On the morbid appearances met with in the brains of thirty insane persons / by J.B. Tuke and William Rutherford.

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THE MORBID APPEARANCES

MET WITH IN THE

BRAINS OF THIRTY INSANE PERSONS.

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MORBID APPEARANCES

IN

THE BRAINS OF THIRTY INSANE PERSONS.

During the last four years we have examined microscopically the brains of thirty persons, all of whom had been the subjects of *chronic* insanity, in one or other of its forms. The autopsies were made within thirty-six hours after death. The specimens of nervous matter were immediately immersed in spirit, and twenty-four hours afterwards in a solution of chromic acid. The sections were in most instances coloured with an ammoniacal solution of carmine, rendered transparent by spirit of turpentine, and set up in Canada balsam or glycerine. The parts of the brain examined were the tips of the frontal and occipital lobes, the convolutions on either side of the fissure of Rolando near the vertex, corpora striata, optic thalami, cerebellum, pons Varolii, medulla oblongata, and any portion which was manifestly the seat of disease. The brains examined were those of patients whose deaths occurred consecutively, and were in no way picked on account of any peculiarity. The forms of disease under which the subjects had laboured were as follows: —general paralysis, dementia with paralysis, chronic dementia, epileptic insanity.

In every case we noticed a marked departure in one form or another from the healthy structure of the brain. And this, although only a *small part* of the brain, was examined in any case.

In our observations hitherto we have occupied ourselves almost exclusively with the detection of morbid conditions, and have only lately begun the greater work of attempting to localize the seat of disease in different cases, but as yet the materials are too limited to admit of any definite statement. The morbid appearances which we have observed are as follow :—

1. Gray degeneration or sclerosis.
2. Miliary sclerosis.
3. Holes of various sizes.
4. Changes in nerve-cells.
5. Changes in nerve-tubes and fibres.
6. Changes in bloodvessels.

7. Granulations on surface of cerebral convolutions, medulla oblongata, and lining membrane of ventricles.
8. Amyloid bodies.
9. Changes in nuclei of neuroglia.

1. *Gray Degeneration or Sclerosis.*

This lesion has been observed by us in various parts of the brain. The order of its occurrence as to frequency has been—

(1.) The white matter of the corpus striatum; (2.) That of the cerebrum and cerebellum; (3.) That of the pons and medulla oblongata. In cases of epileptic insanity it was very frequently found in the last-named organ. Out of the thirty brains examined by us, we have found this lesion in eighteen instances. In nine cases the patients had been the subjects of chronic dementia, of chronic mania in three, of general paralysis in three, and of epileptic insanity in three.

When nerve-tissue, which is the seat of this degeneration, is hardened, and thin sections of it rendered transparent by turpentine are held up between the eye and the light, gray tracts of various shapes and sizes can usually be perceived by the naked eye. If, however, the case be one of recent standing, the microscope is required for their detection. The tracts, whatever be their shape and extent, are invariably less transparent and denser than the surrounding healthy tissue. Rokitansky[1] believes that the primary and essential change is an increase in the amount of the connective tissue (neuroglia) which separates the nerve-elements and vessels. Its nuclei proliferate, and the almost homogeneous matrix which surrounds these becomes distinctly fibrillated and increased in quantity, so as to press upon the nerve-tubes, and cause their atrophy and disintegration; these break up into fatty particles, and often form colloid bodies. Leyden,[2] however, considers that the increase of connective tissue is more apparent than real. He believes that the first change is atrophy of the nerve-tubes, and that, on account of the disappearance of these, the fibrous matrix in which they are embedded appears to be increased. According to Friedreich[3] the place of the nerve-elements is taken by a delicate fibrous tissue, the fibres of which do not, however, lie free, but are embedded in a gray granular substance, in which, after the addition of acetic acid, round or oval nuclei, each containing from two to four nucleoli, may be seen. In a case of sclerosis of the posterior columns of the spinal cord, in which the

[1] Über Bindegewebswucherung im Nervensystem. Sitzungsbericht der math: naturwissenschaft: Cl. der Wiener Akad, band xxiv. heft 1-3. Wien, 1857.

[2] Über graue Degeneration des Rückenmarks. Deutsche Klinik, 1863, No. 13; Canstatt's Jahresbericht, bd. iii., 1864, p. 15.

[3] Über degenerative Atrophie der Spinalen Hinterstränge. Virchow's Archiv, bände xxvi. and xxvii.

first stage of the morbid change was seen, Charcot and Bouchard[1] observed an amorphous, finely granular material, with numerous "myelocytes," amyloid bodies, and proliferated nuclei in the walls of the capillaries. In the opinion of Rindfleisch[2] the following are the morbid changes which constitute gray degeneration: (1.) The nuclei in the walls of the capillaries and larger vessels proliferate; this he regards as the starting-point. (2.) The nuclei of the neuroglia around the vessels proliferate. (3.) A quantity of molecular matter accumulates around these proliferated nuclei of the neuroglia, so as to give rise to the appearance of nucleated cells similar in appearance to the many-nucleated elements of the marrow of bones, as described by Robin and Kölliker. (4.) The perinuclear plasm and the matrix of the neuroglia undergo transformations, which result in the production of cell-like bodies, with numerous delicate fibrous processes. The atrophy of the nerve-elements Rindfleisch ascribes to interference with their nutrition, resulting from the changes in the vascular walls.

We have observed this lesion only in the *white matter* of the brains examined by us. As to the nature of the morbid change, our observations lead us to agree with Rokitansky in regarding it as primarily a modification of the connective tissue. In the spinal cord, medulla oblongata, and pons, it appears to us that the connective tissue or neuroglia is a nucleated, finely-fibrillated structure. In the cerebrum and cerebellum, however, we have not been able to see anything more than a nucleated transparent homogeneous non-fibrillated matrix, representing the fibrillated connective tissue of the spinal cord. Owing to the extreme fineness of the nerve-tubes of the white matter of the brain, as compared with those of the spinal cord, an inquiry into the diseased conditions of the white matter of the former is much more difficult than in the case of the latter; but a careful inspection of numerous finely-prepared sections by means of a magnifying power of 800 diameters linear (Hartnack's immersion lens No. 10, eye-piece No. 3) has resulted in the demonstration that fibrillation and increase of the neurogliar matrix, together with proliferation of its nuclei, are the essential changes in gray degeneration, as Rokitansky[3] has already pointed out. Sometimes proliferation of the nuclei precedes fibrillation of the matrix, at other times the converse holds good. Sometimes there is a marked proliferation in the nuclei of the capillary walls in the diseased tracts, but we have not been able to confirm Rindfleisch's[4] observation that the diseased process invariably starts from these. Indeed, our specimens show that the morbid change just as often begins at a distance from, as in the immediate

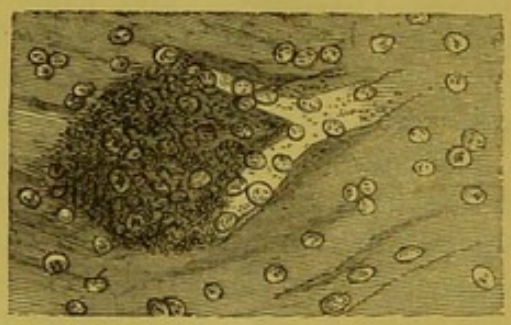
[1] Gazette Médicale, 1866, No. 7, quoted in Centralblatt für die Med. Wissenschaften, 1866, p. 268.

[2] Rindfleisch, Histologisches Detail zur grauen Degeneration von Gehirn und Rückenmark. Virchow's Archiv, band. xxvi.

[3] Rokitansky, *loc. cit.*

[4] Rindfleisch, *loc. cit.*

neighbourhood of, the vessels. Regarding the fate of the nerve-tubes in the diseased tracts in the white matter of the brain, our observations, owing to the fineness of these elements, scarcely enable us to speak with confidence. They *appear*, however, to undergo atrophy, and this need scarcely be doubted, seeing that they certainly do so under similar conditions in the spinal cord. We have seen no evidence of the production of fatty particles from the wasted tubes in the brain. Colloid bodies sometimes appear in degenerated tracts, but these are not of frequent occurrence. In one case we found a lesion which appeared at first sight to be ordinary gray degeneration, such as we have described, but which, on careful examination, proved to be a lesion not hitherto described. In the specimens in our possession it forms patches or spots, one of which is represented in the woodcut. They are sometimes close to, at other times somewhat distant from, the vessels.



Section of corpus striatum, showing a patch in which the nuclei of the neuroglia are proliferated, and surrounded by molecular material. A vessel is seen near the spot. × 300 diam.

Everywhere throughout the section, the nuclei of the neuroglia, and those of the vascular walls, have undergone marked proliferation. The proliferation is, however, especially marked in the spots, and these are embedded in a semi-transparent, finely-granular material which takes the place of the fibres in gray degeneration. The granular material is not arranged around the nuclei so as to form cell-like masses, so that this lesion does not present the characters of gray degeneration, as described by Rindfleisch.[1] It differs from gray degeneration inasmuch as the proliferation of the nuclei of the neuroglia is more marked, and granular material is formed instead of the fibres which are characteristic of gray degeneration or sclerosis. The granular material appears to result from some transformation of the neurogliar matrix, and perhaps the nerve-tubes also. It takes the place of these elements, not because it pushes them aside as if it were proliferated and pushed out from a centre, but as if it resulted from some transformation of them.

It may be, that this is a variety of gray degeneration. We were inclined to suppose that MM. Charcot and Bouchard[2] had already seen it. We, however, took the precaution of showing it to the

[1] *Lib. cit.* [2] *Lib. cit.*

former of these gentlemen, and ascertained that he had not previously seen the lesion.

2. *Miliary Sclerosis.*

We propose the above title for the lesion elaborately described by us in the number of this Journal for September 1868. We would guard the reader against the assumption that this term indicates that this is a form of gray degeneration (the sclerosis of French writers). We adopt the term because it simply indicates rounded hardened patches.

It consists of semi-opaque whitish spots resembling very small millet-seeds. They vary in size from 1-40th of an inch downwards, and, like gray degeneration, and the lesion we have just described, are almost confined to white nerve-matter. When this lesion is far advanced in its development, the spots are readily discernible with the naked eye. They consist of semi-opaque molecular material lying amid a few exceedingly delicate colourless fibres. The lesion is due to the formation of cell-like masses of molecular material, in each of which a nucleus is sometimes discernible. By the formation and growth of these cell-like bodies, the nerve-tubes and bloodvessels are pushed aside, and these may in consequence be seen curving round the diseased tracts. We have not yet been able to decide as to the origin of the cell-like masses. They certainly do not originate in the nuclei of the vascular walls. More probably they originate in the nuclei of the neuroglia. We thought at first that this lesion is that described by Rindfleisch[1] as gray degeneration; but he says that the nuclei of the neuroglia first proliferate, and then molecular material appears around each nucleus, and with the molecular material are connected numerous delicate fibres. The lesion described by us differs from that mentioned by Rindfleisch, inasmuch as no proliferation of the neurogliar nuclei can be seen in the first stage of its development. A *single* molecular cell-like body making its appearance first of all, it may be that it results from a transformation of a neurogliar nucleus. Other cell-like bodies make their appearance, these resulting from division of the first, or arising close to the first one by a process similar to that which gave it origin. Fibres are not connected with the cell-like masses, nor is there any increase of the connective tissue or neuroglia—a fact which at once distinguishes it from gray degeneration, as described by Rokitansky and by Rindfleisch.

We must refer the reader to our drawings and description of this lesion in this Journal for September 1868. When we described the lesion a year ago, we had met with only one case in which it was found. It occurred in a case of atrophy of one-half of the cerebellum. The lesion was found in the white matter of the cerebellum. Since then we have met with it in five out of the thirty cases examined

[1] *Lib. cit.*

by us. We have found it in the white matter of the convolutions in four cases, and in the white matter of the cerebellum in the case already referred to. Dr Kesteven[1] has noted a case in which he observed this lesion in the medulla oblongata.

It may be well to mention that this lesion is not the same as that described by Dr Lockhart Clarke[2] under the title of "transparent granular degeneration." In that degeneration *transparent* granular spots are found. We have shown our preparations to Dr Clarke, and he agreed with us in regarding the lesions as essentially different.

3. *Holes.*

We have observed holes of sizes varying from the 1-50th of an inch downwards. These have only been observed by us in the white matter of the brain. We have most frequently seen them in the corpus striatum, but have also found them in the pons Varolii and the white matter of the convolutions. These holes have ragged edges owing to the abrupt termination of nerve-elements at their margins. The various elements of the brain look as if they had been eaten away. In our sections, which have been hardened in a solution of chromic acid, and set up in Canada balsam, the holes are quite empty. No doubt they are filled with some matter during life, but we are as yet unable to say anything regarding its nature. Nor can we pronounce any definite opinion as to the mode in which these holes are developed. Probably they are due to a disintegration of nerve-tissue, the results of which are removed by the solution employed in hardening the tissue. These holes are quite different from those recently described by Dr Lockhart Clarke at the meeting of the Medico-Psychological Association, held at York (August 1869), inasmuch as they have no apparent connexion with bloodvessels, and are manifestly due to a solution of the continuity of nerve-elements, as is evident from the ragged character of their walls.

It is well known that where portions of the central nervous system have been macerated in spirit for a long time, holes with ragged edges are formed, due to the action of the spirit. In this case the holes contain numerous crystals and broken-up portions of nerve-tissue, which were not discernible in the holes just described. Moreover, we have observed these holes in brains hardened in a chromic acid solution. In our experience, this hardening agent does not cause a solution of nerve-tissue, even when it is macerated in it for at least two years.

4. *Changes in Nerve-cells.*

Atrophy of the pyramidal cells of the convolutions of the vertex

[1] Brit. and For. Med.-Chir. Review, April 1869.
[2] On Tetanus, Medico-Chirurgical Transactions, vol. xlvii., 1866, p. 264.

has been observed in three cases. They had shrunk to at least one-eighth of their normal size, but presented no appearance of granular degeneration.

The pigmentary degeneration of nerve-cells, described by Van der Kolk, Meschede, and others, was likewise frequently observed in the pyramidal and other cells of the cerebral convolutions in the cells of the corpora striata and the corpora dentata of both cerebellum and medulla oblongata. The name of *fuscous degeneration* is suggested as definite and in accordance with its characteristics. Generally the reddish-brown granules appear first at the nucleus, and in such cases the nucleolus has been observed as a black spot. They gradually extend to the periphery of the cell, implicate the processes, and at last nothing but a granular reddish-brown, somewhat angular mass remains to mark the position of the original cell. In some cases this mass has been found larger than the cell which it represents. These changes have been observed both in fresh and prepared brains, and are easily demonstrable in either condition. The cells of the cellular layer of the cerebellum have never been observed to have been the seat of abnormality.

In certain cases the nerve-cells have been noticed surrounded by clear spaces. Although it is impossible to say whether this appearance is morbid or not, it is thought worthy of mention.

5. *Changes in Nerve-tubes.*

Atrophy of the tubes was frequently observed. In a case of chronic dementia, complicated with chorea, the nerve-tubes of the anterior and posterior roots of the spinal nerves were found to have undergone a pigmentary degeneration similar to that noticed in the cells, and to which allusion has just been made.

6. *Changes in Bloodvessels.*

Fatty degeneration of the vessels of the pia mater and cerebrum was very frequently observed, more especially near their bifurcation. In general paralysis, tortuosity and aneurismal dilatation of capillaries were almost constantly present. On the walls considerable proliferation of neurogliar cells and deposits of hæmatoidin were not unusual. Marked dilatation of the perivascular canals was observed in the case of paralytic dementia, the immediate cause of whose death was apoplexy. All the canals of the vessels of the cerebrum which were examined were much dilated, the vessels lying distinctly on one side, as if adherent. The difference between the calibre of the vessel and canal varied from 1-8th to 1-12th. The space was clear of any organized contents. As far as we are aware, this condition of the canals has not yet been described.

7. *Granulations.*

Granulations of the lining membrane of the ventricles, which have

been described by Dr Lockhart Clarke[1] and others, of the pia mater of the parietal and occipital lobes, and of the medulla oblongata, were observed in many cases of general paralysis, and old standing mania and dementia. In whatever portion of the brain they occurred, they closely resembled each other, and were evidently the result of changed epithelium. In the more recent cases they resembled villi, and were semi-transparent. In the oldest, they presented the appearance of rough irregular nodules on the free margins, the epithelial cells being noticeable on their extreme outer edge. They seemed to contain a homogeneous substance, and as this substance has been seen to extend some distance into the brain matter, it is probably exuded lymph, which has raised up the superjacent epithelial layer. As yet we believe these granulations have only been noticed on the floors of the ventricles, but many sections in our possession demonstrate their existence on the surface of the posterior and parietal convolutions and medulla oblongata.

8. *Amyloid and Colloid Bodies.*

These bodies were seldom absent from the brains of old-standing cases. There appeared to be two kinds of bodies, one of which was readily dyed by carmine, while the other remained unaffected thereby after being submitted to its influence for many hours. The latter were also larger, some of them being ten times, the former never exceeding twice, the size of a human blood-corpuscle. These smaller coloured bodies we have alluded to as "amyloid," and the larger and uncoloured as "colloid," without reference to theory, simply for the sake of distinction between them. The *amyloid* bodies have been found chiefly on the surface of the convolutions, medulla oblongata, and spinal cord, held down by the pia mater. Occasionally they were found in the brain substance. A very frequent seat is the posterior longitudinal fissure of the medulla oblongata. We have failed in obtaining any reaction from the application of iodine, and the existence of concentric rings is doubtful. In a case of locomotor ataxia, the atrophied posterior columns of the cord were represented by an immense aggregation of these bodies.

The larger and uncoloured bodies are more frequently met with in the substance of the brain. They are observable in both gray and white matter. Virchow holds that one or other or both of these bodies are normal, or, at least, the result of natural decay. But the fact that they are more common in the brains of the insane than the sane, and the immense numbers in which they occur, suggests that they are actual morbid products.

9. *Changes in Nuclei of Neuroglia.*

In some cases we have observed a diminution in the number of these bodies; proliferation is, however, more common. The pro-

[1] Beales's Archives, vol. iii.

liferated nuclei form either in rows or clusters. There are usually three or four in a cluster, but in one instance we observed as many as twenty in one group. The bodies which result from the proliferation closely resemble the original nucleus; like it, they are coloured by carmine. This proliferation is doubtless the result of irritation. When it is very decided the whole nerve-substance has an unusually granulated and cloudy appearance. In connexion with this subject it is necessary to guard against a somewhat misleading appearance presented by very transparent thick sections; in such the nuclei appear as if increased in number, although really they may have undergone no multiplication.

In conclusion, we beg to offer the opinion that these morbid appearances are only the more crude and apparent pathological changes which are yet to be demonstrated in the brains of the insane. Thanks to the earnest and fruitful labours of Lockhart Clarke more especially, we are now in possession of great facts as to the normal structure of the brain. This great histologist has enabled us to differentiate between the structure of the various convolutions; he has laid open many of the hitherto secret communications of the cerebro-spinal nerves; and the knowledge which he has so freely given to the world places it within the reach of the pathologist to recognise morbid from healthy structure. It is to be hoped that soon he will place the most important anatomical observations of this generation within the reach of all students.

There is still much to be overcome ere a definite opinion can be given as to the nature of the neuroglia and its morbid changes. In this lies the main difficulty; so also, in a less degree, with regard to nerve-cells and nerve-fibre. Patient and continuous observation of morbid brains must be undertaken. Experimental physiology must conjoin with pathology to reduce to logical deduction our knowledge of the functions of the various organs of the brain. After the mere examination of pathological changes has been pushed to its utmost extent, the greater task of localizing the lesions still remains to be accomplished. To this end the most careful record of facts by a host of witnesses is necessary. It is no good to follow in the old rut of naked eye observation. Nothing but the most careful microscopic dissection can serve to bring to light the secrets still unknown. The foot-rule and the pound-weight must give way, and elaborate research, assisted by finer and more accurate instruments, must be brought to bear upon this most important subject. When we know that the arrangement of the layers of the gray matter of the occipital convolutions differs from that of other parts of the encephalon, and that the pyramidal cells of the parietal lobes have an arrangement peculiar to themselves,—when the nerves have been traced to their ultimate origins, and their close relationship demonstrated,—the fallacious crudities of the pathological theatre must be things of the past. We are entering on a new era of cerebral pathology.

We are far from regarding the morbid appearances we have here described as the *causes* of insanity. It is much more than likely that they are the results of we kened or perverted evolution of energy of the nerve-plasm. Nor do we regard these lesions as confined to cases of mental insanity, for we are well aware that certain of these morbid appearances occur in subjects where the insanity has only affected the muscles, and where the mental faculties have remained unimpaired. We believe that the exhausting influences of painful disease, long-continued anxiety (which in itself is not far removed from disease), or old age, may cause many of the degenerations which have here been mentioned, without the manifestation of abnormal mental symptoms—old age, more especially. Let one instance be brought forward—that of Dr Whewell, late Master of Trinity. He worked up to within a few days of his death at the most abstruse subjects; dissection showed great general atrophy of the brain-substance, with a compensatory amount of serum, atheromatous arteries, etc. Now, had this philosopher been the subject of hereditary predisposition to insanity, or had he been liable to the worrying anxiety of the work-a-day world, it is more than probable that he would have evinced greater symptoms of mental aberration than in him were apparent. This case is instanced only to show how very narrow is the neutral ground between mental and physical insanity. It still lies open for demonstration what morbid appearances may be presented in cases of recent and acute mental insanity. The opportunities offered for observation are comparatively rare. Should the microscope fail in detecting any abnormalities in such cases, we must come to the conclusion that the molecular changes are beyond our ken. But we hold that it is of no mean importance that, in so long a series as thirty cases of various forms of chronic insanity, actual morbid changes in structure have been demonstrated. We trust that it will tend to place mental insanity in its proper position as a bodily disease and a pathological entity.

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