependyma and choroid plexus (80.654).

Whether the degenerative changes in the ependyma are the result of inflammatory processes, whether some marked 'trophic change is the sole cause, or whether there is a bacillary element present, we must leave to further investigations to decide. Probably all three factors are more or less concerned.

Having thus briefly glanced at the main factors associated with morbid changes in the ependyma, we must turn to the consideration of the "granular ventricle".

2. SPECIAL CONDITION: THE GRANULAR VENTRICLE.

The most important change in the ependyma is the presence of the so-called "granulations", or as they are termed in France "chagrinée". These little bodies are of such frequent occurrence, and are objects of so much interest, that we shall consider them in some detail.

The condition may be described as a morbid change of the lining membrane of the cerebral ventricles, characterized by the formation of small prominent tumours on its surface.

HISTORICAL.

These granulations have been known for a long
time. They were discovered by Brunner in 1694. They were first and very fully described in general Paralysis by Bayle in 1826, and mentioned by Galmeil in the same year and by Daveau in 1830. In 1861 they were the objects of an imagined discovery by Joire, who believed that they were always found in, and were peculiar to, general Paralysis. They were described by Rokitansky and Virchow in 1862; and have been referred to and described by many writers since that date. Among the latter may be mentioned Westphal, Wilks, Moxon, Gallopain, Mickle, Tuke, Clouston. (See 29.114)

**FREQUENCY of OCCURRENCE.**

The granulations are by no means limited to cases of general Paralysis, as some have supposed, but are found in a large majority of cases of brain disease. Most pathologists hold that they are a special feature of progressive or general Paralysis, but that they may exist in other maladies also.

They are not common in epilepsy, but are frequent in chronic insanity - atrophy of the brain consequent on long dementia -, in the hydrocephalic ventricles of idiots, in syphilis, and sometimes are seen in the brains of patients dying from exhaustion following acute mental disease as mania. Clouston mentions (25.432 & 474) their occurrence in a case of syphilitic mania, and also in a case of epilepsy with syphilitic and alcoholic history. Woodhead (16.387) describes them in a case of hystero-epilepsy. Baroncini (40. April 1889.119) found granulations in "alcoholic
phrenosis," "consecutive dementia" and "paralytic phrenosis". Lyle (40. Oct. 1880. 385.) describes the lateral and 4th ventricles as being rough with granulations in a case of brain tumour, probably a gumma. Fagge (20. Vol. 1. 675) says the ependyma is often granular in tubercular meningitis. He also mentions them as occurring in the 4th ventricle in a case of chronic diffused inflammation of the brain in a girl aged 14, (20. Vol 1. 646). They are found in hydrocephalus due to brain wasting in old age, according to Rokitansky (14. 365). Wilks and Moxon state that they occur in some cases of acute hydrocephalus (19. 211).

The preceding references shew how varied is their occurrence; they however, most commonly observed in general Paralysis, though even in this disease they are not always present, even when the clinical signs have been well marked. See tables in section 5.

Glouston (25. 382) says that in general paralysis the "normally delicate epithelial linings are toughened and roughened in an extraordinary degree."

According to Howden (40. April 1871. 87) in 235 post mortems of insane persons, 64 showed "well marked crystalline granulations" on the lining membranes of the ventricles; of the 64, 40 were males and 24 females. Gallopain (40. April 1878. 139) found them in every one of 16 cases of general Paralysis. Bullen (40. Jan 1890. 35) gives some interesting statistics with regard to their frequency in various mental diseases. He says that the granular condition "is met with in all varieties of mental diseases, but is,
beyond all others, a feature of general Paralysis,” occurring in “31% of its cases. It is next often found in those of organic dementia, but here in less than one-fourth the proportion of the preceding. In epilepsy, dementia and chronic melancholia, the percentage is in each about 5.7%.

Acute mania has twice the ratio possessed by the chronic form, this last being only 2%” . These statistics are from an “Abstract of 1585 post mortems examinations of the brain performed at the Wakefield Asylum during a period of eleven years” (40. Jan 1890.15). The granular condition would seem to be about equally distributed in acute mania and melancholia; while in chronic melancholia there are more instances than in chronic mania. In 650 postmortems, of which 62 were paralytics, Dr. Baroncini observed true granulations in 32 cases only, (40. April 1889.119).

In our experience the granular condition seems to bear some relationship to the state of adhesion of the membranes to the cerebral cortex, an inverse ratio in fact. If the cortical adhesion is well marked, the ventricles are less granular, and vice versa. The granulations also seem to be more common in men than in women.

SITE.

As regards their site; they may occur in any part of the cerebral ventricular cavities, from the calamus scriptorius of the 4th. ventricle to the furthest part of the lateral ventricles. We have never seen them, or anything of their nature in the canal of the spinal cord.

The granulations seem to be most frequent in the
anterior part of the lateral ventricles; they may be found, in this situation, in small clusters or patches in the majority of cases of chronic brain disease with enlarged ventricles; they are probably often overlooked here, as they are usually very fine and inconspicuous.

The 4th. ventricle alone seems to be the next most frequent site; more especially in the region of the calamus, along the central furrow, and in the lateral recesses of the ventricle between the cerebellum and the bulb; in this last situation a little patch of fine glistening points may generally be found. Clouston (25.382) says they are "usually most marked in the floor of the 4th ventricle." They frequently occur on the sides of the central furrow in the 4th ventricle, and may form bridges across it; very often they obliterate it altogether.

They may occur over the whole of the floor of the 4th ventricle; or over the greater part of the outer wall of the lateral ventricles. Or they may be found throughout the ventricles, that is, the 4th.ventricle, the iter, the 3rd. ventricle and the lateral ventricles - outer wall and septum lucidum. The iter and 3rd. ventricle never seem to be affected alone, but always associated with one or both of the other two, viz: the 4th and lateral ventricles.

In our experience, granulations on the walls of the 3rd. ventricle are almost peculiar to general paralysis.

The descending horns of the lateral ventricles rarely shew any; the posterior horns seldom. The canal of the spinal cord seems to be free from them; its upper part being
as a rule more or less blocked by proliferated epithelial cells &c.

Baroncini, in 32 cases, found them in all the ventricles in 30 cases, and in the 4th. ventricle only in the other two,(40. April 1889. 119). Cornill and Ranvier (17. 376) state that in general Paralysis they occur most frequently in the 4th. ventricle.

According to Wilks and Moxon (19, 216) a few granulations may nearly always be found on the “septum lucidum about the entrance of the vein of this septum into the choroid plexus”; these, they think, are “equivalent to internal Pacchionian bodies”. We cannot say we have noticed these.

The following table gives an idea of the sites at which the granulations are usually seen; the first being most frequent, and decreasing downwards:

1. Anterior part of lateral ventricle only.
2. Floor of 4th. ventricle only.
3. Outer wall of lateral ventricle, and floor of 4th. ventricle, together.
4. Inner and outer walls of lateral ventricles, 3rd. ventricle, iter and 4th. ventricle.

Granulations are also seen on the arachnoid membrane over the cerebral cortex; they, however, do not concern us here.

NAKED-ENEO APPEARANCES.

Many and varied have been the terms used by different writers to describe the granular appearance. It has
frequently been compared to fine sand sprinkled on the ventricular surface. Moxon (19.216) (20.Vol.1.652) likened the ependyma to the “leaf of an ice-plant.” Ziegler (11.282) speaks of “reticulate and arabesque patterns” on the surface. Bucknill and Tuke (28.431) describe it as covered with fine sand, or “converted into the resemblance of fine shagreen”. Clouston (25.382) likens the less marked cases to frosted glass; while Mickle (29.111) refers to the pearly, sanded, jewelled appearance observable, especially in the 4th. ventricle. The condition has also been compared to the capsule of the liver in perihepatitis, (20. Vol.1.659). We have, also, frequently come across such terms as “grey granulations” (11.282), “warty granulations” granulations” (28.174), “dewdrops” (40.Jan.1884.533); the last being a designation given to the granulations in Holland. Rokitansky, in his treatise on Pathological Anatomy (14.358) (40.April 1889.119) describes five different forms of ependymal change as occurring in chronic hydrocephalus, viz:

1. “The lining membrane sometimes appears covered with a granular film, like the finest sand, which has a transparent crystalline or an opaque, greyish-white appearance.” “It may occasionally be seen at every part of the lateral, 3rd. or 4th. ventricles, but it is generally most developed at particular spots, as the corpus striatum and taenia semicircularis, and especially in the anterior cornu of the lateral ventricle.” We have already remarked on the frequency of occurrence in the last named situation.
2. Coarse granulations of rarer occurrence; these are "more prominent, and in time become modules attached by a pedicle." These he considers "analogous to the false growths of the same kind which occur on other serous membranes, and to the Pacchi-onian bodies on the arachnoid."

3. Sometimes the new tissue is smooth, membranous, and superficially attached, and forms separate, round, white, opaque islands or 'plaques', which are not unfrequently thinner in their middle, and, as it were, perforated — latticed."

4. "At other times the tissue is similar in its character, but instead of forming separate islands, it is continuous, and the whole seems knitted or areolar, and forms an adherent network of false membrane, which may generally be easily raised from the surface."

5. It may form "false membranes of considerable and nearly uniform thickness, which are, for the most part, intimately united with the lining membrane."

He further says (14.359) "In some very rare cases of chronic hydrocephalus in children, the cerebral substance protrudes into the ventricle at various spots, probably those where the ependyma is relatively thinner, and forms rounded, smooth bosses, with broad bases, as large as hempseed or peas." We have never met with this condition in sections we have examined. There seems every reason to believe, from microscopic examination that these five forms, as described by Rokitansky, are merely degrees of one and the same condition, viz: A fibrous overgrowth which at first forms
small rounded tumours, these later on fuse together and form patches, or an areolar network, and finally may end in a more or less complete false membrane.

Experience goes to show that Rokitansky's descriptions cannot be much improved upon. We have practically met with every form in varying degrees; many of them are well shewn in the photographs of the ventricular surface in Section 4. See photographs AF.AI.BC.DE.DG.DI.DJ.DK.DM.DR.FB., which show fine and coarse granulations, also linear forms and areolar networks.

We suggest the following division into three types, as being simpler, and convenient for practical and microscopical purposes.

1. The granulations may be very fine, and often only visible when the ventricle is held with the light falling on it in a definite direction. These fine forms may occur a. in small, isolated groups, scattered here and there - e.g. in the lateral ventricle or in the lateral recesses of the 4th. ventricle; b. in fine lines running above and with some of the subjacent vessels - e.g. in the lateral ventricle wall; and c. as isolated points - e.g. in the central furrow of the 4th. ventricle.

2. MEDIUM type. These cover larger areas, and give the "sanded" appearance to the ventricle. It is a common form in the lateral and 4th. ventricles. The little tumours are distinct, rounded, but not pedunculated; sometimes they form fine linear projections. In both this form and the preceding one the granulations may be clear
and crystalline, or whitish and opaque.

3. **COARSE** type. These are rounded and knobby, or conical, or flattened, masses, often pedunculated - especially in the knobby forms -, and appear as distinctly visible, separate tumours. They are most frequently seen in the calamus scriptorius of the 4th. ventricle, and in the neighbourhood of the foramina of Monro in the lateral ventricles, but they may occur anywhere in the ventricles or iter. They may bridge over or occlude the central furrow in the 4th ventricle. Sometimes they fuse into linear masses - we have seen them about one-fourth of an inch in length - or they may form a reticular or areolar network over the surface of the ventricle; these conditions seem to be most common in the 4th. ventricle. Rarely the ependyma may be covered by a thick layer of fibrous tissue forming a false membrane over it.

It is not uncommon to find coarse granulations, with areolar masses, in the calamus scriptorius and lower one-third of the 4th. ventricle, while the upper two-thirds of the same ventricle is covered with the finer "sanded" granulations. All three types may exist together in varying degrees.

In the coarser forms, the ventricular surface feels decidedly rough to the touch; on being pulled asunder, it is often tough and leathery.

**SIZE.**

As regards the actual size of the granulations, this, as we have seen, varies from a mere point, which is
barely visible, to a tangible tumour. The largest granulation we have met with, was hanging from the roof of the iter; it measured 800 micro millimetres in diameter. According to Wilks and Moxon (19.216) in some cases of chronic hydrocephalus, the whole of the ependyma was "covered with large translucent granulations," which in one case were "as large as hempseeds." Gallopain (40. April 1878.139) speaks of granulations amounting to papilla. Gowers (23. 1742) states that some of the "warty granulations" in degenerative brain diseases may attain the size of a pea. In our experience they are not common above the size of a small pin's head.

SHAPE.

As to their shape, they may be rounded, linear, or in the form of "plaques"; they may be knobby and pedunculated, or sessile. In section they may be conical, rounded, squarish or flattened; this will be more particularly referred to under the head of microscopical structure.

MICROSCOPICAL STRUCTURE.

Varying statements have been made regarding the minute structure of these little bodies. Essentially they seem to be fibrous tissue tumours of a non-malignant type; the epithelium being rarely, if ever, actually involved.

We shall, first, briefly review the opinions that have been put forward by various writers regarding their structure. Some look upon them as due to a proliferation of the epithelial layer, while others describe them as being connective tissue formations; the latter seems to
be the more generally accepted view. Rokitansky in 1850, (14.358) in speaking of chronic hydrocephalus, says that the "plastic exudations" remaining upon the surface of the ependyma after acute hydrocephalus, become converted into a "cellular or fibroid tissue and covered with a layer of tesselated epithelium". Buckmill and Tuke in 1858, (28.431) describe the change as due to a "modulated deposit of fibro-albumen." Wilks and Moxon (19.216), nearly 20 years later, call them "warty or papillose states" having much the same structure as the ependyma. Lockhart Clarke (13.506) says "they consist of globular aggregations of the ordinary epithelial cells, which, in a natural or healthy state, are arranged side by side, and form a smooth or level surface on the floor of the ventricle." Cornil & Ranvier (17.376) state that they consist of "embryonic elements traversed by a few capillary vessels." Balfour (40. Apr. 1874. 59) believes them "most commonly to be due to small collections of fluid below the membrane, and not, as a rule, to an organic deposit, for in stripping off the membrane no traces of the granulations remain when it is examined under the microscope." Gallopain (40. April 1878. 139) looked on them as formed of connective tissue. Gowers (23.1742) described the ependyma as being infiltrated with "cells of new formation." Clouston (25.382), in describing the microscopic examination of a granulation, says that the "single normal layer of delicate epithelium has become enormously hypertrophied, and has thrown itself up into great nodular masses of epithelial cells, arranged in some
cases in layers of one hundred cells deep. In the deeper layers the cells have become flattened and hardened, so that they have a fibrous appearance, and the brain substance on which they rest has undergone a process of sclerosis. These granulations are, in fact, innumerable epitheliomata growing over a fibroid membrane. More recently (40. Oct. 1894. 668) he believes the granulations to be formed by a localised over-growth of the subepithelial neuroglia; the normal epithelial covering having often disappeared in places.

Batty Tuke in 1884 (23.720) in an article on the "Morbid Histology of Insanity", described the "ground glass appearance" frequently seen in the ventricular ependyma as being due to three different morbid conditions, which he states in their order of frequency, as:

1. Proliferated epithelium: 2. Lymph exudations and 3. Crystalline deposits. When change in the epithelium is the cause of the granulations, a vertical section shews simply a proliferation of cells projecting into the ventricle like villi. When lymph exudations have pushed the ependyma upwards, it presents the appearance of rough, irregular, bullae-like nodules, consisting of the layer of epithelial cells and a greenish homogeneous stroma. According to Obersteiner (3.153) they depend upon "an over-growth of the subepithelial connective tissue, which, breaking through the epithelium, appears uncovered in the ventricular cavity." Mickle (30.538), in an article on general Paralysis, looks on the granulations as composed of connective tissue and due to an over-growth of it. Ziegler
(11,282) describes them as consisting in a new formation of neuroglia, the fibrous felt-work being exceptionally dense in proportion to the number of cells or nuclei present; the cylindrical epithelium, which invests the ventricle, sometimes continuing to cover the prominences, sometimes falling away and leaving them bare. Hamilton (12, Vol. 2, 574) in his "Pathology 1894," says they appear to be entirely cellular, and are devoid of blood vessels. Woodhead and Tuke (30, 910) in an article on Pathology, state the formation of granulations to be usually "associated with proliferative or other changes of the cells of the ependyma, or with proliferation or increased new formation of the subjacent connective tissue." They describe three forms; the simplest and commonest being a "simple throwing into folds of the ependymal covering;" the second being a "kind of granulation tissue in which the young connective tissue first projects the ependymal cells before it into the cavity of the ventricle, and then breaks through, leaving a solution of continuity of the cellular layer;" the third form appears to consist in "simple swelling, accompanied by vacuolation of the ependymal cells." Woodhead in his "Pathology" (16, 891) in describing a section from a case of hystero-epilepsy, says, "growing into the 4th ventricle are the masses of granulation tissue. They are masses of small, round cells, which grow up beneath the epithelium of the ependyma, pushing the latter before them, or breaking through the epithelial layer, and continuing to grow for some time; eventually, in either case, they fall to one side, either to
the floor of the ventricle or towards a similar granulation. In consequence of this, cavities lined with a layer of epithelium are frequently found near the base of these granulation masses. Running into the masses of granulation tissue small vessels may be seen, very similar to the vessels in the floor of a granulating wound." Again (16,393) he states that the cells of which the granulations are composed are "continuous with those deeper down in the pad of tissue which is found in the floor of the 4th ventricle." Dr. Beadles in an article on the "Nature of granular ependyma" (40 Jan 1875.46) says the granulations are "small, roundish, solid, connective-tissue, tumours which spring from the ependyma and project into the cavity of the ventricle. They are usually composed of a dense fibrous tissue," and the epithelium is often modified over them, and may be degenerated.

Reviewing the above descriptions of the structure of the granulations, we can only say that in practically all the cases we have examined, in which they occur, we have found them to be tumours composed either of an embryonic or of a fully formed fibrous tissue. We are decidedly of opinion that they are never produced by the proliferation of existing epithelial cells, as some writers have stated; and we are strongly inclined to believe that, though they are produced in the subepithelial layer, they are not "of" that layer. We follow the statements of Obersteiner, Ziegler, Mickle and others, in that we look upon the true "granulation" as being composed of a fibrous tissue "overgrowth" in the subepithelial layer of the ependyma.
An overgrowth in which, in our experience, both the epithelium & its subjacent neuroglia play a more or less passive part.

We have, in one case only, seen small rounded swellings of the ependyma, which might give the appearance of granulations to the naked eye. They were merely bulgings of the ependyma over subjacent vessels with thickened walls, each rounded bulging corresponding to a vessel. The epithelium was intact over them; there were no cell elements or fibrous tissue near them. We have mentioned this condition here, as it seems to be similar to the 1st type of Woodhead and Tuke (30.910). See case AG in section 3.

Beadles (40. Jan 1895.40) in a paper on “Degenerative lesions of the arterial system” says that vessels of medium size shewing atheromatous conditions “may often be met with beneath the ependyma of the ventricles, when they cause an elevation of the thickened lining, and give rise to a false appearance of granulation.”

We must now consider the results of our own observations on the granular ependyma. The details of each particular case we have examined are given in section 3.

Here we shall limit ourselves to the general features underlying the appearance and structure of granulations as a whole. In some cases a microscopical section shews only one or two granulations, while, in other cases, the tumours are so numerous that the whole ventricular surface, from side to side, is one mass of them.

We have already alluded to their size. Microscopically, they vary from a mere bulging of the epithelium to
rounded tumours of 400 to 800 micro-millimetres in a diameter. They vary much in shape on section. See micro-sketch 23, which is a low power view of a portion of the ventricular surface. Of the isolated tumours, some are mere flattened excrescences—see micro-sketches 13 and 32—; some are conical, and tall like a sugar-cone—this form is very well shown in micro-sketches 22 and 39; others are rounded, with or without a peduncle—see micro-sketches 12 and 26, and photomicrographs 6, 7, and 8; or squarish, forming cube-like blocks of tissue on a broad base—see micro-sketches 35, 36, and 43. In addition to these types, all sorts of forms are produced by the coalescence and fusion of the tumours. A tall tumour falls over and becomes united to the adjacent ependyma, “including” its epithelium—micro-sketch 26 shews this very well; or in falling it comes in contact with another tumour, and the two then fuse together to form one large mass, the intervening epithelium being enclosed between them—see micro-sketches 27 and 42. Sometimes a tumour of slender dimensions, which has grown from one side of the central furrow in the 4th. ventricle, falls over and completely bridges across the furrow, forming a distinct arch; we have seen this arch duplicated, producing a kind of viaduct—see micro-sketches 20 and 24; or two tumours, growing up alongside one another, may become fused together as a consequence of their growth. Sometimes the fibrous masses appear to grow horizontally and form shallow, flattened, bands of tissue, which run for considerable distances over the ependymal
surface - see micro-sketch 19; or they may grow over the surfaces of the "ependymal convolutions" and unite them together - see micro-sketch 29.

These various forms are interesting as showing the diversity of growth of the tumour masses; but, so far as we are aware, they have no significance beyond the general fact that the flatter forms often appear in the more expanded parts of the ventricle, while the taller forms occur in and near the deeper portions, as the calamus in the 4th. ventricle, and the foramina of Monro in the lateral. This not, however, an absolute distinction.

Structure of the tumour. Under this head we shall consider, firstly, the general structure of the granulation tumour, and then, in the order here given, the changes affecting a. the epithelium, b. the subepithelial neuroglia, and c. the subependyma and its vessels. The tumours vary from a small collection of cell-elements, which produces but a slight bulging of the epithelium - this is a very early form - to a fully developed tumour of considerable size, composed of dense fibrous tissue. Between these two extremes there is every gradation of the fibro-cellular tumours; in the younger forms the cell-elements predominate, while in the older ones the cells have largely given place to, or have become transformed into, fibres.

If we examine a very young tumour, we find that it consists merely of a small cluster or collection of cells with deeply stained nuclei, producing slight bulging of the epithelium above it. This little cluster lies in the
ependyma, the fibrils of which are rather more distinct and defined in its neighbourhood, than in the normal condition. The examination of a more fully developed granulation, of fibro-cellular type, reveals a nucleus of new tissue, bounded externally by a thin stratum of the subepithelial neuroglia, supporting the single layer of columnar epithelium - the epithelial layer will probably be broken in its continuity. The tumour is well nucleated as a rule.

See micro-sketches 22, 25, 35, and 39, and photomicrographs 6 and 7. The new tissue will be seen to consist of elongated cells with a faintly stained protoplasm, and a well marked rounded or oval nucleus, along with well-formed fibrous tissue with elongated or rod-shaped nuclei. Generally we find the cellular elements nearer the base of the tumour; this would seem to indicate that this part is the growing portion of the tumour mass. See micro-sketch 25. Occasionally, faintly-stained nuclei of epithelial type are seen in the new growth; these may be due to accidentally involved epithelium, or to a small portion of the surface of the tumour being included in the section.

In the oldest tumours the fibrous tissue predominates, in fact may sometimes form the whole tumour mass. It may be in the form of coarse straight fibrous stands, or of wavy fibrous tissue, or it may take the shape of serpentine or spiral masses of a coarse and dense nature; this last form is frequently present in the tall and conical tumours. In each case the nuclei are of the elongated or rod-shaped type, and the round elements are wanting.
Blood vessels sometimes occur in these tumours; but, in our experience, they are exception. Very frequently, patches resembling colloid degeneration are seen in the outer parts of the tumour. See micro-sketches 19, 29, 42 and 43.

We now come to the changes affecting the epithelium. In the smaller tumours the epithelium is often continuous over their surface, the cells appearing rather flatter than normal. In the majority of cases, however, the tumour, as it grows, bursts through the epithelial layer, so that all we see of the previous single layer are the traces of it which have remained at the sides of the tumour mass; these traces often shew some proliferation of their cells - see micro-sketches 25, 35, 36 and 39. Over the tip of the tumour mass scattered epithelial cells of degenerated type are frequently seen; in some cases these cells shew proliferation, and send distinct tailed processes into the tissue below; as a rule, however, they stain badly, their nuclei are indistinct, and the nuclear contents are shrunken.

The commonest change which we find in the epithelium is that of "inclusion". We have used this term to signify the portions of epithelium cut off by the growth of the tumours. We frequently see small circles or elongated spaces lined by a single, sometimes a proliferated, layer of epithelial cells, identical with the surface epithelium, and almost invariably associated with the growth of the tumour masses. We have seen "inclusions" normally on the extreme lateral aspects of the
4th. ventricle, but they are not common. A tumour grows for a time, projecting itself through the epithelium, and then falls over, cutting off a small area of the epithelial layer; the tumour becomes fused to the surface where it touches and the epithelium becomes "included". It is very common in the bridgings and occlusions in the central furrow of the 4th. ventricle. See micro-sketches 19, 20, 24, 25, 26, 28 and 42.

b. The subepithelial neuroglia. This suffers much the same as the epithelium. Sometimes it is continuous over and around the tumour—see Micro-sketch 12; at others its continuity is broken, along with that of the epithelial layer, on the bursting through of the tumour.

Its nuclei are sometimes increased in number sometimes not. It may shew an increase in the coarseness of its fibres, or it may retain its normal reticular appearance to a large extent. The most important condition in this region is the presence of collections or clusters of cells, with, usually, an associated increase in the definition and distinctness of the adjoining fibrils. These clusters may occur near the bases of existing tumours, or they may be isolated & produce a slight bulging of the epithelium; in the latter case they are probably very young tumours. The cell clusters may however be present, & produce no apparent effect on the epithelium or the surrounding reticular tissue. Sometimes these clusters are large, and markedly elongated. See micro-sketches 14, 17, 18, 21, 25, 31, 33 and 41. 31, which is a sketch from
the lateral ventricle of case DP, shows two clusters of cells, one producing bulging of the epithelium, the other smaller and scarcely causing any change. We shall refer to them later on. Besides these clusters, we have several times noticed in this subepithelial layer, particularly near the tumours, cells of peculiar type. These cells were isolated, elongated in shape, had a homogeneous cell protoplasm and a distinct nucleus. A few of these cells are shown in micro-sketch 49, which is taken from a 4th section ventricle of case HB; this case showed them extremely well. What is the import of these cells, we cannot say. There were, however, similar cells in the lower part of the tumours, and also in the subependymal region, in the same case. We are inclined to believe that both the epithelium and the subepithelial layer—that is, the ependyma—play a passive part in this granular condition; that the effect on them is a secondary one produced by the growth of the tumour.

The subependyma on the other hand seems to give indications of a more active condition. Its nuclei are often, we might say usually, increased in number, at all events in the earlier stages of the tumour growth; in the later stages, that is when the tumour has become fibrous, it is more or less quiescent. We have mentioned previously, the existence of a distinct stratum of small, well-stained nuclei in this region; this stratum shows a decided increase in the number of its nuclei, just subjacent to a young tumour mass. These nuclei, moreover,
frequently encroach on the ependyma, into which they would appear to wander; the neuroglia fibrils, at the same time, shew a definite upward direction, tending to a right angle with the ventricular surface, and the nuclei seem to follow these fibrils. See micro-sketches 14, 17, 21, 33 and 41.

The blood vessels in this region frequently have thickened walls, and sometimes are surrounded by masses of leucocytes. The micro-structure and appearances of the granulations are very well shewn in many of the micro-specimens accompanying the thesis.

(A list of them is given in Section 5.)

As to the origin, and growth of these tumours, there can be little doubt that they arise from the collections or clusters of cells in the subepithelial layer of the ependyma, which clusters we have already referred to. The cells in these clusters multiply, and give rise to a mass of cells, which at first only produces a slight bulging of the epithelial surface; this new-growth proceeds, growing from below, the outer cells becoming flattened and finally fibrous, till it at last bursts through the epithelium, and forms the so-called "granulation". We have seen practically every stage from the tiny cluster of cells to the old fibrous tissue tumour.

We have examined the multiplying clusters, the elongation of their cells, the lengthening of their, at first rounded, nuclei, and the gradual transformation into fibrous elements. Hence we have no doubt as to the mode of growth of these tumours. But where do the collections of
cells come from? This is an extremely obscure point, and one on which we can at present only surmise. There seem to be only three sources for these cells, either a. they are produced by a multiplication of the cells or nuclei already present in the subepithelial neuroglia, b. they come from the epithelial layer, or c. they are foreign to the ependyma, and come from the region of the subependyma.

In a paper including some "Remarks upon the nature of Granular Ependyma" (40. Jan 1895. 48) Dr Beadles says, "Immediately beneath the nodule it is usual to find small blood vessels, and not infrequently here, and at the point from which the growth leaves the ependyma, are collections of deeply staining round nuclei. These same groups of distinctly defined cells are found beneath and in proximity to the granular bodies in the case of hydrocephalus, where they stand out even more prominently against the younger connective tissue of which the nodules are composed. They appear to resemble closely the proliferated epithelium of the ependyma." Again (ibid. 47.), in describing a section of the ependyma from a case of general Paralysis, he says, "where these thickenings of the ependyma exist, there are a few scattered round cells lying in the stroma, but here we see again to a very marked degree definite masses of the more deeply staining cells situated round the lower margin of the forming nodule." Further the slight thickenings of the ependyma above described are very plentiful, and it is a remarkable fact that the groups of deeply staining cells are seldom absent at these places, but are rarely found elsewhere."
Our experience is quite in accord with these statements in Dr. Beadles' paper. He at first thought the granulations originated from the walls of small vessels in the ependyma.

Now, however, in describing a section from the lateral ventricle of a general paralytic, (ibid.47) he says, "in a minute granulation in an early stage, there is but a slight thickening of the ependyma, covered by a layer of much degenerated columnar cells. Dipping down into the stroma at this spot are two small flask-shaped cell groups of an epithelial nature, and in connection with the surface epithelium, although the former are of a spheroidal and glandular type. They closely resemble minute glands". Though he suggests that the "epithelial downgrowths from the surface give rise to the isolated cell masses" he will not go so far as to say positively that this is the true origin of these cells." These statements are based on "an extensive experience of both malignant and extensive growths."

These "epithelial downgrowths", on whatever they may be, are illustrated in micro-sketches 14,17,18,21,25, 31,33,41.

We do not agree with the suggestion that these collections of cells originate from the surface epithelium.

The clusters no doubt are often quite close to the epithelial layer, but we have seen them quite as frequently some distance away from it. The cells in the clusters are said to resemble the epithelial cells; this is certainly the case, but we have, on the other hand, examined numbers of sections in which the cells in the subependyma, and even in
the general neuroglia in the substance of the medulla and pons, resembled epithelial cells quite as closely. And again, we have to account for the connective tissue in the more advanced tumours; the above writer has to fall back on the neuroglia and the outermost coat of the vessels to produce this. Moreover, we have frequently seen these clusters of cells in the ependyma, the epithelium over them being, at the time, to all appearances unaffected. Of course, if an inflammatory process is going on, we should expect some change in the epithelium sooner or later.

Again, we cannot believe that these cell groups originate in the subepithelial layer itself. This layer, with the exception of some greater definition in its fibrils near the cell groups, as already described, especially between the cell group and the subependyma immediately subjacent, appears frequently to remain quite passive. It may often be seen bounding well developed tumours, and at the same time retaining its finely reticular structure. Undoubtedly, in cases where the tumour growths are large and numerous, it is often enough seen to be coarser in texture than normal, but this is a secondary condition. Its nuclei, too, are quite unlike those of the cell groups and shew no tendency to proliferation. We have already suggested, in Section 1, that this layer, from the peculiarity of its formation and the absence, normally, of blood vessels, contains no mesoblastic elements. If this be the case, we can hardly look to this layer for the origin of the cell clusters.
We must, therefore, fall back on the subependyma. A reference to many of the micro-sketches, notably 14, 17, 31, and 33, will shew an increase in the nuclei in this region. This condition, apparently, has, so far, been overlooked by Dr. Beadles & others. In our experience it is almost an invariable accompaniment of early or forming cell clusters. We say accompaniment because we are not in a position to state definitely whether it is the cause of their presence, that is, is the source from which they come, or merely a concomitant condition. The cells in this region—see micro-sketch 17—are increased in number, at the particular spot where the cluster is forming, as compared with the remainder of the subependyma; they are very similar to the cells in the cluster itself; and between the two fine straight fibrils pass with numerous similar cells scattered amongst them. Frequently the straight fibrils and the cells dip down into the neuroglia below the actual subependyma. See micro-sketches 17 and 21. These fibrils seem to us to point to a close connection between the two groups of cell elements, and, when considered along with the peculiar cells we have already mentioned as occurring in the subepithelial layer—see micro-sketch 49—suggest the possibility of the cell groups or clusters originating from the subependyma. Whether these subependymal cells are the result of a proliferation of the cells normally present in that region, or whether they are cells derived from the blood vessels—we have described the distinct line of subependymal vessels in Section 1—we cannot emphatically say. We, however, put
forward the suggestion, that cells of mesoblastic type under the influence of some cause, at present unknown, wander from the subependyma into the looser texture of the subepithelial layer, proliferate, and by their growth give rise at first to cell clusters, and finally to the connective tissue tumours or "granulations," which produce such havoc with the normal contour of the ependymal surface; and, further, that the epithelial and subepithelial layers are passive, and only affected secondary by the spread of the tumour mass.

We do not think there is any similarity, as some have supposed, between these granulations and the granulation tissue in a healing wound. The tumours are not, as a rule, vascular; it is, usually, in the more advanced ones that vessels are found, and even then they are not common.

Causation. There is much diversity of opinion as to what are the causes at work in the diseases in which we find these granulations. Some authorities look on them as inflammatory, while others doubt the possibility of this. On the whole the balance seems in favour of an inflammation, a chronic ependymitis.

Wiglesworth in an article on the pathology of general Paralysis (40. Jan.1833.480) says, "The conclusion, then, finally arrived at is, that general paralysis is a true interstitial inflammation of the brain running a subacute or chronic course, that it is, in fact, a true cirrhosis of the brain altogether comparable to cirrhosis
of other organs, such as that of the liver; in other words, that connective tissue hyperplasia is the primary element in the disease, and the affection of the nerve cells secondary. Ziegler (11.206) states that most authorities regard general Paralysis as an inflammation corresponding in general to what has been described as "chronic meningo-encephalitis." Meschede (13.517); Delaye, Foville, Griesinger and others (29.114), have all referred to inflammatory changes in general Paralysis. Mickle (38. Spring 1894.61) says that "On the whole, we may view general Paralysis as essentially commencing with hyperæmia, and ending with chronic cortical degenerative cerebritis, and usually embryonic-and connective-tissue substitution, the change, fundamentally parenchymatous, affecting all the elements of the past."

According to B. Lewis (24.441) the frequency of morbid adhesions between the cortex and its membranes is "dubitable evidence of inflammatory activity." "Such morbid adhesions," he says "occur in chronic insanity, in chronic mania, in senile mania, occasionally in alcoholic insanity, and especially in the mental derangement associated with traumatism; " in general Paralysis it is so "important a feature as to constitute the one distinctive sign of this disease." If, then, general Paralysis is due to an inflammation affecting specially the interstitial substance of the brain, we cannot be surprised at finding the results of this inflammatory activity in so delicate a structure as the ependyma; and further, as Lewis states that
inflammatory processes go on in other conditions besides general paralysis, we see a reason for the presence of granulation tumours outside the pale of the latter disease. We have, in fact, a slow inflammatory process going on in or near the ependyma, due primarily, we may say, to frequent hyperæmia of the tissue in that region.

Magnan and others (29, 130) have concluded the existence of ependymitis and of diffuse interstitial periependymary encephalitis, particularly in the 4th. ventricle. Rokitansky (14, 366) says that cellular and fibroid formations occur "as inflammatory products on the free surface of the ependyma". According to Maudsley (28, 506) the finely granular condition of the ependyma, "with its frequent adherence to the parts beneath, would seem to bear witness to a previous subinflammatory condition." Baronoini (40, April 1889, 119) believes that the granulations "depend upon a phlogistic process of the ependyma." Ziegler (11, 282) says that in some cases the granulations recall the structure of inflammatory papillomata of the skin.

In the light of the evidence at present before us, we can only assume that these masses of connective tissue formation are the result of some inflammatory process going on in the brain, and in their most advanced forms are the final stages of a tissue degeneration. What this inflammatory process is, or how it originates, we cannot say. There may be some irritant material in the cerebrospinal fluid, as a result of altered nutrition in the brain, & this acting on the ependymal surface may produce the
results we have seen, causing a diapedesis of lymph cells out of the vessels, and ending in the metamorphosis of these cells into connective tissue. On the other hand, the irritant may be in the blood, and may act from within, the resulting conditions being much the same, namely the escape of cells & their migration into the tissues of the ependyma, with a consequent transformation into granulations. There is, moreover, the possibility of an organism being the cause; of this we have no evidence, though we have frequently stained sections from the brains of general paralytics with the object of localising it.

Dr Beadles, in the paper we have already referred to (40. Jan 1895. 48), believes these granulations "owe their origin to an irritative cause - possibly some chemical substance contained in the fluid of the ventricles or present in the blood."

We are inclined to favour the theory that the irritant is in the blood. For the present, however, we must leave it an open question.

Whether the granulations are the cause of any clinical symptoms or not is doubtful. Take & Woodhead (30.911) say "the strong probability is that they interfere with the free movement of the upper part of the brain over the base, and that the friction generated by the rubbing together of the two surfaces, or even by the passage of fluid through the ventricular cavity in cases of sudden movement, may cause considerable irritation and excitation of the areas covered by these granulations. They will
certainly impede the free movements of fluid, and also of the brain, so necessary to keep up compensatory changes in connection with alterations in the blood supply of the various parts of the cerebral cortex; they will thus interfere, not only with the nutrition, but also with the actual function of the nervous tissues."

In concluding this section, we may say that we have laid special stress on the structure and origin of the granulations on account of the frequency with which they occur, at all events in the brains of those dying insane, and also because of the interest attaching to them as a pathological condition.

We cannot claim to have proved anything with regard to their production, but we have suggested a mode of origin, which, so far as we have been able to find out, has not been put forward before. Much more evidence is required, however, before it can be said that we know everything regarding the pathology of these little bodies, the "chagrinée" or granulations."