

The *pathological physiology* of the disease is scarcely more advanced than its anatomy. Very shortly, I expect I shall have an opportunity of demonstrating the accuracy of this assertion before you. I shall not dwell upon the subject now, as I desire to conclude the clinical history of paralysis agitans by stating what we know with respect to the etiology and therapeutical history of this disease.

*Etiology.*—A. Among *external* causes, two especially have a right to be mentioned, in a tolerably large number of cases. First in order comes the influence of violent shocks of the nervous system—fright, terror, the sudden communication of bad news, &c. Instances of this kind abound in books, and the facts which we have ourselves collected oblige us to put away all scepticism on this subject.

Of the female patients whom we have interrogated many related how their complaint took its rise in the midst of the political commotions by which our country has been agitated. It may be sufficient to mention the case of the gendarme's wife, which we have already referred to, and that of a woman at present occupying bed No. 2 in the Salle St. Alexandre, who began to tremble after a violent emotion occasioned by the events of December, 1851. Besides the instances which came under our own observation we may mention—1st, a case of M. Hillairet (recorded in our memoir) concerning a father who saw his son killed before his eyes; 2d, another case, published by Oppolzer, relating to a burgher of Vienna, terrified by the bursting of a bomb beside him;<sup>1</sup> and 3d, a case given by Van Swieten, where a man was suddenly roused from sleep by a fearful thunder-clap. It would be easy to multiply examples, but this could add nothing to what we have already told you. What it behooves you to know is the fact that, in all these patients, the trembling followed immediately, or almost immediately, on the occurrence of the cause. But the peculiar nature of the cause, be it known to you, does not impress any special character upon the disease.

Let us note, in the second place, the *influence of prolonged exposure to moist cold* in the production of paralysis agitans, an influence which, according to some authors, should suffice to establish

<sup>1</sup> In a work published in 1873 ('Berliner Klin. Wochenschrift,' No. 24, p. 278, etc.), Dr. O. Kohts reports a number of cases of nervous affections, observed at Strasbourg, which the patients attributed to the terror caused by the bombardment of that city. The author, who expatiates complacently on that disastrous event, informs us that the number of bombs showered upon Strasbourg amounted in thirty-one days to 193,722, making, as he calculates, 6249 per day, 269 per hour, or from four to five per minute. Amongst the pathological cases quoted, three appear to relate to paralysis agitans: one is that of a woman, aged fifty years, another that of a woman aged sixty-one years, and the third that of a man aged fifty-six years. (B.)—*Note to the Second French Edition.*

its rheumatic origin. However, one important fact may be alleged against this view, which is that, neither before the development nor during the course of the disease, do we meet with any form of chronic or acute articular rheumatism, some rare cases excepted. We notice, at most, in cases where the influence of cold can be accused, the presence of wandering rheumatic or neuralgic pains. In this connection we may quote the case of a woman to whom your attention was drawn, and whose (elephantine) gait recalls that of the larger pachyderms. This woman, who was engaged in wafer-making, lived for over ten years in a very damp apartment on the ground-floor, and the description she gives of her unhealthy abode leaves no doubt upon the subject. She was, moreover, exposed to frequent chills in carrying on her trade.

There are cases in which this cause is, in our opinion, far from having played the part assigned to it. Such is that recorded by Romberg relating to a man who, in 1813, was stripped naked by the Cossacks in snowy weather. Is the action of cold to be accused in this case, or the influence of terror?

Finally, we will point out a third cause, which has been silently passed over, by most medical writers, in describing this disease, namely, the *irritation of certain peripheral nerves*, supervening in consequence of a wound or contusion. A case mentioned by Haas, from Door, in 1852, and quoted by Dr. Sanders, appears to belong to this etiological group. It relates to a girl of nineteen, under whose right toe-nail a thorn had penetrated. She immediately complained of acute pain, and soon after was seized with trembling, which, though at first limited to the wounded foot, gradually became generalized. This trembling, it is said, completely disappeared in the course of time. A termination so exceptional affords us reason to doubt whether this was really a case of paralysis agitans.

The wife of one of our provincial brethren, whom I attended, received a severe contusion of the left thigh, owing to a fall from her carriage. After some time there supervened in the injured limb acute pain following the course of the ischiatic nerve, and, shortly afterwards, the extremity was affected by trembling throughout its entire extent. This tremor, which was at first temporary, became permanent later on, and finally invaded the other members.

With this case we may place that of a midwife, who was also taken with paralysis agitans. This patient, who was under my care in La Salpêtrière for many years, had experienced a violent pain, limited to the course of the nerves of the leg and foot. The parts so affected were the first seized with tremor. The pain, which had arisen spontaneously, and which was at times intolerable, resisted the most energetic remedies. It persisted until the

death of the patient, on whom, unfortunately, no autopsy could be performed.

B. We have indicated the cases in which the influence of an etiological element may be discerned; but there are others where the most attentive investigations do not lead to any result. Here we are reduced to inquire into the *predisposing influences*, which it now remains for us to review.

In relation to the question of *age*, we should point out that shaking palsy is not, as has been asserted, a senile disease. It is true that it sets in after forty, and consequently at a later period than disseminated sclerosis. This rule, however, is not absolute; some instances may be cited in which the disease showed itself at an early age, at twenty, for example, as in a case which M. Duchenne (de Boulogne) has told us of.<sup>1</sup>

*Sex* appears not to exercise any pathogenic influence; paralysis agitans is found as commonly in males as in females.

We possess no precise information with respect to the influence of *hereditary* predisposition. Unlike locomotor ataxia in certain circumstances, and progressive muscular atrophy, paralysis agitans is not a family disease. The observations which have produced a contrary impression relate to partial tremors that showed no tendency to become generalized, and which pertain rather to the class of convulsive twitchings (*tics convulsifs*).

There is some reason to believe that the Anglo-Saxon *race* (in England and North America) is the most subject to this disease. The accounts which I have received from physicians of the countries mentioned, my personal experience, and especially the information with which my friend, M. Brown-Séguard, has supplied me, all yield support to this opinion.

But even in those countries shaking palsy is not *very common*. Dr. Sanders, in his statistical table, which comprises England and Wales, and reaches from 1855 to 1863, records 205 cases of death by paralysis agitans—that is, an average of 22 deaths per year (fourteen men and eight women). Finally, this disease figures in the fifth place, side by side with locomotor ataxia, on the etiological list of affections treated at La Salpêtrière.

*Treatment.*—A few words, in conclusion, gentlemen, upon thera-

<sup>1</sup> M. Fioupe has published in the 'Journal de Médecine et de Chirurgie Pratiques' (p. 389, 1874) the case of a young girl, under the care of Dr. Siredey, who was stricken with shaking palsy at the age of from fifteen to sixteen years: "Towards the end of the siege of Paris she had one day taken refuge in a cellar to be out of the way of the projectiles, when a shell burst, destroying three or four persons at her side. Seized with violent terror, she fainted away, and when, after a few instants, she came to her senses, it was soon observed that her right arm was shaken by a slight tremor, which in a little time invaded the right lower extremity also." She presents, at present, all the symptoms which denote paralysis agitans: characteristic physiognomy, fixity of gaze, special attitude of head and body, peculiar gait, propulsion, retropulsion, &c. (B.)—*Note to the Second French Edition.*

peutical remedies. It is an incontestable fact that paralysis agitans is sometimes cured. Does this cure take place spontaneously, or because of the remedies employed? The latter hypothesis is but little probable, so far as the majority of these fortunate cases are concerned, for the same drugs, to which the credit of effecting the cure in such cases has been given, have completely failed in other cases. Elliotson administered carbonate of iron, and Brown-Séguard chloride of barium—each of them had a success to chronicle, and, along with that, cases in which the results were negative. M. Duchenne (de Boulogne) has likewise to record the cure of one of his patients. These instances prove that paralysis agitans is not incurable. But we must confess that we are ignorant of the means employed by nature to produce this result.

Everything, or almost everything, has been tried against this disease. Among the medicinal substances that have been extolled, and which I have administered without any beneficial effect, I need only enumerate a few. Strychnine praised by Trousseau ('Journal de Beau'), appears to me rather to exasperate the trembling than to calm it. Ergot of rye and belladonna, recommended on account of their anti-convulsive qualities, have not yielded any very profitable results. The same verdict must be given in reference to opium, which, on the contrary, augments reflex excitability, and which was supposed capable of moderating the tremor because of diminishing the pain. Latterly I have made use of hyoscyamine, from which some patients have obtained relief; its action, however, is simply palliative.

Ogle gave Calabar bean without any advantage. As to nitrate of silver, it has always appeared to us to exaggerate the convulsive condition, and this is the more remarkable, because in disseminated sclerosis it sometimes produces a fairly marked amendment, and diminishes the intensity of the shaking.<sup>1</sup>

Finally, we should mention the application of electricity, which, according to some physicians, has brought about several cures. Neither statical electricity nor the interrupted current is recommended. These agents, though of benefit, it is said, in chorea are, at least according to Dr. Gull, inefficient as against paralysis agitans. The continued current of a galvanic pile is prescribed. It is not necessary, gentlemen, to remind you to-day that the physiological and therapeutical effects differ remarkably as you make use of one

<sup>1</sup> M. Eulenberg has recently recommended the hypodermic injection of a solution composed of one part of arseniate of potash to two parts of water ('Berliner Klin. Wochenschr.', Nov. 1872). This mode of treatment, having been tried by us in M. Charcot's wards, gave no satisfactory results ('Progrès Médical,' 1874, p. 245). We have also prescribed bromide of camphor in the case of two patients in the same ward, whose disease had lasted for several years. In the first weeks there was amendment of some symptoms, but this improvement did not persist. It might, perhaps, be well to recur to this therapeutic agent in less advanced cases. (B.)—*Note to the Second French Edition.*

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.

### 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.<sup>1</sup> I do not find it indicated in any of the standard works published in that country, not even in Dr. Gull's valuable collection.<sup>2</sup>

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 Turek published, in 1855, examples of lesions manifestly belonging to disseminated sclerosis; still the physiological aspect of it alone engaged his mind;<sup>3</sup> Rokitansky indicates them in his treatise;<sup>4</sup> Frerichs<sup>5</sup> and Valentine<sup>6</sup> record two observations; Rindfleisch,<sup>7</sup> Leyden,<sup>8</sup> and Zenker,<sup>9</sup> present in their turn

<sup>1</sup> This lecture was delivered in 1868.

<sup>2</sup> Cases of Paraplegia in 'Guy's Hospital Reports,' 1856-1858.

<sup>3</sup> "Beobachtungen über das Leitungsvermögen des Menschlichen Rückenmarks," 'Sitzungsberichte der Kais. Akademie der Wissenschaften, Math. Natur. Class.,' t. xvi, 1855, p. 229.

<sup>4</sup> 'Lehrbuch der Pathologischen Anatomie,' 1856, Zweiter Band, p. 488.

<sup>5</sup> 'Haeser's Archiv,' Band x.

<sup>6</sup> "Ueber die Sclerose der Gehirns und Rückenmarks" ('Deutsche Klinik,' 1856, No. 14).

<sup>7</sup> "Histologische Detail zu der Grauen Degeneration von Hirn und Rückenmarks" ('Virchow's Archiv,' B. xxvi, Heft und 6, p. 474).

<sup>8</sup> "Ueber graue Degeneration des Rückenmarks" ('Deutsche Klinik,' No. 13, 1867).

<sup>9</sup> "Ein Beitrag zur Sclerose des Hirns und Rückenmarks" ('Zeitschrift für Rat. Medizin,' B. xxiv, Heft 2 und 3).