noted, I shall only make special mention of the modification which the nerve cells experience when, on the gray substance being invaded, they become comprised within the area of a sclerosed patch. These cells do not become the seat of nuclear proliferation, contrary to what under similar circumstances occurs in the cells of the connective tissue whose nuclei generally multiply; and this is, in fact, a characteristic which might, if needed, be a help to distinguish one from the other of these two orders of anatomical elements. The nerve-cells undergo a peculiar alteration which may be designated by the term *yellow degeneration*, on account of the ochreous tint which they assume, and which is occasionally somewhat intense; in this state they cease to be coloured by carmine as in the normal state; the nucleus and the nucleolus seem to be formed by a substance having a vitreous and brilliant appearance. It is the same as regards the body of the cell, which, besides, appears as if composed of concentric strata.

Finally, all parts of the cell are seized by atrophy, which may lead to a comparatively considerable diminution of its bulk, whilst, at the same time, the cell processes dwindle away and disappear.[1]

In the encephalon, and also in the optic and olfactory nerves, the sclerosed patches present essentially the same characters as in the cord; hence we do not think it would be of any advantage to enter into details in relation to them.

Now that we have reached the conclusion of our study, we may try to array, in their natural order of sequence, the phenomena which go to make up the alteration in question, and thus endeavour to determine the pathological method by which this morbid change is produced.

Undoubtedly, the multiplication of nuclei and the concomitant hyperplasia of the reticulated fibres of the neuroglia constitute the initial, fundamental fact, and necessary antecedent; the degenerative atrophy of the nerve elements is consecutive and secondary; it had already begun when the neuroglia gave way to the fibrillary tissue, though the wasting afterwards proceeded with greater rapidity. The hyperplasia of the vascular parietes plays merely an accessory part.

In what consists the affection of the neuroglia which marks the beginning of this series of derangements? It is easy to discover there all the characteristics of formative irritation. But, after recognizing the fact that disseminated sclerosis is a primary and multilocular chronic interstitial myelitis or encephalitis, it remains for us to determine the histological characters which distinguish it from other forms of sclerosis of the nerve-centres, and also from several kinds of myelitis or encephalitis which, having their starting-

[1] Frommann, *loc. cit.*; Vulpian, 'Cours de la Faculté,' 1868; Charcot, 'Société de Biologie,' 1868.

point likewise in the neuroglia, nevertheless do not issue in fibrillary metamorphosis. We will endeavour, at an opportune moment, to fulfil this duty. At present, gentlemen, we hasten to leave the department of pathological anatomy for that of clinical observation in order to show you by what array of symptoms disseminated sclerosis of the nervous centres makes its existence known.[1]

LECTURE VII.

DISSEMINATED SCLEROSIS: ITS SYMPTOMATOLOGY.

SUMMARY.—Different aspects of disseminated sclerosis, considered from a clinical point of view. Causes of error in diagnosis.

Clinical examination of a case of disseminated sclerosis. Tremor: modifications caused thereby, in the handwriting; characters which distinguish it from the tremor of paralysis agitans, chorea, general paralysis, and the motor incoördination of ataxia.

Cephalic symptoms. Disorders of vision: diplopia, amblyopia, nystagmus. Impeded utterance. Vertigo.

State of the inferior extremities. Paresis. Remissions. Absence of disorders of sensibility. Commixture of rare symptoms; tabetic phenomena; muscular atrophy. Permanent contracture. Spinal epilepsy.

IN the preceding lecture we minutely described the anatomical lesions of multilocular sclerosis of the nervous centres. Leaving aside, therefore, this portion of its history we shall proceed, to-day, to point out the series of symptoms by which it makes its existence clinically known.

I.

A. It is singular that a morbid state which possesses so distinct and so striking an anatomical substratum, and which, in short, is

[1] In a note published in the 'Archives de Physiologie' (1873, p. 753), one of Professor Charcot's students, Dr. Debove, has shown cause for the modification of the generally received opinion in reference to the histology of disseminated sclerosis. According to his researches, the sclerosed parts are formed of fibrillæ and of flat cells, quite similar to the cells of common connective tissue. He has succeeded in demonstrating this, through having employed the method of interstitial injections.

These facts are very different from what was believed with respect to the structure of the neuroglia (see note, p. 138), before M. Ranvier demonstrated that the connective tissue of the nerve-centres does not essentially differ from that of other organs; the only striking peculiarity being, according to M. Ranvier, the small diameter of the fibrillary fascicles.—(*Note to the Second French Edition.*)

not a rare disease, should have escaped clinical analysis for such a length of time. Yet nothing is simpler, as I trust to show you, than to diagnose the affection in question, by the bedside of the patient, at least when it has reached its typical period of perfect development.

If it be asked what cause so long deferred the recognition of disseminated sclerosis and its admission into nosological charts where it should occupy a place beside other better-known forms of primary sclerosis of the nervous centres, it is proper to point to the diversity of aspects under which it may be encountered in the hospitals. It is, in fact, an eminently polymorphic affection.

Our anatomo-pathological studies ought to have made you anticipate that it would be so. You remember that the patches or islets of sclerosis sometimes occupy the spinal cord exclusively, that in other cases they predominate in the cerebral hemispheres and the medulla oblongata, and that, finally, there are cases in which they are dispersed throughout all the departments of the nervous centres. These varieties of position induced us to recognize, from an anatomical point of view, the three following forms: 1st, the *cephalic form;* 2d, the *spinal form;* and 3d, the *mixed* or *cerebro-spinal form.* It was easy to foresee that each of these forms would be represented by a group of symptoms peculiar to itself.

B. Let us first, if you please, concentrate our attention on the cerebro-spinal form. It is, in truth, the most interesting in every respect and that which you will have occasion most frequently to observe in practice. Well, even when considered in this type, the disease may assume a variety of masks. Allow me, in support of this assertion, to mention an anecdote which one of my colleagues recently related to me.

A very distinguished physician, one, however, who was but little familiar with the symptomatology of disseminated sclerosis, had come to visit my friend in the clinical department over which he presides. In order to do him honour, my colleague presented him a case of the new disease,—a very fine specimen of the cerebro-spinal type The patient, leaving his bed, took a short walk down the ward. "This is an ataxic," said the visitor. "Perhaps so," replied my colleague, "but what do you think of the rhythmical movements by which the hand and upper extremities are shaken?" "True," said the visitor, "he is also affected with chorea, or perhaps with paralysis agitans." The patient was then questioned. He replied, but, in replying, showed a marked difficulty of enunciation; he scanned the syllables in a very peculiar manner; and the utterance of a word was often preceded by a slight trembling of the lips. "I understand," said the physician, "you wished to puzzle me by presenting a most complicated case. Here are symptoms which belong to general paralysis. Pray don't proceed any further; your patient probably is a living conpendium of all nervous pathology."

Now, gentlemen, I repeat it, this was simply a case, though a very complete one, of the cerebro-spinal form of disseminated sclerosis.

C. Paralysis agitans is especially the disease with which this form of sclerosis has been the most persistently confounded, and for which it is, undoubtedly, still the most frequently mistaken. It was because of this confusion that, at the time we laboured to draw forth disseminated sclerosis from the chaos of chronic myelitic affections, we urged M. Ordenstein, then one of our students, to tabulate in parallel columns the opposite characters that divide this disease from paralysis agitans, for the better understanding of the contrast.[1] How M. Ordenstein acquitted himself of this duty is known to you, and I do not hesitate to declare that his dissertation marks a serious progress in the clinical history of chronic diseases of the nervous system.

In recent days, Herr Baerwinkel, a distinguished physician of Leipzig, after having related a very interesting example of cerebro-spinal sclerosis, which, however, presented no tremor (as sometimes happens), seems to insinuate that M. Ordenstein was pleased to create difficulties which had no real existence, in order to give himself the facile satisfaction of surmounting them. According to him, there is no analogy whatever between the two diseases. Dr. Baerwinkel must, doubtless, have forgotten that in 'Canstatt's Jahresbericht' he gave, some ten years ago, the analysis of a case observed under Skoda's care,—in that case, paralysis agitans had been diagnosed during life, whilst, on post-mortem examination, patches of disseminated sclerosis were found in all parts of the cerebro-spinal axis. The case appears to have been noted with the greatest fidelity. It is stated, and this point deserves remark, that the tremor, contrary to what occurs in ordinary cases of paralysis agitans, only showed itself when voluntary movements were made, and subsided when the patient was at rest.[2]

Nor can Herr Baerwinkel have overlooked the case recorded by Herr Zenker in Henle's Journal. Here again the existence of multilocular sclerosis was only revealed by the post-mertem examination.[3] During life, Professor Hasse had made a diagnosis of paralysis agitans, and yet, in the symptomatological description, there is stress laid on the nature of the tremor, which only showed itself under the influence of emotion or on the occasion of voluntary movements.

These examples suffice, I presume, to show you that, in spite of

[1] "Sur la Paralysie Agitante et la Sclérose en Plaques Généralisée," Paris, 1867.
[2] 'Vein. Med. Halle,' 13, 1862.
[3] Zenker, 'Zeitschrift für Medizin,' Band iii, Reihe, 1865, p. 228.

the opinion of Herr Baerwinkel, it is possible to confound the two diseases, since such confusion has been committed by clinical observers whose skill is above all question.

That being established, I am ready to concede that the different disguises assumed by disseminated sclerosis are coarse masks, and that to-day, when recent works[1] have illuminated the field of diagnosis, it is scarcely permissible to be caught in the snare. But it is time, gentlemen, to place you in a position to distinguish the characters by means of which cerebro-spinal disseminated sclerosis may be separated from those diseases which more or less closely resemble it.

II.

You are not unaware, gentlemen, of what value you must set on clinical descriptions, eloquently detailed at a distance from the bedside of the patient. They seldom succeed, whatever the effort, in doing more than giving origin to indistinct images which generally leave but a vague and transient impression on the mind of the auditor.

In order to avoid, as much as possible, falling into the fault I have just mentioned, I will proceed in your presence to the methodical examination of a patient who presents all the symptoms of the cerebro-spinal form of disseminated sclerosis, in the period of perfect development.

Mademoiselle V—, aged 31, has been suffering for about eight years under the affection which forms the object of the present study. Admitted to La Salpêtrière three years ago, she was bequeathed to me by M. Vulpian when he left this hospital, and he, at the same time, gave me, in reference to her case, a detailed and most valuable note. The invasion of the disease dates, we have said, from eight years ago; it is, therefore, a case of old standing. I will tell you afterwards of the different changes which characterized the early phases of the evolution of symptoms. For the moment I wish to confine myself to an analysis of her actual condition.

One symptom which, doubtless, struck you all from the first on seeing the patient enter, assisted by a nurse, was certainly the very special rhythmical tremor by which her head and limbs were violently agitated whilst she was walking.

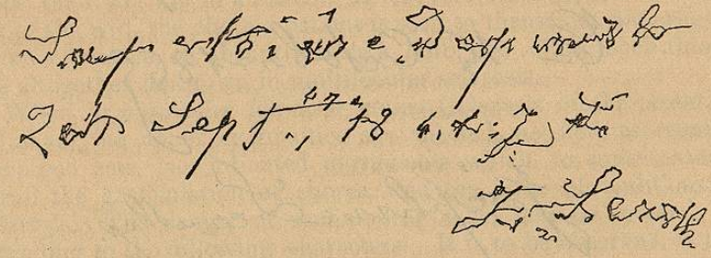
You have likewise noticed that when the patient sat upon a chair, the tremor disappeared at once and completely from her upper and lower limbs, but only partially from the head and trunk. I lay stress on this latter point, whilst calling your attention to the fact that the new attitude, assumed by the patient, is

[1] Bourneville et L. Guerard, "De la Sclérose en Plaques Disséminées," Paris, 1869; Bourneville, "Nouvelle Étude sur quelques Points de la Sclérose en Plaques Disséminées," Paris, 1869.

far from being one of absolute rest as regards the muscles of the body and neck. Besides, we must make allowance for the existence of emotion which undeniably plays a certain part here. I shall have occasion to show you Mademoiselle V— when reclining in bed, and in complete repose; you will then be able to assure yourself of the utter absence of all trace of tremor in the different parts of her body. To cause the rhythmical agitation again to appear throughout the body, it will suffice to make the patient rise from her seat. To bring it back merely in a partial manner, in one of the upper extremities for instance, I will request her to lift a glass full of water, or a spoon, to her mouth. You can see that, in the several acts prescribed by the will, the tremor increases in direct ratio with the extent of the movement executed. Thus, when the patient wishes to lift a glass full of water to her lips, the rhythmical agitation of the hand and forearm is scarcely noticeable when taking hold of the object; but it becomes more and more exaggerated as the glass is brought nearer to the eyes; and at length proceeds to such an extent that, at the moment when the goal is being attained, the glass is, as you observe, dashed with violence against the teeth, and the water is flung out to a distance. This great disorder is not shown, I repeat, save in the performance of movements of a certain amplitude. As regards petty operations, such as sewing or ravelling linen, the oscillations, on the contrary, are almost null. Some time ago, the patient could still write distinctly enough; the letters, indeed, were tremulous, but perfectly readable.[1]

[1] We give below two specimens of the handwriting of a patient named Leruth, who succumbed to disseminated sclerosis in M. Charcot's wards. This woman was admitted to La Salpêtrière September 24, 1864. In May, 1865, M. Charcot obtained this fragment of the writing (fig. 13).

Fig. 13.



From the month of June, Leruth was placed under the nitrate of silver treatment (two milligrammes, then four, being administered). Under the influence of this medicine the tremor diminished in a notable manner, as may be judged from an examination of the following specimen of her writing (fig. 14).

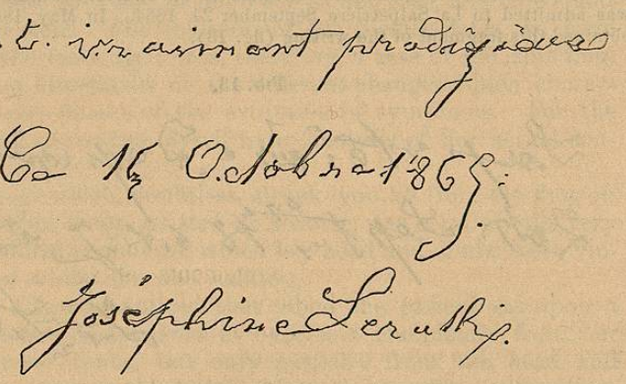
Remark, also, that in May, 1865, the patient was greatly fatigued after writing the three lines, of which a fac-simile is given above; whilst in October she was

To sum up, *the tremor* in question *only manifests itself on the occasion of intentional movements of some extent; it ceases to exist when the muscles are abandoned to complete repose.* Such, gentlemen, is the phenomenon which I have been led to regard as one of the most important clinical characters of cerebro-spinal disseminated sclerosis. I do not, indeed, pretend to put this forward as a pathognomonic symptom; I am not unaware that a tremor showing itself, with somewhat similar characters, is occasionally observed in affections other than disseminated sclerosis, as, for instance, in mercurial poisoning, in chronic cervical meningitis with sclerosis of the cortical layer of the cord, in primary or consecutive sclerosis of the lateral columns, etc. It is not, as we shall see, a constant symptom. But what I wish at present to place prominently before you is the fact that, in disseminated sclerosis, when no other complication supervenes, the tremor, if it exist at all, presents itself always with the characters which I have assigned to it. In some this is a symptom which, by itself alone, would suffice to distinguish multilocular sclerosis of the nervous centres from some affections which so nearly resemble it as to render confusion possible. In reference to this subject I shall enter into some details.

The tremor of *paralysis agitans* exists as well when the members are in a state of repose as when they are set in motion by the will. I present a patient in whom the tremor has persisted for long years, without cessation or truce, during the patient's waking

able to write a dozen lines with ease. We have selected, for the second specimen, the first and last lines of what she wrote.

Fig. 14.



Judging from the specimens in our possession, it is difficult to form an opinion on the characteristics of the handwriting of patients affected with disseminated sclerosis. Generally, indeed, we have examined the patients at an advanced stage of this disease; then it is almost impossible to obtain anything beyond a scribble without significance, the more so because we have no term of comparison.—(B.)

hours. It never stops save when this unfortunate woman is plunged in profound sleep. There are cases of shaking palsy where the tremor only shows itself intermittently, but, singularly enough, it is just in such cases that the tremor shows itself rather when the limbs are at rest, and ceases when they are set in motion by the will. You can perceive in another patient, whom I submit to your observation, this peculiar characteristic of paralysis agitans. Remark, also, in both these women, that the head takes no share in the trembling; or, if it seem shaken by the oscillations, these are plainly communicated to it by the agitation of other parts of the body,—there is transmission of shocks from the affected members and trunk. The absence of tremor of the head seems to me an almost constant fact in shaking palsy. I will add that in this affection the jerks are of much less extent, more regular, rapid, and serried, if I may so speak, than in multilocular sclerosis. In the latter, the oscillations are larger, and resemble, in many respects, the gesticulations of chorea; this analogy is so close that before the publication of the works which have caused it to be admitted into clinical lists, disseminated sclerosis has been sometimes designated under the names of rhythmic chorea and choreiform paralysis.

It is, however, always easy to distinguish the odd and disorderly movements of *chorea*, properly so called, from the rhythmical oscillations of multilocular sclerosis. Note, firstly, that in the latter case, if the action of the upper extremity when lifting an object to the lips be considered, the *main direction of the motion persists in spite of the obstacles caused by the jerks of the tremor*, which, as we have just said, augment as the hand approaches its goal. In chorea, on the contrary, the *main direction of motion would be disturbed from the outside by contradictory movements*, quite disproportionate in magnitude, *which cause the goal to be missed.* Add to this that the movements of chorea show themselves suddenly and unexpectedly, when the limbs are in a state of perfect rest; thus, apart from any act of the will, the choreic patient is seen to thrust out his tongue, make a grimace, or abruptly raise a limb, etc. Now, such things are altogether unknown in multilocular sclerosis.

When, in *progressive locomotor ataxia* (sclerosis of the posterior columns), the upper extremities are affected, we find, as regards purposed acts, incoördinated movements which, to some extent, recall the gesticulation of chorea, and the jerks of multilocular sclerosis. The danger of confounding them may be avoided by attending to the following characters. It is to be observed, at the outset, that in the incoördination of the ataxic patients we do not, properly speaking, find any tremor or rhythmical jerks, but rather gesticulations of different degrees of disorder, abruptness, and extent. Examine studiously, in the case of the patient whom I place before you, the movements of the hand when in the act of taking

hold of a small object, and you will find truly characteristic peculiarities. You see how, at the moment of grasping, the fingers separate excessively, and are extravagantly extended, bending towards the back of the hand. Then the object is seized suddenly, with a dash, in an almost convulsive manner by the abrupt and disproportionate flexion of all the fingers. This is a symptom of ataxia; you will never observe anything of the kind in disseminated sclerosis. Lastly, I would add—and this final trait is truly decisive—that, in ataxia, the closing of the eyes has always the effect of exaggerating in a very marked manner the incoördination of the movements, whilst it does not at all modify the rhythmical jerks of multilocular sclerosis.

We should not, however, forget that some of the symptoms of ataxia are found occasionally mixed up with those of disseminated sclerosis, when the sclerosed islets in certain regions of the cord spread over a certain height of the posterior columns. A case, the history of which may be found recorded at length in Cruveilhier's 'Atlas d'Anatomie Pathologique,' may be cited as an example of this class.[1] It is the case of the patient Paget. In order to grasp and use a pin she required to have her eyes open, otherwise the pin dropped from her fingers. On a post-mortem examination, it was found that one of the sclerosed patches occupied a considerable extent of the posterior columns in the cervical enlargement of the cord. But I shall not now dwell at any greater length upon this point, to which we shall have several opportunities of again referring

We have hitherto, almost exclusively, studied the question of tremor in its connection with the upper limbs; but we also know that it may affect the head, the body, and the lower extremities. It presents itself, in these different parts, with all the characters that we have described in reference to the upper limbs, that is to say, it is absent in repose, and shows itself on the occasion of purposed movements, or in case of attitudes which cannot be maintained except by the active and more or less energetic tension of certain muscles or sets of muscles.

In order to complete the characteristics of this symptom, we must enter into a few details. Tremor, gentlemen, as I long ago declared, is an almost constant symptom in the cerebro-spinal form of disseminated sclerosis. It must not be forgotten, however, that exceptional cases exist, in which—though the fact is as yet inexplicable—no tremor presents itself amongst the symptomatological group. I have myself observed several cases of this kind. But you should note, gentlemen, that tremor may have existed, to a greater or less extent, at a certain anterior epoch of the disease, and may have disappeared at the time when the patient offers himself for examination. It is, therefore, necessary, on this account, to question with the greatest care those patients in whom this symptom is apparently absent.

[1] Cruveilhier, 'Atlas d'Anatomie Pathologique,' livraison 38, pp. i et ii.

It is the rule that the tremor disappears when the members are immobilized by permanent contracture, at a more or less advanced period of the disease. Though the tremor sometimes shows itself almost from the very beginning, yet it must be acknowledged that it is usually a late symptom. In conclusion, gentlemen, it is very frequent and almost customary that the tremor shall not last as long as the disease; it grows less marked as the patients decline in strength, and it sometimes completely vanishes before the fatal end arrives.

III.

You are now acquainted, gentlemen, with one of the most original and most important symptoms of sclerosis in generalized patches. A deeper and more circumstantial study of the case which we have before us will enable us to collect many other indicia which are not less valuable. We shall discover in our patient a whole group of symptoms, which I propose to call *cephalic*, as opposed to *spinal* symptoms. This group comprises certain disorders of vision, of speech, and of intellect.

A. Let us first apply ourselves to the question of visual disorders. These are diplopia, amblyopia, and especially nystagmus.

a. Diplopia, as happens also in locomotor ataxia, is an initial symptom, usually quite transient, but yet deserving of passing notice.

b. Amblyopia, on the other hand, is a persistent, and indeed a more frequent symptom of cerebro-spinal disseminated sclerosis. I believe I may affirm that, contrary to what takes place in posterior sclerosis, it very rarely issues in complete blindness.[1] This is a peculiarity worthy of notice, especially if you remember that patches of sclerosis have been found, after death, occupying the whole thickness of the nerve-trunk, in the optic nerves, in cases where, during life, an enfeeblement of sight simply had been noted.[2] This apparent disproportion between the symptom and the lesion constitutes one of the most powerful arguments which can be invoked to show that the functional continuity of the nerve-tubes is not absolutely interrupted, although these, in their course through the sclerosed patches, have been despoiled of their medullary sheaths and reduced to axis-cylinders.

[1] In a case reported by M. Magnan ('Archives de Physiologie,' t. ii, p. 765) there was papillary atrophy of both eyes, with complete blindness.

[2] Case of the patient, Aspasie Byr, communicated by M. Vulpian. This observation is recorded, *in extenso*, in a work by M. H. Liouville, entitled "Observations detaillées de deux cas de sclèrose en îlots multiples et disséminés du cerveau et de la moelle épinière" ('Mémoires de la Société de Biologie,' 1868, p. 231).