On the Degenerative Lesions of the Arterial System in the Insane, with Remarks upon the nature of Granular Ependyma.

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The degenerative changes in the tissues of lunatics are more or less well known, at any rate the grosser or naked-eye lesions that are to be expected, but even amongst these there are some points that, I venture to think, may receive further attention. Of histological changes we can say more positively that much light may yet be thrown on their nature. As to their cause—the cause of the degeneration of nerve cells, for instance—we are lamentably ignorant.

In the following paper I propose to draw attention to the widespread signs of arterial degeneration that are present in the bodies of persons dying insane.

If one observes a large number of lunatics one is early struck with the fact that their appearance as to age is slightly in excess of what is in reality the case. Of course there are individual exceptions to this rule, often very striking; but on the whole the fact remains that insane persons taken as a class have aged, and, when advancing in years, show more early than is natural the changes characteristic of old age.

The appearance of ageing is nothing more or less than an early stage of senile decay, and is dependent on the nutritive supply of the tissues. In other words, it depends upon the character of the blood and the conditions of the vessels through which the blood courses. Definite indications of degeneration of the arterial system are very manifest in a large percentage of the insane. It is shown by the prominent and rigid arteries and the concomitant cardiac signs that are present. Signs of hypertrophy and dilatation, with or without murmurs that point to valvular disease, are far from rare in asylum patients, and often without any definite evidence of the foregoing there may be clear indications of weakness of the cardiac muscle; with it may be fatty degeneration. The weakened heart makes itself manifest in the feeble pulse, tachycardia, and syncopeic attacks to which lunatics are liable, and grave symptoms of cardiac failure and even sudden death therefrom are by no means infrequent.

https://doi.org/10.1192/bjp.41.172.32 Published online by Cambridge University Press

FIG. 1.

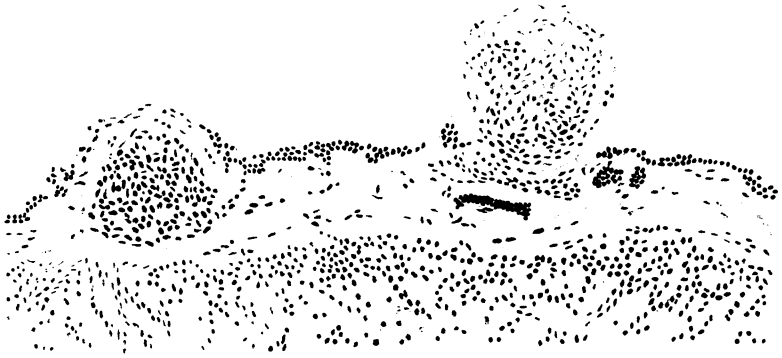

FIG. 2.

FIG. 3.

FIG. 4.

I am unable to give the precise proportion of our patients in whom the organ is recognizably affected, but I find that for the last five years at Colney Hatch Asylum 5·8 per cent. of the males presented definite signs of valvular disease of the heart on admission. Dr. R. H. Wright, of the Alabama Hospital for the Insane, informs me that, as a result of a careful physical examination on 702 white patients, he found valvular heart disease among the men in 10·9 per cent.; among the women in 12·4 per cent. with a percentage of 11·7 on the total. Out of the 82 cases showing the lesion, 56 had mitral insufficiency and 16 aortic stenosis. I am indebted to Dr. Wright for the following table showing the distribution of the lesion, and by its side I have placed the male cases from Colney Hatch referred to above, which were 81 in number.

	Alabama. Both Sexes.	Colney Hatch. Males.
Mania	8	5
Melancholia ...	33	30
Dementia	28	10
Imbecility	2	1
General Paralysis ...	7	12
Epilepsy	4	3

Seeing that the total cases of mania were much more numerous than those of melancholia, the fact is brought out that the latter are the most liable to cardiac troubles; or can the explanation be that heart disease more frequently leads to melancholia? In dementia we probably have a more advanced age to deal with, and consequently must expect senile changes.

A morbid state of the arteries is observed also in chronic Bright's disease, and in that condition so commonly present in young dements which is nearly allied to Raynaud's disease, where the hands and feet are continually cold and of a blue colour, pointing to a sluggish circulation. Hæmatoma auris is another rarer manifestation. Here we have the rupture of a diseased vessel either spontaneously or as the

effect of a slight injury, which in a person with healthy arteries would produce no ill-effect, resulting in a blood effusion and followed by a life-long swelling and deformity. Why should "insane ear" be looked upon as of ill-omen? Surely only for the reason that it proves the existence of advanced arterial degeneration. The ease with which bruises are produced in lunatics, their extensive character, and the length of time they take in disappearing, show, too, a morbid condition of the arterioles and capillary vessels, and the ease with which they rupture and give rise to extravasations of blood.

Malnutrition is further exemplified by the brittleness of the bones and the decay of the teeth, for how seldom do we find a good set of teeth in an asylum patient!

But these and allied signs of deterioration it is not now my intention to study further, but rather to pass on to the signs indicative of vascular degeneration that may be met with in the body after death.

I will at once note that it has so far been my experience, when making post-mortem examinations on persons dying in a lunatic asylum, to find only as the rarest exceptions the thoracic and abdominal organs free from disease of a degenerative nature. This applies not only to old persons, but to those also of a middle or comparatively young age; it also refers to both sexes. The diseased state of the organs can, in a large percentage of the cases, be explained by the existence of a general arterio-capillary fibrosis.

If we wish to know the state of the small arteries, there is no easier method than by examining the kidney, for that organ forms an admirable index to the condition of the arterioles throughout the whole body. In fact, there is no organ better suited to study arterio-capillary fibrosis in, and, owing to its peculiar structure, it enables us to form a rough and ready estimate thereof without calling the microscope to our aid.

In the insane I have rarely found the kidneys perfectly healthy. Most often there have been indications of chronic interstitial nephritis, represented by a variable degree of granular contraction. Especially frequent is an adhesion of the capsule and a granular state of the surface. A normal condition of this organ is far rarer than would seem to be the case with patients dying at a general hospital.

Out of a total of 150 autopsies I found the kidneys presenting distinct evidence of disease in 106, or over 70 per

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cent. of the cases. These do not include simple congestion of the organ. The proportion did not greatly differ in the males and females. It was rather to have been expected that there would have been a greater predominance on the male side, for it is well known that men suffer more frequently from chronic Bright's disease, and are more liable to diseases of the arteries than are women, but in the insane this fact does not appear to hold good. The high percentage here disclosed is remarkable, and it should be remembered that this result is entirely dependent on the rough examination made in the post-mortem room, and that no systematic histological examination was undertaken.

I will not stop to consider the state of the other abdominal organs, for it is impossible from a cursory glance to record the condition of their nutritive arteries.

I now come to the condition of the heart and great vessels. Again, as was the case with the kidney, what would at a general hospital be defined as a healthy heart is from my observation phenomenally rare in lunatics. Although in post-mortem reports it is not unusual to find that organ described as healthy or normal, I believe that if due care had been taken in its examination there might have been detected some slight indication of disease.

In the number of cases already quoted, I met with an abnormal condition of the heart in 136, that is to say in over 90 per cent. In a large proportion of these cases valvular disease was present, thickening or puckering of the mitral flaps with atheromatous changes being most frequent, resulting in an incompetence of the valve, less commonly in mitral obstruction. The aortic valve suffered if anything rather more frequently in the males than did the mitral. A slight degree of atheroma was seldom absent, co-existing with disease of the intima of the aorta immediately above the orifice. The wall of the left ventricle was more often than not hypertrophied, associated with a more marked dilatation, though the latter was at times absent. There were rarely wanting indications of weakness of the cardiac muscle. The myocardium in a large number of instances was soft and flabby, often pale, with signs of degeneration. Associated with this not uncommonly was an excess of adipose tissue deposited beneath the epicardial covering, at times accumulated in masses on the surface, and occasionally presenting a gelatinous character. What is popularly described as a fatty heart is common in lunatics,

and accounts for the syncopeic and fainting attacks to which many are liable, and is a great means of bringing life to a close when such are attacked by catarrhal affections of the lungs, whether it be pneumonia, bronchitis, or influenza.

Actual fatty degeneration of the muscle fibres is, then, usually present, especially noticeable towards the ventricular apices, but it occurs in patches elsewhere; the myocardium is transformed into soft, fatty tissue, which presents a pale, dirty-yellow tint. The liability in such cases to rupture of the heart is referred to in a paper which appeared in the Transactions of the Pathological Society for 1893.[1]

It occurs invariably in the wall of the left ventricle on the anterior surface; in this it is opposed to rupture due to violence, the latter resulting in a rent on the right side of the organ. Where rupture of the heart has taken place in lunatics it has seldom been preceded by any violent exercise, but the patient has been quietly dressing, or sitting in a chair partaking of food. Several times I have found ecchymoses in the wall of the ventricle, either beneath the endo or epicardium, which without doubt could readily form the starting point of a rupture.

I have attempted to show that a disordered state of both the heart and kidney is exceedingly common in persons dying insane. My figures are set forth in greater detail in the accompanying table :—

	Males.		Females.		Totals.	
	No. of Cases.	Per-centage.	No. of Cases.	Per-centage.	No. of Cases.	Per-centage.
No. of Autopsies ...	90		60		150	
Heart abnormal ...	82	91·1	54	90·0	136	90·6
Kidney „ ...	62	68·8	44	73·3	106	70·6

Are these high percentages carried out in the experience of others? The result of a search through some autopsy books gives a percentage of 58·2 for the heart and 43·2 for the kidney in a total of 2,610 cases. That for females in both was much the highest. In the case of the heart changes are noted in 49·3 per cent. of the males and in 71·2 per cent of the

females. Although these percentages fall considerably short of my own experience, yet they still remain very high. I may point out that one cannot be entirely guided by such figures, for it is necessary to take into account the personal equation of the investigators, some observers having seldom recorded a heart that is not healthy, while others find the healthy organ only on the rarest occasion. If all the reports made by some had been excluded, the results would have practically coincided with my own. I may also mention that the percentage given for cardiac disease is probably nearer the truth than is that for the kidney, for it is evident that the heart has received greater care in its examination than has the latter organ. Still, slight changes have doubtless frequently passed unrecorded. Of the large arterial trunks I have already referred to the commencement of the aorta as displaying early or advanced atheroma, but when progressed it usually extends much beyond the arch. I should state that hearts are not included above where atheroma of the aorta beyond the valves has alone been noted; were such the case the number would be greatly increased.

A small percentage only of asylum inmates are certified as dying from cardiac disease, chronic Bright's disease, or other diseases connected with the vascular system. Although, as I have pointed out, there is often an advanced degree of degeneration, sufficient apparently to account for death, yet there has generally been some co-existing malady to which death could be readily attributed. Such are phthisis, pneumonia, exhaustion of diarrhœa, cerebral or meningeal hæmorrhage.

Some of these admittedly certifiable causes of death are in reality only symptoms of the general disease of the circulatory organs, and even many of those diseases that at first sight appear distantly related to the heart may, in fact often do, owe their fatality, if not their existence, to the weakened state of the heart and blood-vessels. In death from exhaustion of insanity from long duration, as well as in that of chronic brain disease and senile decay, there are usually to be found degenerative changes in the coats of the arteries, and these may often be seen if looked for in cases where death has occurred early from exhaustion of acute mania or melancholia.

The following table is compiled from the "death tables" of the four London asylums—Hanwell, Colney Hatch, Ban-

https://doi.org/10.1192/bjp.41.172.32 Published online by Cambridge University Press

stead, and Cane Hill—for the five years 1889-1893 inclusive[1b]:—

Cause of Death.	No. of Cases.	Percentage.
From Cardiac Disease	204	5·51
„ Renal Disease	47	1·27
„ Diseases referable to Arterial Degeneration	146	3·94
From Senile Decay...	310	8·38
„ Chronic Brain Disease ...	569	15·39
„ General Paralysis	950	25·69
Total number of deaths	3,697	

Here I have included besides deaths due to heart and kidney disease those assignable to extensive disease of the arteries, which for the most part were cerebral or meningeal hæmorrhages. There are also shown the deaths from such causes as are invariably accompanied by marked arterial degeneration—senile decay, chronic brain disease, and general paralysis. The same would apply to many certified as "exhaustion of mania" and of "melancholia," but it is impossible from the data given to extract those in which cardiac or vascular degeneration is likely to have existed.

Passing on to the consideration of the vessels within the cranium, how commonly do we observe the arteries at the base of the brain presenting evidence of degeneration. Their walls are often thickened or opaque, and frequently rigid with earthy deposits, and this in persons whose age is not sufficient to account for the condition alone.

In 60 brains from females I found the basal arteries distinctly diseased in 32, viz., over 53 per cent.; in 90 brains from men the number was 45, or 50 per cent. These included all forms of insanity. Dr. St. John Bullen, in an analysis of the morbid changes exhibited in 1,565 brains of lunatics,[2] says that atheroma of these vessels was recorded in 410 cases, or 26 per cent. of the total. He states that in

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general paralysis disease of the basal arteries is relatively infrequent, and the percentage is little more than that in epileptics and the acute insane states. In dementia, on the other hand, atheroma is present nearly five times as often as in general paralysis.

A percentage of only 18 is obtained from a total of 310 brains analyzed by Drs. Howden[3] and B. Tuke.[4] In a table of 333 cases showing the percentages of the lesions found in different forms of insanity, Dr. Balfour[5] includes the condition of the basal arteries. These I have extracted and placed side by side with Dr. Bullen's and my own.

	Bullen.	Balfour.	Beadles.
Dementia	53·0	19·5	16·8
Chronic Melancholia ...	36·0	19	15·5
„ Mania	31·8	9	37·6
General Paralysis	12·4	10·6	23·3
Epilepsy	10·5	5·8	6·4

Drs. Bullen and Balfour agree only in that atheroma of the vessels was most common in dementia, and in the percentage for general paralysis. The ratio which those present to mania, melancholia, and epilepsy is remarkable for their want of uniformity. The extraordinary differences here revealed form a convincing proof to my mind of the valueless nature of such collections of figures, and bear out the statement already made that observers are never alike in their manner or accuracy in recording morbid specimens. As Dr. Balfour himself remarks, in speaking of the condition of the brain, "little dependence can be placed upon records regarding this, seeing that what may be to one observer a deviation from the normal standard will to another be perfectly healthy." The old difficulty of classifying insanity also presents itself, and must be borne in mind, and it is possible that some cases classed as chronic mania in my own table might have been defined as dementia.

If we come to examine the smallest ramifications of the cerebral arteries in microscopical sections of the brain of lunatics, I believe it is exceptional to find the vessels in a

perfectly healthy state. There may usually be found some change in the walls of the small arteries, all the coats of which are liable to suffer.

The innermost coat of the artery may show a variable amount of proliferation, by which the calibre is much diminished, and it may proceed to such an extent as to entirely occlude the vessel. Syphilis is a great producer of such a condition; it affects the very smallest vessels as well as those of larger size. In the case of a medium size branch of the anterior cerebral artery, where there was a distinct syphilitic history, the lumen is occupied by a young connective tissue growth, and the elastic layer is much destroyed. Most frequently it is the middle coat which shows the most marked changes. The wall may be much thickened by a proliferation of the muscular and fibrous tissue, or there may be deposited in its wall material of a fatty nature, as in the larger arteries. The tissues forming the vessel wall appear to become fused, assume a homogeneous aspect, and the cell nuclei disappear. When this atheromatous change has taken place the vessel may become narrowed in places, dilated in others, producing kinking and aneurismal dilatations. Medium size vessels showing these abnormalities to a marked degree 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, which is to be distinguished from the true glandular ependyma. Of the latter I shall have occasion to speak shortly.

The smallest arterioles in all forms of insanity are liable to the conditions described as existing in those of medium size. There are, however, in the case of the former the familiar collections of small round cells in the perivascular spaces and immediate neighbourhood. In addition, the diseased state of these and the capillaries is not infrequently shown by the extravasation of blood, or altered pigment in their proximity, and the small foci of softening so commonly present in the insane brain.

Sclerosis of arterioles is always followed by overgrowth of connective tissue around them, which appears to originate from the outer coat of the vessel, and this gives rise to a hardening and shrinking of the organ. Thus may be accounted for such a condition of the brain. The point Dr. Goodall has lately endeavoured to prove,[6] that the "spider cells" are merely connective tissue cells in the pro-

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cess of fibrous tissue formation, appears to me the most reasonable. In that light it is clear that they owe their existence secondarily to the diseased state of the vessels.

Although slightly apart from the subject under consideration, I may briefly refer to a form of pigmentary degeneration, depending as it is does on the state of the blood and vessels. It is a pigmentary condition of the pia mater over the medulla oblongata and upper part of the cervical region of the spinal cord, which is somewhat common in lunatics. I have not been able to find any reference to this condition in general works on pathology or those special to insanity. Dr. Edwin Goodall makes no provision for such a circumstance in the very full scheme of a "table for the examination of the brain and its covering" which he recently published in the "Journal of Mental Science",[7] and he has been unable to give me any information on the subject.

Now, I have found a marked degree of pigmentation of the membrane in this region on many occasions. To the naked eye the pia mater presents a brownish colour, varying in intensity according to the amount of pigment present, occasionally of a deep brown tint, but usually pale, and not readily distinguishable from a congestion of the minute vessels. The condition appears to bear no relation to any particular form of insanity, although it is undoubtedly most marked in general paralytics.

Under the microscope the colour of the pia mater is found to depend on many connective tissue cells, containing brown pigmentary granules. These cells vary much in form; many are elongated, some long spindle-shaped, and others irregular and branching. They have a large oval nucleus which produces a bulging, and is usually freer from brown granules than the remainder of the cell. When few in number the cells are generally clustered around or lay near a small blood-vessel. Some pigment cells can more often than not be found even when they are not sufficient in amount to give a tint to the membrane; they are then most frequently situated near one of the longitudinal fissures of the cord, especially the posterior. This condition of the pia mater is not limited to the insane, for one of the most marked specimens I ever saw was from a non-insane female who died from phthisis. Pigment cells occur normally in the pia mater of the medulla oblongata, and their existence is well known to physiologists, but this only to a slight degree, and such a condition as to give rise to a distinct colour of

the membrane is, I venture to think, of far greater frequency in the insane than in any other class of cases. It is merely another sign of degeneration, beyond which there is little importance to be attached to its presence.

Having considered the widespread degeneration in the arterial system throughout the bodies of insane persons, let us now briefly pause to find an explanation. We are at once confronted by several important questions. Is this a primary disease or a secondary, dependent on the condition of the nervous system or the state of the patient? If an initial lesion, to what is it due? Is it in any way a causative agent in the production of insanity?

The minute structure of the brain cells has lately received much attention, and rightly too, and recent investigators have proved a diffuse degeneration and vacuolation of the cortical cells. Observers, moreover, are unanimous that where this is the case the small vessels of the brain show definite signs of degeneration also. This point has been specially noted by Dr. Campbell.[8] They usually exist together, though some brains have been described with deteriorated blood-vessels in which no vacuolation of the cortical cells or the presence of spider cells were found; yet I believe the latter conditions have never been observed without the co-existence of extensive alterations in the walls of the vessels. In fact, in those cases where the cells are extensively diseased, there the vessels are most profoundly affected.

The most recent writers are agreed that cell degeneration is not characteristic of one form, but is present in all varieties of insanity, and is seldom absent even in the most acute cases. Since Dr. Bevan Lewis first described this morbid change in epileptic insanity,[9] many workers have been studying this point. It has been found in all regions of the cerebral cortex, but the intensity of the vacuolation appears to vary in its site in different brains. Dr. Skae[10] detected it in 80 per cent. of the brains he examined, taken indiscriminately from almost all kinds of insanity. This condition, however, is not entirely characteristic of the insane brain, for it has been met with in some persons who have died from toxic poisoning or febrile diseases.

Dr. Carter[11] draws attention to the fact that in general paralysis the changes in the vessels and in the cells co-exist. He says: "These changes go, to a great extent, hand in hand; where the vessels are most thickened and cellular,

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the dissolution of the surrounding nerve-tissue will be most evident as a rule." He regards the changes in the vessels as of secondary importance, although he states they are often far more noticeable than any disorganization of the nerve-cells. With his statement that in some brains of general paralysis the vessels are practically healthy, I am not able to agree, nor can I fall in with the remark that "the appearance of thickened, proliferated, and cellular vessel-walls is not so common a feature, and is not met with in a well-marked state in any other condition of brain disease." Taking this as a fact, he ventures the opinion that "as this feature is not so constant as the dissolution of the nervous tissues to which ultimately the symptoms of the disease must be referred, I repeat that the probability is in favour of a purely nervous origin."

Dr. Campbell [12] is inclined to refer the condition of the nerve-cells to the direct action upon them of a toxic principle in the blood. He would, moreover, account for the diseased state of the heart in the insane as depending upon a primary lesion of the vagi nerves. He says: "In addition to the clinical evidence of cardiac affections, I have been able to demonstrate anatomically the existence of most profound changes in the muscular elements of the heart in cases in which the vagi nerves were diseased;" and to the toxic infection of the nerves he attributes the cardiac troubles met with in general paralysis.

In the recent paper already cited, Dr. Skae lays stress upon the disease of the heart, blood, and blood-vessels which he has found in the insane. These, he believes, by giving rise to some obstacle in the proper supply of the blood to the brain, cause deficient oxidation and result in a fatty degeneration of the cells followed by vacuolation. From this it is to be gathered that in his opinion a diseased condition of the arterial system precedes the nerve degeneration and does not result from it. With this I am practically in agreement. I do not believe that a diseased state of such important structures as the vessels is without its effect upon the brain as the organ of the mind, and I am inclined to regard it as playing a far greater part in the pathogenesis of mental aberration than for which many would give it credit.

Not forgetting that in some cases and to some extent the condition of the arteries may be a secondary one, I consider there is distinct evidence for believing that it often has a

primary existence, and has long anteceded the onset of the insanity to which the patient has become the victim. Atheromatous changes in the vessels may undoubtedly develop rapidly, but in a large number of the cases disease of the heart and arteries is recognizable long before the onset of any mental symptoms. Surely it is not unreasonable to suppose that the diminished calibre of the vessels conveying nutrient fluid to the nerve elements must seriously affect them in their vitality and function!

I would suggest, therefore, that the vacuolation and degeneration of the nerve-cells is possibly often a secondary result of the want of proper nourishment of the cell, due to the cutting off of the blood supply by diseased or occluded arteries. And this brings me to the cause of this arterial degeneration of which I have been speaking. There are many recognized causes, but especially would this condition appear dependent on some chemical poison floating in the blood. Alcohol and the syphilitic poison are known to be potent factors in this respect, and the recognized frequency of both these as causes of insanity needs no comment from me. They both primarily affect the blood-vessels, and, through acting on the smaller vessels, produce deterioration of structure in all the organs of the body. Richardson [13] says that seven out of every eight cases of kidney disease are attributable to alcohol. Much has been discovered relating to the absorption of ptomaines and allied poisonous substances from the alimentary tract, and lately the question of the manufacture of alkaloidal bodies in the blood itself has been receiving attention. Lauder Brunton [14] has pointed out the relation of the former when absorbed into the system to various cerebral symptoms. That such bodies do, and must, exercise an injurious influence on the vessel-walls in which they exist there can be little doubt.

I may add that the toxic principles to which reference has been made may of course act primarily upon the nerve elements, but, none the less, they cannot be without their effect on the vital tissues of the vessels which convey them to their ultimate destination.

In conclusion, it is to be observed that no mention has been made of the theory held by some that the degenerated state of the cardio-vascular system found in lunatics may be fully accounted for by the strain thrown upon the heart and vessels from the restlessness, excitement, and violent exercise of the patients. This I believe to be a causative agent, if

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at all, in but a very trifling proportion. It would in no way account for the condition in melancholiacs or in primary dementia, whether of senile origin or otherwise.

On the nature of Granular Ependyma.—In the previous remarks on the arterial degeneration in lunatics I incidentally made mention of the granular nature of the lining ependyma of the ventricles of the brain. I now propose to enter briefly into the microscopical nature of these remarkable little bodies that lie scattered over the ventricular ependyma like minute grains of sand.

They have long been recognized and looked upon as a sign of degeneration, but as to their minute structure and exact nature there still appears some doubt. They have been briefly and variously described by Lockhart Clarke,[15] Batty Tuke,[16] Clouston,[17] Mickle,[18] Angel Money,[19] and others.

As is well known, they do not occur in the normal brain. On the other hand, they are found co-existing in a wide diversity of abnormal conditions of that organ. They are most frequently found in some chronic brain disease, and although seldom absent in general paralysis of the insane, they are by no means limited to that form of mental disorder. In fact, they occur at times in all forms of insanity, including the acute states. I do not think that I ever saw them more pronounced than in a recent case of acute and rapidly fatal mania, where the man had shown signs of insanity for little more than three weeks. The condition almost constantly accompanies hydrocephalus, both acute and chronic. In the insane brain it is more often found where the ventricles are only moderately or not at all dilated, where the brain is sclerosed and harder than natural, and the small vessels are extensively diseased.

The authorities named above are by no means unanimous in their opinions. Some regard the granules as primary connective tissue growths, others as solely due to an accumulation of proliferated epithelial cells, while others again consider them of a mixed nature, in which either the epithelium or the connective tissue plays the most important part. It is, therefore, clear that many points are still open to inquiry, and that more light may yet be thrown on the nature and origin of the bodies under consideration.

I first became interested in these granules some six years ago, when making sections from the brain of a hydrocephalic child. I was then inclined to regard them as originating from the walls of small vessels in the ependyma. More

recently I have investigated this subject further, and cannot now hold altogether to that view.

If we study sections of these granulations from a case of general paralysis or chronic brain disease we find that they 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, often more or less granular or homogeneous in nature. Frequently, however, the more central part is of a younger nature, and exhibits numerous round or elongated nuclei. Only very rarely is there any sign of a vessel in their centre, but where this does exist the nuclei and fibrils appear to be arranged concentrically around it, as though the tissue had originated, possibly, from the outer coat of the vessel. The nodules are covered by the columnar-shaped epithelial cells of the lining membrane, which, however, are often modified in form, having become spheroidal or flattened, and although the cells may exhibit distinct evidence of proliferation at the sides of the growth, they are more often than not markedly degenerated, or have entirely disappeared from the summit of a fully developed granulation. Only in rare instances have I seen a marked accumulation of the epithelium cells, and then it could more readily be referred to an obliquity of the section than to an actual increase of the epithelium. The base of the growth blends with the tissues of the thickened membrane, which is of a coarse granular and fibrous nature (Fig. 1).

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 nuclei sometimes appear of a different nature to those of the connective tissue or leucocytes which lie scattered singly about the stroma. They stain more darkly with logwood, and appear in spaces free from the stroma. They do not, however, seem to bear any relation to vessels or vascular spaces.

These same groups of distinctly defined cells are found beneath and in proximity to the granular bodies in the case of hydrocephalus (Fig. 2), where they stand out even more prominently against the younger connective tissue of which the nodules are composed. In some places there are spaces distinctly lined by a layer of the deeply staining cells which have the appearance of glandular epithelium, and are very different to the lining cells (endothelial) of neighbouring capillaries. This is clearly seen in a drawing in the

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"Pathological Transactions" for 1889. They appear to resemble fairly closely the proliferated epithelium of the ependyma, which in the case of the hydrocephalic child is of a more spheroidal character than that of the adult brain.

With a view, if possible, to clearing up the nature of these cells I examined granulations in an earlier stage of their formation. In Fig. 3 is seen a section of the ependyma from a case of general paralysis. The membrane is but slightly raised above the surface in two places, and dips down into the brain substance to about an equal distance. It is of a coarse fibro-granular structure, and is covered by a single layer of columnar epithelium. These thickenings represent two granules in the process of formation, and they show that a change is recognizable in the stroma long before any is observable in the epithelial covering. 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. At a deeper level are many blood-vessels exhibiting more or less signs of degeneration of their walls.

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. Still, their nature remained exceedingly obscure, and it was not until I discovered the specimen which is represented in Figure 4, and a few similar ones, that an explanation was forthcoming, but even now I will not go so far as to say positively that this is the true origin of these cells. The drawing represents a minute granulation in an early stage, there being 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, but I am not aware that glands exist in the normal ependyma of the ventricles.

Whether or not it is a fact that the epithelial downgrowths from the surface give rise to the isolated cell-masses that have been described, I would venture to suggest the following explanation for the formation of the granulations based upon an extensive experience of both malignant and simple growths.

I believe these little nodules are of the nature of small tumours which owe their origin to an irritative cause—possibly some chemical substance contained in the fluid of the ventricles or present in the blood. This constant irritant acting upon the epithelium causes it partly to degenerate and partly to undergo proliferation, which may commence a down-growth into the tissues beneath. The continuity of the surface is thus weakened and the connective tissue in the neighbourhood, derived from the neuroglia and from the outermost coat of the vessels, undergoes active increase, producing wart-like projections upon the surface. In its growth it is conceivable that epithelial cells may become isolated and embedded in the fibrous stroma. Moreover, the blood-supply being impoverished and diminished, partly by the condition of the arteries, the new connective tissue-growth early degenerates into a more or less granular amorphous structure.

If we look for an analogy to such a case as is given by these granules on the ependyma, we easily find one in the case of warts on the skin, and this in more than one way. If the skin is constantly coming into contact with irritating fluid, such as that derived from septic or dead animal matter, we have the warty growths and thickenings produced on the hand, commonly known as dissecting-porter's warts. Such is the result when the irritant acts from without, but we also have a similar effect when it is contained in the blood and operates from within. The latter is exemplified by multiple warts on the hands and face of persons who are habitually constipated. That these warts are clearly dependent on the absorption into the blood of effete products from the alimentary canal is proved by their rapid disappearance after a short course of magnesium sulphate. In all such cases the growth is mainly and almost solely made up of dense fibrous tissue, and there is but slight proliferation of the epithelial covering.

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DESCRIPTION OF ILLUSTRATIONS.

FIG. 1.—Ependyma of lateral ventricle from a G.P. There are two granular bodies seen. That on the right hand is of a granular amorphous nature; that on the left is less advanced, and shows connective tissue cells in the central part (? proliferating cells from wall of a vascular space). The membrane is thickened and the vessels are diseased. Logwood. Obj. ½ inch, Pillischer.

FIG. 2.—Ependyma of lateral ventricle from a hydrocephalic child four years of age. The connective tissue forming the granulations is of a younger nature than that represented in the preceding figure. The central part is the most nucleated, the cell nuclei being more elongated than in the adult brain. There is proliferation of the epithelial lining, and groups of similar-looking cells are situated beneath and at the side of one of the granules. Logwood. Obj. ½ inch, Pillischer.

FIG. 3.—Ependyma of lateral ventricle from a G.P. Two granulations in an early stage. The membrane is only slightly thickened, except where the nodules are appearing, and is evenly covered by a single layer of columnar-shaped epithelium. Beneath the thickenings are groups of deeply-staining cells resembling

that of glandular epithelium. Logwood. Obj. $\frac{1}{2}$ inch, Pillischer.

FIG. 4.—Ependyma of the lateral ventricle from a G.P. Into a very slight thickening of the membrane are two small epithelial down-growths, derived from the surface epithelium. The cells are of a less columnar form, and have assumed a more glandular appearance. Logwood. Obj. $\frac{1}{4}$ inch, Pillischer.

Observations on the Effect of Thyroid Feeding in some Forms of Insanity. By LEWIS C. BRUCE, M.D., Assistant Physician, Royal Asylum, Edinburgh, late Assistant Medical Officer, Derby Borough Asylum.

One of the best and latest descriptions of the functions of the thyroid gland is that by Victor Horsley.* This paper furnishes an account of recent work on the subject, and so fully details the results arrived at by other workers that I use it as my chief reference throughout this paper.

Horsley holds three views with regard to the functions of the thyroid gland.

1. That it is directly a blood-forming organ.
2. That it is indirectly a blood-forming organ.
3. That it modifies or destroys substances which, circulating in the blood, are harmful to the general economy.

Dr. Gibson,† in an article on the function of the thyroid, says, in his original paper, he "gave adherence to the hypothesis advanced by Schiff, that the gland secretes some substance whose absorption into the blood is essential to life; and to the extension of this hypothesis by Sanquirico and Canalis, that the gland secretes some material which is necessary for the nourishment of the central nervous system." Gibson believes this to be the gland's chief function, and explains the anæmia which occurs in animals after thyroidectomy as being due "to the very serious effect that the absence of the thyroid has upon the nervous system and upon the general body metabolism, exercising a depressing influence on the blood formation."‡

Horsley makes no definite statement with regard to the gland's influence on the nervous system, but remarks that

* "Brit. Med. Jour.," Jan. 30, Feb. 6, 1892.
† "Brit. Med. Jour.," Jan. 19, 1893.
‡ "Brit. Med. Jour.," Sept. 23, 1893.