or other of these kinds of currents. However it be, there are at least two cases in which this method of treatment seems to have proved successful. The first pertains to Remak, the second to Dr. Russell Reynolds. It is proper, therefore, when the occasion offers, to have recourse to the continued current.

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## *LECTURE VI.*

### DISSEMINATED SCLEROSIS. PATHOLOGICAL ANATOMY.

SUMMARY.—History of disseminated sclerosis; French period; German period; New French investigations; Macroscopic morbid anatomy; external aspect of the patches of sclerosis; their distribution in brain, cerebellum, protuberantia, bulbus rachidicus, and spinal cord. Patches of sclerosis on the nerves. Spinal, cephalic or bulbar, and cerebro-spinal forms. Characters of the sclerosed patches; their colour, consistence, etc.

Microscopic anatomy; sketch of the normal histology of the spinal cord; Nerve tubes; Neuroglia, its distribution; Cortical layer of the reticulum. Characters of the neuroglia, influence of chromic acid. Arterial capillaries. Histological characters of the sclerosed patches; transverse sections; peripheral zone; transition zone; central region. Longitudinal sections. Alterations of the bloodvessels. Examination of the sclerosed patches in the fresh state. Histological lesions consecutive on section of the nerves. Fatty granulations in sections of the sclerosed patches observed in the fresh state. Modifications of the nerve-cells. Mode of succession of the lesions.

GENTLEMEN: At our last conference I dwelt upon the distinction which should be made between the different kinds of tremor. I mentioned, at the outset, that they could be divided into two groups; one, in which tremor is in some sort permanent; another, in which tremor only supervenes on purposed movements. Then, proceeding from these notions, I cited as an example of the tremor characteristic of the first class, that observed in *paralysis agitans*, the history of which I traced for you. On our way, I noted some of the characters which enable us, in these days, to distinguish this disease from another affection, previously confounded with it, namely, from *disseminated sclerosis*.

To this affection, which offers us an example of tremulation belonging to the second class, *i. e.*, a tremor which only appears under certain conditions, we shall devote the present and succeeding lectures. Anatomically considered, disseminated sclerosis forms a clearly defined pathological species; clinically, the case is different,



and in this connection we shall have many blanks to fill up. Let us begin by a few words on the history of the subject.

### HISTORICAL NOTE.

Disseminated sclerosis is found mentioned, for the first time, in Cruveilhier's 'Atlas d'Anatomie Pathologique,' 1835–1842, an admirable work, which ought to be more frequently consulted by all who desire to avoid the disappointment of making second-hand "discoveries" in morbid anatomy. In Parts 22 and 23 you will observe representations of the lesions found in disseminated sclerosis, and, side by side, you can read the clinical observations which relate to them. I take advantage of this opportunity to commend to your perusal a remarkable chapter on paraplegia. Previous to this epoch, so far as I am aware, there is no trace of disseminated sclerosis to be discovered anywhere.

After Cruveilhier, Carswell in the article on "Atrophy," contained in his 'Atlas,' 1838, has had lesions depicted which pertain to disseminated sclerosis. But this author, who has drawn the materials of his work chiefly from the hospital of Paris, does not relate any clinical case in connection with this subject. Even to-day I do not believe that disseminated sclerosis is known in England.[1] I do not find it indicated in any of the standard works published in that country, not even in Dr. Gull's valuable collection.[2]

Thus, up till that time, the principal documents in connection with this disease had been collected in France. From that period forth, during a lapse of several years, this question dropped into almost complete oblivion, and we have to seek in Germany for new indicia. Ludwig Turck published, in 1855, examples of lesions manifestly belonging to disseminated sclerosis; still the physiological aspect of it alone engaged his mind;[3] Rokitansky indicates them in his treatise;[4] Frerichs[5] and Valentine[6] record two observations; Rindfleisch,[7] Leyden,[8] and Zenker,[9] present in their turn

[1] This lecture was delivered in 1868.
[2] Cases of Paraplegia in 'Guy's Hospital Reports,' 1856–1858.
[3] "Beobachtungen über das Leitungsvermogen des Menschliden Rüchen marks," 'Sitzungsberichte der Kais. Akademie der Wissenschaften, Math. Natur. Class.,' t. xvi, 1855, p. 229.
[4] 'Lehrbuch der Pathologischen Anatomie,' 1856, Zweiter Band, p. 488.
[5] 'Haeser's Archiv,' Band x.
[6] "Ueber die Sclerose der Gehirns und Rückenmarks" ('Deutsche Klinik,' 1856, No. 14).
[7] "Histologische Detail zu der Grauen Degeneration von Hirn und Rückenmarks" ('Virchow's Archiv,' B. xxvi, Heft und 6, p. 474).
[8] "Ueber graue Degeneration des Rückenmarks" ('Deutsche Klinik,' No. 13, 1867).
[9] "Ein Beitrag zur Sclerose des Hirns und Rückenmarks" ('Zeitschrift für Rat. Medizin,' B. xxiv, Heft 2 und 3).

some elements towards the solution of the problem. There were, however, desiderata to be supplied, and new researches were indispensable. It was at La Salpêtrière that the question of disseminated sclerosis once more attracted attention amongst us. In 1862, M. Vulpian and myself placed new examples on record. M. Bouchard, founding his remarks on the cases collected by us at the Salpêtrière, reopened the subject in a treatise which he read before the Medical Congress at Lyons.

In the preceding enumeration of authorities, we have taken count chiefly of the works relating to the pathological anatomy of the subject, as we propose to make mention hereafter of those which contain clinical details. To the items of information culled from the writers whose names are mentioned above, we shall add other information drawn from unpublished sources, and, in order to facilitate the understanding of our studies, we shall place before your eyes the anatomical preparations which we have preserved.

## Macroscopic Anatomy.

Disseminated sclerosis, as I have informed you, gentlemen, is not an exclusively spinal affection. It invades the cerebrum, the pons Varolii, the cerebellum, the bulbus rachidicus, as well as the spinal cord. We shall, therefore, enumerate the alterations which are to be observed, taking the most distinctive cases, in the different parts of the nervous system, viewing them first externally, then in section.

We have here to consider a comparatively coarse alteration, and it is surprising that it should have escaped observation so long. On the plates before you, in which these changes are accurately depicted, you see the spinal cord spotted with grayish patches, having a more or less regular outline, but in every case distinctly circumscribed and contrasting widely with the adjacent portion of the cord.

Sometimes discrete, sometimes confluent, these spots or patches, as you may easily perceive, are disseminated without any apparent order, and as it were by chance, over the whole of the spinal cord. The medulla oblongata itself does not escape, far from it; different portions of the encephalon are also frequently affected.

But we cannot content ourselves with this simple sketch, and we must enter upon the details of a more regular description. At the outset, we should remark that a mere *external examination* will give but a very imperfect idea of the lesion. The spots or patches which we have mentioned are not superficial; they constitute real kernels or foci which penetrate into the substance of the tissues. Frequently, indeed, the section itself will reveal the existence of other spots concealed in the interior.



Let us first examine the *encephalon*. The general appearance of the cerebrum proper has undergone no modification of form, nor, we may add, of colour; for the patches are very rarely found on the gray substance of the convolutions. It is different, however, as regards the central parts. There, in fact, we find the patches, especially on the walls of the ventricles, in the white substance of the centrum ovale, the septum lucidum, the corpus callosum, and finally in certain regions of the gray matter, *e. g.*, the optic thalami, and the corpora striata.

The *cerebellum* generally presents only internal patches, which occupy especially the corpus rhomboideum.

The *bulbus rachidicus*, the *pons Varolii*, and the different districts of the isthmus, are very frequently affected by patches of sclerosis which, in such cases, are both peripheral and deep seated. When the bulbus rachidicus is attacked, the patches are found to affect, either singly or simultaneously, the corpora olivaria, pyramidalia, restiformia, and the posterior region where the nuclei of origin of the bulbar nerves are disposed. As regards the pons, the patches generally occupy its antero-inferior aspect. If we ascend higher, we see the corpora mammilaria (or albicantia) and the crura cerebri affected.

We now come to the *spinal cord*. Through the pia mater we often perceive the gray spots which assume a rosy tint or salmon-colour, on contact with the atmosphere. But it is especially after the removal of this membrane, a removal easily effected, that the lesions are clearly perceived. They affect the whole of the cord, being found in the cervical, dorsal, and lumbar regions; they invade all the different columns indiscriminately, are to be found on the sides of the fissures, and attack the gray substance as well as the white.

The *nerves* themselves do not escape sclerosis. We see them, indeed, sometimes emerge from a sclerosed patch and yet remain perfectly sound; at other times, we find them affected, in their course, by sclerosed patches quite similar to those of the nerve-centres; this is so, at least, as regards those parts of the nerves which lie adjacent to the centres, for the observations of MM. Liouville and Vulpian (which have been frequently verified) leave no doubt upon the subject.

The *cranial* nerves that have been found to present sclerosed patches are the optic, the olfactory, and the fifth pair. As to the *rachidian* nerves we only know that such patches have been observed on the posterior and anterior roots; but we are not aware whether they have been thus affected in their extra-spinal course.

I will not dwell any further, gentlemen, on the topography of the patches of sclerosis; still, I cannot refrain from requesting your earnest attention to the interest which belongs to this question.

You observe, in fact, that these patches, in different cases, occupy very different regions of the nervous centres, and it is clear that this variation of position should be represented by very different functional disorders. It is, indeed, to this fact that the disease owes a large portion of its protean character. We shall return to this subject; at present, you will remark that these differences of position give rise to certain important clinical divisions. Sometimes the patches occupy the spinal cord exclusively (*spinal form*); sometimes they predominate in the encephalon (*cephalic* or *bulbar form*); finally, the simultaneous existence of patches in the encephalon and cord supplies the *cerebro-spinal form*.

In order to close what I have to say respecting the macroscopic anatomy of the disease, it only remains for me to indicate the principal characters which the patches present when considered in themselves.

Sometimes they are salient, and, as it were, turgescent; at other times they are on a level with the adjacent parts; finally, they are sometimes depressed, when of old date.

Their colour resembles that of the gray matter, from which it is difficult to distinguish them; but on contact with the atmosphere they assume a rosy hue, and numerous vessels are observed distributed through them.

These spots have a firm consistence, and, on section, present a clean surface, whence exudes a transparent fluid.

Such, gentlemen, as regards its simple anatomy, is disseminated sclerosis, or sclerosis generalized in patches; we have now to enter upon its minute histological details.

In order to bring to a successful issue this undertaking, which relates to facts demanding a careful exposition, I must beg you to grant me both your entire attention and all your indulgence.

## Microscopic Anatomy.

The method to be followed is simple. We should proceed from a consideration of the normal state of the tissues; that once known, it will be more easy to deduce the morbid alterations. The preliminary knowledge of the characteristics of the normal state, as regards the organs and the elements whose changes we wish to study, is doubtless familiar to you, and we might, if necessary, enter at once upon an examination of the intimate lesions. Nevertheless, as you are aware, the histological anatomy of the nervous centres is, in many respects, quite new; many of the questions which it suggests are still disputed; whilst, on the other hand, for the comprehension of pathological lesions, it is not a matter of indifference to have a more or less well-grounded opinion in relation to these questions. These considerations induce us to remind you, at least in a succinct manner, of certain fundamental facts of normal



anatomy. We shall, however, occupy ourselves chiefly with the spinal cord, an organ of less complexity and more easily studied than the brain. In order to limit the field of our examination we shall not delay to describe the nerve elements, properly so called, whether tubes or cells, nor shall we dwell on their reciprocal relations or modes of grouping, in the formation of what is known as the white and gray substances. We propose to concentrate your attention on the connective gangue (or matrix) which surrounds these elements on every side. To this connective setting a high interest attaches, especially for the pathologist, because we must attribute to it a supreme part in the causation of certain alterations of the nervous centres, and particularly in the cases which at present engage our attention.[1]

### I.

A. It will be, I believe, of advantage to inaugurate this study by an examination of thin transparent sections, taken transversely from segments of the spinal cord, which have been properly hardened in dilute chromic acid and coloured with carmine. Carmine is here a precious reagent. Thanks to it, certain elements which under its influence assume a vivid hue are thereby set in relief, whilst other elements preserve their usual appearance. Thus the ganglionic cells, their nuclei, their neucleoli, and also the prolongations of these cells, are strongly coloured under the influence of this reagent. The connective matrix also becomes tinted throughout its whole extent, but much less vividly; as regards the nerve-tubes, the axis cylinder alone takes the carmine tint, whilst the medullary sheath completely resists its action.

All the details which this mode of preparation brings out may be followed on the plate, copied from Deiters,[2] which I here exhibit; you will afterwards easily find them in the very beautiful sections which I shall have passed before you for inspection, and which I owe to the courtesy of Dr. Lockhart Clarke. These sections should be at first examined with a low magnifying power.

In the preparations, as in the plate, the portions pertaining to the white substance of the cord seem to you at first sight almost entirely composed of small regularly rounded bodies, like disks, placed side by side, and having all nearly the same diameter. These are thin cylindrical segments, resulting from section of the

[1] It is known that the first studies of the connective matrix of the spinal cord date from 1810, and are due to Keuffel; but it is less known that Cruveilhier in his article on apoplexy in the 'Dictionnaire de Médecine et de Chirurgie pratiques,' published in 1820, mentioned it:—"Le tissu cellulaire séreux extrêmement délié qui unit et sépare les fibres cérébrales et qui forme une trame excessivement tenue" (*loc. cit.*, p. 209).

[2] O. Deiters, 'Untersuch. über Gehirn und Rückenmark,' Braunschweig, 1865, Pl. iii, fig. 12.

nerve-tubes, which tubes are, in that part of the cord, disposed longitudinally, having the same direction as the greater axis of the organ, and are here, like the prisms of a basaltic causeway, placed parallel each to each. In the centres of these disks, which are chiefly formed of non-tinted medullary matter, having a brilliant and transparent appearance, you will see a point or rather a little globule, *i. e.*, the axis cylinder, coloured carmine.

A somewhat more careful scrutiny soon enables you to note that the disks in question are not exactly in contact, and that they are, on the contrary, more or less plainly separated, each from its neighbour, by an apparently homogeneous substance, which the carmine colours faintly, and which seems to fill like a cement all the interstices that the nerve-elements leave between them. This substance is nothing other than the connective gangue (or matrix) as we called it a little while ago, the neuroglia of Virchow, and the reticulum of Kölliker. In studying its mode of distribution and arrangement, in the different parts of the section, you will readily perceive that it constitutes an important portion of the mass of the organ. Observe, in the first place, that in the peripheral part of the section it forms a ring or rather a zone of some thickness, from which the nerve-tubes are altogether absent. This zone is covered externally and enveloped, as it were, by the pia mater, with which it contracts only some frail attachments; it is, besides, perfectly distinct as regards structure from the latter membrane, which is composed of fibrillary connective tissue and is, therefore, built up quite differently from the neuroglia. This zone has been carefully described by Bidder, and by Frommann,[1] who term it the *cortical layer* of the reticulum (*Rindenschlicht*); we shall see, further on, that, considered from a pathological point of view, it is of incontestible interest.

From the internal border of this zone or cortex we see septa arise and proceed, at certain intervals, which direct their course towards the centre of the cord, which they divide into triangular compartments of almost equal size, whose bases are at the circumference, and whose apices are lost in the gray matter. Each of these septa gives off secondary dissepiments, and these tertiary, which are again subdivided. Their ramifications get interwoven, crossing and anastomosing, so as to produce a web or network with meshes of unequal size. Each of the largest of these meshes may inclose a fasciculus of eight or ten nerve-tubes, or even more, whilst each of the smaller meshes usually contains only one. The reticulated character described becomes especially evident in those portions of the preparation where, owing to the peculiar distribution of the nerve-tubes, the connective skeleton persists alone.

[1] C. Frommann, 'Untersuch. über die normale und patholog. Anatomie des Rückenmarks,' Jena, 1864.



The neuroglia plays, probably, a more important part in the gray substance than in the white; there are, in fact, some regions almost exclusively formed by it, as, for instance, the borders of the central canal and the column of the ependyma. It is also predominant in that part of the posterior cornua known as the gelatinous substance of Rolando; in the posterior commissure, which consequently takes, almost throughout its whole extent, a rosy tint in the preparations coloured with carmine, whilst the anterior commissure, on the contrary, in consequence of the numerous transverse nerve-tubes it contains, is much less affected by the reagent. In the gray substance also, as in the white, the neuroglia presents a reticulated appearance; but, in the former case, the greater intricacy of the trabeculæ causes the meshes to be notably smaller, and the whole to assume the appearance of a spongy tissue. In both states, however, it serves as a framework and support for the bloodvessels.

B. It is incumbent on us now to investigate, by means of more powerful lenses, what is the histological constitution of this connective gangue or web, of which we only know as yet the most superficial appearances. Have we here a common connective tissue (laminous or fibrillary)? Certainly not. All observers are agreed upon this point. But, beyond this purely negative notion, almost everything else is disputed in the histological history of the neuroglia. However, one opinion tends to become prevalent here, and this opinion, if I may judge from impressions arising from personal observations, closely approximates to the truth. According to this view the neuroglia would be formed, like the stroma of lymphatic glands, for instance, after the type of simple reticulated connective tissue (Kölliker); that is to say, it would be essentially composed of stellate cells, generally poor in protoplasm, having slender prolongations, ramified several times, whose branches unite with other, so as to bind into one system the several cells, and to render them, as it were, joint-partners [Kölliker,[1] Max Schultze, Frommann].[2] In this form of the connective tissue there exists but very little amorphous matter in the meshes of the reticulum, and the intermediate fibrillary substance, which is one of the fundamental characteristics of the laminous tissue, is completely deficient here.

Let us now see what direct examination enables us to discern in thin sections of the cord hardened by chromic acid and coloured with carmine. As in the case of the stroma of lymphatic glands, which we have just taken for example, it becomes us here to distinguish, in the first place, the cells, and, in the second place, a network of fibroid trabeculæ, which binds these cells together. Let us first take note of what is observed in the white substance. The

[1] Kölliker, 'Geweblehre,' 5e Ed., Leipzig, 1867, § 108.
[2] *Loc. cit.*

points of the reticulum, where several trabeculæ meet, form here and there swellings or nodes of different degrees of thickness, situated at almost equal distances from each other. Now, all these nodes, but especially those remarkable by their great size, present towards their central portion a definite, rounded, and somewhat oval corpuscle, more vividly coloured by carmine than the adjacent parts. These bodies are nuclei, having a well-defined border; they are finely granular, are devoid of nucleoli, and measure each on an average from 0.004 m. to 0.007 m. They are soluble in acetic acid, which causes them to shrink in every direction, and diminishes their diameter sometimes by one half; they are known by the name of *myélocytes* (Ch. Robin),[1] or *neuroglia nuclei* (Virchow).[2] A thin layer of protoplasm, having no distinctly cellular appearance, usually surrounds these nuclei (*myélocytes, variété noyau*), which, at other times on the contrary, are inclosed in a genuine rounded or stellate cell (*myélocytes, variété cellule*), and furnished with more or less numerous prolongations (from three to ten, according to Frommann), of different lengths.[3]

The prolongations appear to unite with the trabeculæ of the reticulum, which continue them, as it were, without any perceptible line of demarcation. In cases where the cellular form is not distinct the nuclei, either naked or covered only with a thin layer of protoplasm, look like centres whence arise the trabeculæ of the reticulum, and whence they radiate in different directions.

The trabeculæ should be studied in their turn, and considered independently of the connections they have either with the nuclei or with the cells which occupy the nodes of the reticulum; their texture varies somewhat, according as we examine them in transverse and in longitudinal sections. In the first case they have the appearance of thin homogeneous and brilliant dissepiments of a fibroid nature. Anastomosing, they form meshes, the smallest of which is still large enough to inclose a nerve-tube. Suppose we observe a longitudinal section? The trabeculæ are seen to ramify to an indefinite extent, and produce a network having much finer meshes. This network is disposed in the form of dissepiments, which separate the nerve-tubes from each other and inclose them, like a sheath. The interstices which exist here and there between these sheaths and the nerve-tubes seem to be filled up by a small quantity of finely granular amorphous matter. In the normal state we meet nowhere, amongst these trabeculæ, with the slender fibrillæ which constitute an integral part of laminous tissue.[4]

[1] Robin, 'Programme du Cours d'Histologie,' 1864, p. 46; 'Dictionnaire Encyclopédique,' 2e Série, t. i, 1re part; art. Lamineux, p. 284.

[2] Virchow, Die Krankhaft, Geschwülste, 1864–5, t. ii, p. 127.

[3] In reference to this subject see Hayem and Magnan, 'Journal de la Physiologie, etc., No. 1, 1876. Hayem, 'Études sur les diverses formes d'Encéphalite,' 1868.

[4] The term *tissu lamineux* was applied in 1799 by Chaussier to the tissue recently and still commonly known as cellular tissue, which we now call connective tissue. Professor Robin still makes use of Chaussier's term, alleging it to be the best, because he says the ultimate elements of this tissue are long filaments, somewhat flattened, thin, slender, soft, and hyaline, smooth, slightly elastic, fasciculated. (Sigerson.)



In the gray substance the neuroglia is disposed on the same general plan; the meshes of the fibroid network are, however, and especially in parts where the nerve-elements disappear, more serried than in the white substance, and from this cause a spongy appearance results, which we have already noticed. Let us add that the stellate cells abound in greater number than elsewhere in certain regions of the gray substance, and that they sometimes attain such a development that it becomes very difficult to distinguish them from nerve cells; but we shall have occasion to refer to this point again.

A dense fibroid network, with close meshes and numerous cells, is found also in those parts of the white substance where no nerve-tubes exist, in the cortical layer (*Rindenschlicht*), for example, and in the greater septa which arise from it.

If we can depend upon the preceding description it is incontestable that the neuroglia deserves to be classed with the reticulated connective-tissue type, whose essential characters we noted a little while ago.

But this description has been chiefly traced out, as you have not forgotten, from observations made on fragments of spinal cord that have been subjected to the action of chromic acid for a greater or less extent of time. Now, can it be asserted that the results obtained by this method of preparation are beyond the reach of criticism? Such is not the opinion of some authors, amongst whom we must cite, in the foremost place, such masters as Henle and Ch. Robin.[1] According to these, the fibroid reticulum, above described, has no real existence, but is an artificial product.

In the fresh state, before the application of reagents, the spaces between the nerve-tubes are filled (according to them), not by solid trabeculæ, arranged so as to form the meshes of a network, but simply by a soft, grayish, finely granular substance, in the midst of which the myelocytes are, as it were, held in suspension.

This substance has the property of hardening, without loss of volume, under the influence of alcohol and different reagents, of chromic acid in particular; and it is owing to this circumstance that it presents a reticulated appearance in preparations treated by the latter reagent. To these objections, arguments or rather facts have been opposed, some of which possess, we think, almost absolute authority. It is conceded that in the normal state an amorphous matter exists, interposed between the nerve-elements, though in scanty proportion (Kölliker), and that this matter possesses the

[1] 'Dict. Encyclopédique,' *loc. cit.*

properties which have been described. It is also conceded that, in the fresh state, the reticulum is less distinctly defined than in preparations hardened by the use of acids. But it is not the less true that, even in the fresh state, thin sections of the white substance of the cord, when placed in iodized serum and dilacerated under the microscope, permit us clearly to discern on their borders the fibroid tractus of the connective tissue (Kölliker, Frommann, Schultze). This result, which it is easy to arrive at in the normal state, is still more readily obtained in certain pathological conditions when the normal arrangements are exaggerated, without being radically altered (Virchow).

This is what takes place, for instance, as we shall point out, in sabacute interstitial myelitis and in sclerosis proper, when the alteration has not as yet exceeded the first phases of its evolution.

From all this it has been concluded, and we think the conclusion legitimate, that the chromic acid has no other specific effect than to bring out into better relief the reticulated texture of the connective gangue or setting of the spinal cord. The arrangement was previously in existence; it is not produced from nothing by the action of the reagent.

In order to conclude the remarks which I have thought it my duty to offer you, in reference to the normal histology of the spinal nerve centre, I have only a word to add concerning an anatomical peculiarity of the smaller vessels, and principally of the arterial capillaries, in the substance of this organ. They possess, like the intra-encephalic arterioles, that supernumerary coat which is commonly known as the lymphatic sheath or Robin's sheath. This sheath is separated, as you are aware, from the adventitious coat by a free space, filled by a transparent fluid in which float some definite elements. You will soon recognize the interest belonging to this anatomical arrangement, when we come to the question of interpreting certain lesions.[1]

[1] Since this lecture was delivered, several works have been published on the structure of the neuroglia (see in reference to this subject a critical review by Gombault, 'Archives de Physiologie,' 1873, p. 458). In an important work, M. Ranvier, whose labours have contributed so much to our knowledge of the connective tissue, has shown that the cells, described by Golgi and Boll, are probably artificial products, due to the preparatory method adopted. The connective tissue of the nerve centres is but little different in structure from that of other regions (Ranvier, "Sur les éléments conjonctifs de la moelle épinière," in 'Comptes-Rendus de l'Académie des Sciences,' Décembre, 1873). The neuroglia is composed of little connective bundles of from 0.001 mm. to 0.002 mm. in diameter. "They do not anastomose," says M. Ranvier, "but in some points they cross each other to the number of four, five, six, seven, eight, and even more. At this crossing there is often a round or oval nucleus, having little nucleoli, which is flattened and surrounded by a granular zone. With a good immersion object-glass, magnifying from 600 to 800 diameters, it is easy to perceive all these details and to discern in the granular zone a lamina of protoplasm which, with the nucleus, constitutes a little flat cell of the connective tissue. Beneath and above this cell the little fasciculi follow each other. It does not seem doubtful to me," M. Ranvier adds, "that this grouping has been taken for a ramified cell; but that is an error which will be abandoned, I am sure, by all who accurately follow the same method" (which he indicates). On other points of the same preparation may be seen isolated cells, and again (stellate) crossings without cells; these appearances leave no doubt as to what should be the proper interpretation of the foregoing facts. The reader will be less surprised at the numerous conflicting opinions published as regards the neuroglia, if he will recall the numerous discussions excited by the question of the structure of the connective tissue of the peripheral organs. The real nature of this structure has been only revealed by recent researches. (*Note to the Second Edition.*)



## II.

After these preliminaries, it becomes easy for us, gentlemen, to enter upon the study of the histological alterations of the spinal cord in *disseminated sclerosis*. The description of these changes, which we are about to give, will be based, principally, on the results of the investigations to which M. Vulpian and myself have long devoted our attention. We shall also have special opportunities of using, after due revision, the researches made, previously or since, on the same subject by Valentiner,[1] Rindfleisch,[2] Zenker,[3] and especially by Frommann,[4] who, in reference to the examination of a small fragment of spinal cord, has written a large volume, adorned with remarkable plates, and enriched with valuable documents.

We shall describe in the first place the appearances which may be discerned: 1st, on transverse sections; and 2d, on longitudinal sections of fragments of the cord hardened by chromic acid. Then we shall describe, from the examination of fresh specimens, certain peculiarities which are not observable in hardened sections. In both cases the coloration of the parts, effected by means of the ammoniacal solution of carmine, will be here, as well as in the case of normal specimens, an auxiliary of great utility of which it is proper to avail ourselves.

A. When you examine with the naked eye a segment of spinal cord affected by a patch of sclerosis, the morbid part appears divided from the healthy portion, in an abrupt manner, without transition, by a definite line of demarcation. Now this is an illusion. Microscopical examination, even when a low power is used, enables us to state that the apparently healthy region bordering the sclerosed patch really presents, to a certain width, very plain traces of alteration. When you pass the apparent limit of the sound parts the lesions become more marked, and they augment gradually in intensity as you approach the centre of the patch,

[1] Valentiner, 'Deutsche Klinik,' 1856, p. 149.
[2] Rindfleisch, 'Virchow's Archiv,' 1863, t. xxvi, p. 474.
[3] Zenker, 'Zeitsch. der Ration. Mediz.,' 1865, Bd. xxiii, 3 Reih. p. 226.
[4] Frommann, 2 Theil, Jena, 1867; see also Rokitansky, 'Sitzungsber.,' K. M. Klasse, t. xiii, 1851, p. 136; Charcot, 'Soc. de Biologie,' 1868; Bouchard, 'Soc. Anat.,' 1868; Hayem, 'Études,' etc., *loc cit.*, p. 121.